

TRANSGENDER PARTICIPATION IN SPORT

Medical Background

1. **Evidence Supporting the Biologic Nature of Gender Identity**
Saraswat et al., 2014
2. **Testosterone therapy for transgender men**
Irwig, 2016
3. **Sport and Transgender People: A Systematic Review of the Literature Relating to Sport Participation and Competitive Sport Policies**
Jones et al., 2016
4. **Prevalence and Types of Gender-Affirming Surgery Among a Sample of Transgender Endocrinology Patients Prior to State Expansion of Insurance Coverage**
Kailas et al., 2017
5. **Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline**
Hembree et al., 2017
6. **LITERATURE REVIEW: SCEG Project for Review and Redraft of Guidance for Transgender Inclusion in Domestic Sport 2020**
Carbmill Consulting, 2020
7. **Effect of gender affirming hormones on athletic performance in transwomen and transmen: implications for sporting organisations and legislators**
Roberts et al., 2020
8. **Transgender Women in the Female Category of Sport: Perspectives on Testosterone Suppression and Performance Advantage**
Hilton & Lundberg, 2020
9. **Fit Transitioning: When Can Transgender Airmen Fitness Test in Their Affirmed Gender?**
Chiccarelli et al., 2022
10. **Transgender Women Athletes and Elite Sport: A Scientific Review**
Research hub for gender+ equity in sport, 2022
11. **Joint position statement of the International Federation of Sports Medicine (FIMS) and European Federation of Sports Medicine Associations (EFSMA) on the IOC framework on fairness, inclusion and non-discrimination based on gender identity and sex variations**
Pigozzi et al., 2022

12. **The current knowledge on the effects of gender-affirming treatment on markers of performance in transgender female cyclists**
Bigard, UCI, 2022
13. **Transwomen Elite Athletes: Their Extra Percentage Relative to Female Physiology**
Heather, 2022
14. **The Biological Basis of Sex Differences in Athletic Performance: Consensus Statement for the American College of Sports Medicine**
Hunter et al., 2023
15. **A Scoping Review of Transgender Policies in the 15 Most Commonly Played UK Professional Sports**
McLarnon et al., 2023
16. **Disparities in sport participation of transgender women: a systematic and scoping review protocol**
Hamdan et al., 2023
17. **Comment on: “Transgender Women in the Female Category of Sport: Perspectives on Testosterone Suppression and Performance Advantage”**
Hamilton et al., 2023
18. **Sex differences and athletic performance. Where do trans individuals fit into sports and athletics based on current research?**
Oberlin, 2023

EVIDENCE SUPPORTING THE BIOLOGIC NATURE OF GENDER IDENTITY

Aruna Saraswat, MD¹; Jamie D. Weinand, BA, BS²; Joshua D. Safer, MD^{1,3}

ABSTRACT

Objective: To review current literature that supports a biologic basis of gender identity.

Methods: A traditional literature review.

Results: Evidence that there is a biologic basis for gender identity primarily involves (1) data on gender identity in patients with disorders of sex development (DSDs, also known as differences of sex development) along with (2) neuroanatomical differences associated with gender identity.

Conclusions: Although the mechanisms remain to be determined, there is strong support in the literature for a biologic basis of gender identity. (*Endocr Pract.* 2015;21:199-204)

Abbreviations:

BDNF = brain-derived neurotrophic factor; **BSTC** = bed nucleus of the stria terminalis; **CAH** = congenital adrenal hyperplasia; **DES** = diethylstilbestrol; **DSD** = disorder of sex development; **MTF** = male-to-female; **FTM** = female-to-male

INTRODUCTION

Gender identity is a fundamental human attribute that has a profound impact on personal well-being. Transgender individuals are those whose lived and identified gender identity differs from their natal sex. Various etiologies for transgender identity have been proposed, but misconceptions that gender identity can be altered persist. However, clinical experience with treatment of transgender persons has clearly demonstrated that the best outcomes for these individuals are achieved with their requested hormone therapy and surgical sexual transition as opposed to psychiatric intervention alone (1). In this review, we will discuss the data in support of a fixed, biologic basis for gender identity.

METHODS

This traditional literature review was conducted using a search of PubMed and Google Scholar for the following key terms: gender identity, gender dysphoria, transsexual, transgender, transmen, and transwomen.

RESULTS

Disorders (or Differences) of Sex Development (DSDs)

A seminal study by Meyer-Bahlburg et al involving outcomes of XY individuals raised as females due to severe nonhormonal, anatomic abnormalities of sex development provided the most convincing evidence that gender identity is fixed (2). These congenital abnormalities include penile agenesis, cloacal exstrophy, and penile ablation. For many years, female gender assignment along with surgical feminization was the dominant approach for these patients. In this study, 78% of all female-assigned 46 XY patients were living as females. While the majority of these patients did not initiate a gender change to male, none of the 15 male-raised 46 XY patients initiated a gender change to female. Thus, the risk of questioning gender identity was higher in

Submitted for publication August 28, 2014

Accepted for publication December 11, 2014

From the ¹Section of Endocrinology, Diabetes and Nutrition, Boston Medical Center; ²Boston University School of Medicine; ³Section of Endocrinology, Diabetes and Nutrition, Boston University School of Medicine.

Address correspondence to Dr. Joshua D. Safer, Endocrinology, Room M-1016; Boston University School of Medicine; 715 Albany Street, Boston, MA 02118. E-mail: jsafer@bu.edu

Published as a Rapid Electronic Article in Press at <http://www.endocrinepractice.org> on August 6, 2014. DOI: 10.4158/EP14351.RA

To purchase reprints of this article, please visit: www.aace.com/reprints.

Copyright © 2015 AACE.

This material is protected by US copyright law. To purchase commercial reprints of this article, visit www.aace.com/reprints. For permission to reuse material, please access www.copyright.com or contact the Copyright Clearance Center, Inc. (CCC).

those 46 XY subjects raised as females than in those raised as males. The same group examined the degree of satisfaction with surgical intervention reported by patients with 46 XY genotypes and found that those subjects raised as boys were considerably more comfortable with their gender identity (3).

Another seminal study relevant to this topic was by Reiner and Gearhart (4). In their review of 16 XY genotype subjects with cloacal exstrophy who underwent female gender reassignment surgery, 4 of the 14 individuals raised as girls announced they were male, and 4 later chose to live as boys when they became aware of their genotype. The 2 individuals who were raised as males identified as males throughout life. The sexual behavior and attitudes of all 16 subjects ultimately reflected strong masculine characteristics regardless of gender assignment. Thus, children who were born genetically and hormonally male identified as males despite being raised as females and undergoing feminizing genitoplasty at birth. Although the cohort sizes in these studies were small, the data provide the strongest evidence for the biologic underpinnings of gender identity.

In congenital adrenal hyperplasia (CAH), the adrenal glands produce excessive amounts of androgens, causing genital virilization with a spectrum of different phenotypes in 46 XX neonates. Dessens et al (5) reported that the prevalence of male gender identity in 46 XX female-raised subjects with CAH was higher than the prevalence of female-to-male (FTM) transgender individuals in the general population of chromosomal females. In this study, the large majority (95%) of 250 female-raised patients later maintained a female gender identity. However, 13 (5.2%) had serious problems with their gender identity. Deficiencies of 5 alpha-reductase-2 and 17-beta-hydroxy-steroid dehydrogenase-3 are similar conditions in which the synthesis and conversion of testosterone to dihydrotestosterone is inhibited, preventing the development of external male genitalia and resulting in potential genital ambiguity. As with CAH, affected individuals are often raised as females. In a study of affected subjects, gender role changes were reported in 56 to 63% of cases with 5 alpha-reductase-2 deficiency and 39 to 64% of cases with 17-beta-hydroxy-steroid dehydrogenase-3 deficiency who were raised as girls (6). These data support the concept that gender identity might be attributed to hormone milieu during intrauterine development.

Data from DSDs highlight the potential influence of abnormal hormone exposure on the development of transgender identity in some individuals. However, it is important to note that most transgender individuals develop a gender identity that cannot be explained by atypical sexual differentiation. It is possible for individuals with normal sexual differentiation to develop transgender identity later in life.

Neuroanatomical Differences

Many of the current hypotheses for the biologic origin of transgender identity are based on atypical sexual differentiation of the brain. The perception of one's own gender is linked to sexual differentiation of the brain, which differs from the body phenotype in transgender individuals (7). Swaab et al have proposed that this discrepancy could be due to the fact that sexual differentiation of the brain takes place only after sexual differentiation of the gonads in early fetal life (8). Along these lines, the degree of genital masculinization may not reflect that of the brain.

The notion of transgender-specific cerebral phenotypes is further supported by postmortem brain studies investigating the underlying neuroanatomical correlates of gender identity (9,10,12). The vast majority of these studies have compared particular regions of interest only in male-to-female (MTF) transgender individuals (13-15). These studies support the hypothesis that atypical cerebral networks in transgender individuals have a neuroanatomical basis.

Gray Matter Studies

Studies of cerebral gray matter in transgender individuals have provided the strongest neuroanatomical case for transgender gender identity. Postmortem brain studies suggest that some subcortical structures are feminized in MTF individuals. One of the earliest and most influential studies in this area investigated the bed nucleus of the stria terminalis (BSTc), which was reported to be a sexually dimorphic nucleus in humans with a larger volume in males than in females. In 1995, Zhou et al reported that the size and number of neurons in the BSTc of 6 MTF estrogen-treated transgender individuals was typical for the size and neuron numbers generally found in control females (9). The authors further reported that these findings could not be explained by differences in adult sex hormone levels.

A similar study by Kruijver et al provided further data supporting the role of the BSTc in transgender identity (10). They examined tissue from the same 6 MTF estrogen-treated transgender persons studied by Zhou et al and found that the number of neurons in the BSTc was more similar to genetic XX female controls. BSTc neuron number was also in the male range in the 1 FTM androgen-treated transgender individual studied.

Most transgender individuals experience feelings of gender dysphoria that begin in childhood. However, in a study of BSTc volume in postmortem brains of 50 control subjects, Chung et al reported that sexual dimorphism in the BSTc did not develop until adulthood (11). Yet, the same group remarked that changes in fetal hormone levels could have delayed effects on BSTc volume and neurons in adulthood, thereby suggesting a role for BSTc as a marker for gender identity. Still, delayed development of

sexual dimorphism in the BSTc would not explain childhood development of gender dysphoria or gender identity discrepancy.

In 2008, Garcia-Falgueras and Swaab were the first to report a sex reversal in the uncinate nucleus. They examined the third interstitial nucleus of the anterior hypothalamus (INAH 3), which is a sexually dimorphic component of the uncinate nucleus, in relation to the brains of transgender individuals (12). They reported that the mean INAH3 volume and neuron number in 11 MTF transgender subjects were in the female ranges.

The above studies are limited by the fact that they involved postmortem examinations of a small number of brains from MTF individuals, some of whom had either received hormone treatment or surgery. Therefore, the study findings may represent confounding effects from exogenous hormones in a small group of transgender individuals. Despite their small sample size, these studies provide valuable evidence that gender identity is linked to neuroanatomy.

Studies by Luders et al provided further evidence that transgender identity is associated with distinct cerebral patterns (13,14). In 2009, the group analyzed magnetic resonance imaging (MRI) data of 24 MTF transgender individuals who had not yet begun hormone treatment. These subjects were shown to have a pattern that was more similar to control males. However, they also observed a significantly larger, more “feminized” volume of regional gray matter in the right putamen in these subjects. In 2012, the same group observed thicker cortices in 24 MTF transgender individuals who had not yet received exogenous hormones compared with 24 age-matched control males in a number of regions across the lateral and medial cortical surfaces. The data supported a dichotomy between MTF transgender individuals and gender congruent males with regard to brain structure.

Differences in brain volume and cerebral activation patterns have been proposed as potential explanations for transgender identity. In 2011, Savic et al examined brains of 24 living MTF transgender individuals and found significant volume reductions of the putamen in MTF transgender individuals and significant increases in gray matter volumes compared with male and female controls (15). Although these findings differ from the findings of smaller, “feminized,” putamens in MTF transgender individuals, they still indicate that certain brain areas in the transgender group have characteristic structural features compared with controls.

The same group investigated 12 living MTF transgender individuals who smelled 2 steroidal compounds: the progesterone derivative 4,16-androstadien-3-one (AND) and the estrogen-like compound estra-1,3,5 (10), 16-tetraen-3-ol (EST). These compounds have been reported to activate the hypothalamic networks in a sex-differentiated way. MTF transgender individuals who had not received

hormone treatment were found to respond similarly to female controls, with AND activating the anterior hypothalamus (16). Another study by Gizewski et al showed a similar cerebral activation in MTF transgender individuals relative to female controls while they viewed erotic stimuli (17). While the above studies only involved MTF transgender individuals, they nonetheless provided evidence of neuroanatomical pathway alteration as an explanation for transgender identity.

The following 2 studies were unique from the aforementioned ones because they included both MTF and FTM transgender individuals who had not received hormone treatment. Zubiaurre et al reported that FTM transgender individuals showed evidence of subcortical gray matter masculinization in the right putamen, while MTF transgender individuals had feminized cortical thickness (18). In 2013, Simon et al reported differences in gray matter in 17 living transgender subjects compared with controls (19). Differences were seen in transgender patients in the cerebellum, angular gyrus, and parietal lobe compared with controls, independent of their biologic gender.

White Matter Studies

Although an early study by Emory et al (20) found no difference in the whole corpus callosum or splenium region between MTF and FTM transgender individuals, the following MRI studies of white matter brain characteristics of transgender individuals suggested a strong neuroanatomical explanation for transgender identity. Yokota et al reported that the pattern of corpus callosum shape in both FTM and MTF transgender individuals was closer to subjects with shared gender identities than to subjects who shared the same natal sex (21). Among FTM transgender individuals who had not received hormone treatment, certain white matter fasciculi involved in higher cognitive functions were closer to the pattern of control males than to control females (22). Among MTF transgender individuals who had not received treatment, diffusion tensor imaging revealed an intermediate white matter pattern that was between those of male and female controls (23).

Genetic Factors and Exposures

Although limited in size and scope, the role of genetic factors in transgender identity is supported by small studies of gene abnormalities associated with steroid hormones, twin case studies, neuroproteins, and prenatal exposures.

Steroid Hormone Genetics

Select genes have been associated with transgender identity. Although these studies have been small, they are most convincing findings to date linking atypical genes with transgender identity in both MTF and FTM transgender individuals. The *CYP17* gene encodes the 17-alpha hydroxylase enzyme and is associated with elevated serum levels of estradiol, progesterone, and testosterone. In a

case-control study of 151 transgender individuals, Bentz et al reported a significant association between the *CYP17* gene and FTM transgender individuals but not in MTF transgender individuals (24). Another study by the same group examined a polymorphism in the gene coding for 5- α reductase and found no association in a sample of both MTF and FTM transgender individuals (25).

Various groups have investigated steroid hormone receptor gene variants to determine if they confer risk of developing transgender identity. Steroid hormones exert profound influences on fetal sexual development and act via specific receptors. It is therefore plausible that abnormal sex hormone receptor function may predispose to transgender identity. However, the existing studies on this topic have been contradictory and require replication. Henningson et al found an association between MTF transgender individuals and a dinucleotide CA polymorphism in the estrogen receptor beta gene (ERb) (26). However, 2 subsequent studies by separate groups reported different results. Hare et al performed a larger study of MTF transgender individuals and found no relationship with the ERb, but they did find a significant association with an androgen receptor repeat (27). In a similar study of 242 MTF and FTM transgender individuals, Ujike et al examined sex steroid receptor genes and found no association with transgender identity (28).

There have been several small case reports of atypical sex chromosomes in transgender individuals. The most common association reported was with disomy-Y (47, XXY); however, no statistically significant association between particular genes has been described (29). Two recent studies of MTF and FTM transgender individuals reported that aneuploidies are slightly more common in transgender individuals than in the general population, but neither was controlled. In the first, karyotype abnormalities were found in 2.5% of the 368 transgender individuals studied (30). A second study of 302 transgender individuals also showed a low overall incidence (1.5%) of chromosomal abnormalities (31).

Twin Studies

Twin literature supports the potential contribution of genetic factors to the development of transgender identity. In 2 separate retrospective studies of twin pairs, Bailey et al and Coolidge et al demonstrated a strong heritable component among twins with transgender identity (32,33). Hylens et al performed a similar study of 23 monozygotic twin pairs and showed that 9 were concordant for transgender identity compared to no concordance among dizygotic twin pairs (34). Two small studies (35,36) also demonstrated a higher concordance for transgender identity among monozygotic twins versus dizygotic twins. Nevertheless, the overall prevalence of monozygotic twins

discordant for transgender identity still outnumbers those who are concordant.

Neuroproteins

Brain-derived neurotrophic factor (BDNF) is a member of the growth factor family involved in synaptic plasticity and neuronal development. Altered BDNF signaling is thought to be a contributor to psychiatric conditions. Fontanari et al (37) reported that serum BDNF levels were 15% lower in an uncontrolled study of 45 MTF transgender individuals. However, all study subjects were treated with hormones, and no female subjects were included.

Neurokinin B (NKB) is a potent regulator of gonadotropin-releasing hormone secretion, which is essential for reproductive function. A postmortem brain study of 4 MTF transgender individuals by Taziaux et al (38) showed a mean infundibular NKB volume similar to control females. The observed feminization may have been explained either by medical estrogen therapy or lack of androgens due to orchiectomy.

Prenatal Exposures

Dessens et al (39) reported that 3 prenatally anticonvulsant-exposed subjects were transgender individuals. For many years, researchers have been assessing the impact of prenatal exposure to the estrogenic antimiscarriage drug DES (diethylstilbestrol) on the development of gender dysphoria in affected offspring. While the vast majority of DES-exposed children have not developed transgender identity, a 5-year online study of DES-exposed sons by Kerlin et al reported at least 150 cases of moderate-to-severe gender dysphoria among 500 sons with confirmed or suspected prenatal DES exposure (40).

Although no studies to date demonstrate mechanism, multiple studies have reported associations with gender identity that support it being a biologic phenomenon. Table 1 organizes areas studied by study type and lists the associations that have been made.

CONCLUSION

Current data suggest a biologic etiology for transgender identity. Studies of DSD patients and neuroanatomical studies provide the strongest evidence for the organic basis of transgender identity. Because the sample sizes of most studies on this subject were small, the conclusions must be interpreted with caution. Further research is required to assign specific biologic mechanisms for gender identity.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

Table 1
Evidence for a Biologic Basis of Gender Identity

Studies showing rigid gender identity in patients with disorders (or differences) of sexual development (DSD)

- Congenital, nonhormonal conditions Penile ablation/agenesis, cloacal exstrophy

Studies showing that gender identity may be associated with prenatal hormone exposure in some (perhaps otherwise predisposed) individuals

- Congenital adrenal hyperplasia
- Hormone deficiencies 5 alpha-reductase-2,
17-beta-hydroxy-steroid dehydrogenase-3

Studies with gender identity associated with neuroanatomical differences

- Gray matter studies BSTc
Uncinate nucleus
Putamen volumes
Cortical thickness
Hypothalamic response to odorous steroids
- White matter studies Corpus callosum
Microstructure differences

Studies with gender identity associated with genetic factors and exposures

- Steroid hormone genetics Genes: CYP17, SRD5A2, ERb, androgen receptor
- Sex chromosome aneuploidy Disomy-Y
- Twin case studies
- Neuropoteins BDNF, NKB
- Prenatal exposures Anticonvulsants, DES

Abbreviations: BDNF = brain-derived neurotrophic factor; BSTc = bed nucleus of stria terminalis; CYP17 = cytochrome P-450 17 alpha gene; DES = diethylstilbestrol; ERb = estrogen receptor beta gene; NKB = neurokinin B; SRD5A2 = steroid-5-alpha reductase, alpha polypeptide 2 gene.

REFERENCES

1. **Sanchez NF, Sanchez JP, Danoff A.** Health care utilization, barriers to care, and hormone usage among male-to-female transgender persons in New York City. *Am J Public Health.* 2009;99:713-719.
2. **Meyer-Bahlburg HF.** Gender identity outcome in female-raised 46 X,Y persons with penile agenesis, cloacal exstrophy of the bladder, or penile ablation. *Arch Sex Behav.* 2005; 34:423-438.
3. **Meyer-Bahlburg HF, Migeon CJ, Berkovitz GD, Gearhart JP, Dolezal C, Wisniewski AB.** Attitudes of adult 46, XY intersex persons to clinical management policies. *J Urol.* 2004;171:1615-1619.
4. **Reiner WG, Gearhart JP.** Discordant sexual identity in some genetic males with cloacal exstrophy assigned to female sex at birth. *N Engl J Med.* 2004;350:333-341.
5. **Dessens AB, Slijper FM, Drop SL.** Gender dysphoria and gender change in chromosomal females with congenital adrenal hyperplasia. *Arch Sex Behav.* 2005;34:389-397.
6. **Cohen-Kettenis PT.** Gender change in 46,XY persons with 5 alpha-reductase-2 deficiency and 17 beta-hydroxysteroid dehydrogenase-3 deficiency. *Arch Sex Behav.* 2005;34: 399-410.
7. **Swaab DF.** Sexual differentiation of the brain and behavior. *Best Pract Res Clin Endocrinol Metab.* 2007;21:431-444.
8. **Bao AM, Swaab DF.** Sexual differentiation of the human brain: relation to gender identity, sexual orientation and neuropsychiatric disorders. *Front Neuroendocrinol.* 2011;32: 214-226.
9. **Zhou JN, Hofman MA, Gooren LJ, Swaab DF.** A sex difference in the human brain and its relation to transsexuality. *Nature.* 1995;378:68-70.

10. **Kruijver FP, Zhou JN, Pool CW, Hofman MA, Gooren LJ, Swaab DF.** Male-to-female transsexuals have female neuron numbers in a limbic nucleus. *J Clin Endocrinol Metab.* 2000;85:2034-2041.
11. **Chung WC, De Vries GJ, Swaab DF.** Sexual differentiation of the bed nucleus of the stria terminalis in humans may extend into adulthood. *J Neurosci.* 2002;22:1027-1033.
12. **Garcia-Falgueras A, Swaab DF.** A sex difference in the hypothalamic uncinate nucleus: relationship to gender identity. *Brain.* 2008;131:3132-3146.
13. **Luders E, Sánchez FJ, Gaser C, et al.** Regional gray matter variation in male-to-female transsexualism. *Neuroimage.* 2009;46:904-907.
14. **Luders E, Sánchez FJ, Tosun D, et al.** Increased cortical thickness in male-to-female transsexualism. *J Behav Brain Sci.* 2012;2:357-362.
15. **Savic I, Arver S.** Sex dimorphism of the brain in male-to-female transsexuals. *Cereb Cortex.* 2011;21:2525-2533.
16. **Berglund H, Lindström P, Dhejne-Helmy C, Savic I.** Male-to-female transsexuals show sex-atypical hypothalamus activation when smelling odorous steroids. *Cereb Cortex.* 2008;18:1900-1908.
17. **Gizewski ER, Krause E, Schlamann M, et al.** Specific cerebral activation due to visual erotic stimuli in male-to-female transsexuals compared with male and female controls: an fMRI study. *J Sex Med.* 2009;6:440-448.
18. **Zubiaurre-Elorza L, Junque C, Gómez-Gil E, et al.** Cortical thickness in untreated transsexuals. *Cereb Cortex.* 2013;23:2855-2856.
19. **Simon L, Kozák LR, Simon V, et al.** Regional grey matter structure differences between transsexuals and healthy controls—a voxel based morphometry study. *PLoS One.* 2013;8:e83947.
20. **Emory LE, Williams DH, Cole CM, Amparo EG, Meyer WJ.** Anatomic variation of the corpus callosum in persons with gender dysphoria. *Arch Sex Behav.* 1991;20:409-417.
21. **Yokota Y, Kawamura Y, Kameya Y.** Callosal shapes at the midsagittal plane: MRI differences of normal males, normal females and GID. *Conf Proc IEEE Eng Med Biol Soc.* 2005;3:3055-3058.
22. **Rametti G, Carrillo B, Gómez-Gil E, et al.** The microstructure of white matter in male to female transsexuals before cross-sex hormonal treatment. A DTI study. *J Psychiatr Res.* 2011;45:949-954.
23. **Rametti G, Carrillo B, Gómez-Gil E, et al.** Effects of androgenization on the white matter microstructure of female-to-male transsexuals. A diffusion tensor imaging study. *Psychoneuroendocrinology.* 2012;37:1261-1269.
24. **Bentz EK, Hefler LA, Kaufmann U, Huber JC, Kolbus A, Tempfer CB.** A polymorphism of the CYP17 gene related to sex steroid metabolism is associated with female-to-male but not male-to-female transsexualism. *Fertil Steril.* 2008;90:56-59.
25. **Bentz EK, Schneeberger C, Hefler LA, et al.** A common polymorphism of the SRD5A2 gene and transsexualism. *Reprod Sci.* 2007;14:705-709.
26. **Henningsson S, Westberg L, Nilsson S, et al.** Sex steroid-related genes and male-to-female transsexualism. *Psychoneuroendocrinology.* 2005;30:657-664.
27. **Hare L, Bernard P, Sánchez FJ, et al.** Androgen receptor repeat length polymorphism associated with male-to-female transsexualism. *Biol Psychiatry.* 2009;65:93-96.
28. **Ujike H, Otani K, Nakatsuka M, et al.** Association study of gender identity disorder and sex hormone-related genes. *Prog Neuropsychopharmacol Biol Psychiatry.* 2009;33:1241-1244.
29. **Nielsen J, Wohler M.** Sex chromosome abnormalities found among 34,910 newborn children: results from a 13-year incidence study in Arhus, Denmark. *Birth Defects Orig Artic Ser.* 1990;26:209-223.
30. **Inoubli A, De Cuypere G, Rubens R, et al.** Karyotyping, is it worthwhile in transsexualism? *J Sex Med.* 2011;8:475-478.
31. **Auer MK, Fuss J, Stalla GK, Athanasoulia AP.** Twenty years of endocrinologic treatment in transsexualism: analyzing the role of chromosomal analysis and hormonal profiling in the diagnostic work-up. *Fertil Steril.* 2013;100:1103-1110.
32. **Bailey JM, Dunne MP, Martin NG.** Genetic and environmental influences on sexual orientation and its correlates in an Australian twin sample. *J Pers Soc Psychol.* 2000;78:524-536.
33. **Coolidge FL, Thede LL, Young SE.** The heritability of gender identity disorder in a child and adolescent twin sample. *Behav Genet.* 2002;32:251-257.
34. **Heylens G, De Cuypere G, Zucker KJ, et al.** Gender identity disorder in twins: a review of the case report literature. *J Sex Med.* 2012;9:751-757.
35. **Sadeghi M, Fakhrai A.** Transsexualism in female monozygotic twins: a case report. *Aust NZ J Psychiatry.* 2000;34:862-864.
36. **Knoblauch H, Busjahn A, Wegener B.** Monozygotic twins concordant for female-to-male transsexualism: a case report. *Arch Sex Behav.* 2007;36:135-137.
37. **Fontanari AM, Andreatza T, Costa ÂB, Salvador J, et al.** Serum concentrations of brain-derived neurotrophic factor in patients with gender identity disorder. *J Psychiatr Res.* 2013;47:1546-8.
38. **Taziaux M, Swaab DF, Bakker J.** Sex differences in the neurokinin B system in the human infundibular nucleus. *J Clin Endocrinol Metab.* 2012;97:E2210-20.
39. **Dessens AB, Cohen-Kettenis PT, Mellenbergh GJ, vd Poll N, Koppe JG, Boer K.** Prenatal exposure to anticonvulsants and psychosexual development. *Arch Sex Behav.* 1999;28:31-44.
40. **Kerlin S.** Prenatal exposure to diethylstilbestrol (DES) in males and gender-related disorders: results of a five-year study. Available at: www.desaction.org/documents/SCOTTKERLINRpt2005.pdf. Accessed July 5, 2014.

Testosterone therapy for transgender men

Michael S Irwig



Testosterone therapy is a cornerstone of medical treatment for transgender men who choose to undergo it. The goal of testosterone therapy is usually to achieve serum testosterone concentrations in the male reference range. Testosterone has several desired effects as well as undesired and unknown effects. The desired effects include increased facial and body hair, increased lean mass and strength, decreased fat mass, deepening of the voice, increased sexual desire, cessation of menstruation, clitoral enlargement, and reductions in gender dysphoria, perceived stress, anxiety, and depression. Achievement of these goals comes with potential undesired effects and risks including acne, alopecia, reduced HDL cholesterol, increased triglycerides, and a possible increase in systolic blood pressure. An additional benefit of testosterone therapy (with or without mastectomy) is a reduced risk of breast cancer. Most of the effects of testosterone start to develop within several months of starting therapy, although facial hair and alopecia continue to develop after 1 year. A major limitation in the study of testosterone therapy for transgender men is a paucity of high-quality data due to a shortage of randomised controlled trials (partly because of ethical issues), few prospective and long-term studies, the use of suboptimum control groups, loss to follow-up, and difficulties in recruitment of representative samples of transgender populations.

Introduction

Many transgender people seek medical care to obtain hormone therapy for masculinisation or feminisation. The mainstay of treatment is testosterone for a transgender man (also referred to as transman or female-to-male transgender) or oestrogen and antiandrogens for a transgender woman (also referred to as transwoman or male-to-female transgender). However, access to hormone therapy varies greatly by country and many transgender individuals do not choose to pursue hormone therapy. For example, findings from one study in Thailand showed that only 35% of transgender men were taking testosterone and that hormone therapy was often taken without medical supervision.¹ Testosterone therapy is typically started after puberty and might be initiated in mid-to-late adulthood for individuals coming to terms with their gender identity later in life.

Over the past few years, awareness and acceptance of transgenderism (also called transsexualism) has substantially increased in many countries, particularly those in western Europe, North America, and Australasia. Nevertheless, there are still many regions of the world where transgender individuals must keep their gender identity hidden due to lack of cultural acceptance, stigma, and overt discrimination. Barriers to receiving culturally competent transgender care are common. In 2015, a representative survey of endocrinologists (n=80) in the mid-Atlantic region of the USA found that 59% did not have any transgender patients under their care, only 50% felt somewhat or very comfortable discussing gender identity or sexual orientation, and 33% did not feel competent to provide transgender care.²

Estimation of the true prevalence of transgenderism is difficult because some transgender individuals come to terms with their gender identity later in life and others do not openly identify as transgender because of societal pressures and stigmatisation. A 1996 study of patients treated at a specialised gender clinic in the Netherlands estimated a prevalence of one in

12 000 men assigned male at birth and one in 30 000 women assigned female at birth.³ In 2010, results from a population-based household probability study of more than 28 000 adults in Massachusetts, USA, showed that one in 215 people identified as transgender.⁴

Transgenderism has a biological component, as evidenced from anatomical and genetic studies. Data from one anatomical study showed that the volume of the central subdivision of the bed nucleus of the stria terminalis in transgender women was similar to that of natal (also referred to as non-transgender) women rather than non-transgender men.⁵ Results of a genetics study that included 23 pairs of identical twins and 21 pairs of non-identical twins showed 39% concordance of transgenderism between identical twins and 0% between non-identical twins.⁶ Nonetheless, the precise genetic foundations of transgenderism are not clear. Investigators have examined several sex hormone-related genes, including CAG repeat length in the androgen receptor gene, CA repeat length in the oestrogen receptor β gene, and TTTA repeat length in the aromatase gene. Although results from some of these studies have suggested an association between transgenderism and particular genetic variations, findings have not been replicated in other studies and the evidence is inconclusive.⁷⁻⁹

In this Review, I focus on the effects of testosterone therapy on various organ systems in adult transgender men. Because the extent of the effects of testosterone can vary by type of testosterone formulation, this information is included where possible. Where applicable, comparisons will be made with the effects of testosterone therapy in men with hypogonadism and natal women. These comparisons have limitations because of the different host environment in natal men and the lower doses of testosterone that are given to natal women. Importantly, endogenous testosterone concentrations are generally 10–20 times higher in men than in women. Detailed information about the diagnostic criteria for transgenderism or gender dysphoria and general care has been

Lancet Diabetes Endocrinol 2016

Published Online

April 12, 2016

[http://dx.doi.org/10.1016/S2213-8587\(16\)00036-X](http://dx.doi.org/10.1016/S2213-8587(16)00036-X)

Center for Andrology and Division of Endocrinology, George Washington University, Washington, DC, USA (M S Irwig MD)

Correspondence to: Dr Michael S Irwig, Division of Endocrinology, GW Medical Faculty Associates, 2150 Pennsylvania Ave NW, Washington, DC 20037, USA mirwig@mfa.gwu.edu

published by the World Professional Association for Transgender Health¹⁰ and in clinical guidelines from the Endocrine Society¹¹ and the Royal College of Psychiatrists.¹² Table 1 shows a summary of the recommendations and evidence quality from the Endocrine Society's clinical practice guidelines. A major limitation in the study of transgender medicine is a paucity of high-quality data. Difficulties in obtaining such data stem from the scarcity of randomised controlled trials (partly because of ethical issues), few prospective and long-term studies, the use of suboptimum control groups, loss to follow-up, and difficulties in recruitment of representative samples, including people disenfranchised from society and medical care. In this Review I do not address care of transgender adolescents, which may include suppression of the gonadal axis for a period of time before hormone therapy is started.

Intended effects of testosterone therapy

Overview

The overall goals of testosterone therapy for transgender men are to obtain secondary sexual characteristics of natal men, to live their lives as men, to improve their wellbeing, and to decrease gender dysphoria. Because androgen receptors are widely distributed, testosterone therapy has diverse effects throughout the body, affecting both physical and psychological characteristics (figure). No standard practice exists for starting doses or maintenance doses of testosterone. In clinical practice, I usually initiate therapy at a low dose (ie, 50 mg intramuscular testosterone cypionate every 2 weeks) and gradually increases the dose to a full

adult male replacement dose (ie, 200 mg intramuscular testosterone cypionate every 2 weeks), as if treating a man with hypogonadism. Periodic hormone measurements are obtained to aid in the titration. Testosterone therapy is generally regarded as safe in the short term, but much less is known about its long-term effects. Table 2 shows the doses, advantages, and disadvantages of the principal formulations of testosterone that are available around the world. Although many formulations of testosterone exist, research about transgender men has mainly been restricted to intramuscular esters, long-acting intramuscular testosterone undecanoate, and topical gels. The effects of testosterone therapy in transgender men should not be generalised to men with hypogonadism or postmenopausal women, who are given much lower doses.

Body composition and strength

Testosterone therapy changes body composition towards that of natal men who, on average, have more muscle and less fat than do natal women. Specifically, the magnitude of increase recorded during 1–2 years of testosterone treatment across several studies was 2.2–3.5 kg in bodyweight, 1.7–6.0 kg in lean mass, and 0.8–2.0 kg/m² in BMI.^{13–19} Results from most studies^{13,14,18,19} showed a decrease in fat mass of 2.3–4.0 kg. However, investigators of some studies^{15,16,18} noted no change in BMI with the intramuscular testosterone undecanoate formulation. In one prospective study,¹⁸ intramuscular testosterone undecanoate therapy given for more than 1 year increased grip strength by 18%, as well as increasing the cross-sectional area of the forearm and calf muscles.

	Quality of evidence
Before hormone therapy	
Confirm the diagnostic criteria of gender dysphoria or transgenderism and the eligibility and readiness criteria	Moderate
Evaluate and address medical conditions that can be exacerbated by hormone depletion and cross-sex hormone treatment	Moderate
During hormone therapy	
Maintain cross-sex hormone concentrations in the normal physiological range for the desired gender	Low
Review the onset and time course of physical changes induced by cross-sex hormone treatment	Low
Implement regular clinical and laboratory monitoring every 3 months during the first year and then once or twice per year	Low
Measure complete blood count and liver function tests at baseline and every 3 months for the first year and then one to two times per year thereafter; monitor weight, blood pressure, lipids, fasting blood sugar (if family history of diabetes), and HbA _{1c} (if individual has diabetes) at regular visits	Not stated
Assess bone mineral density if risk factors for osteoporosis exist, specifically in those who stop hormone therapy after gonadectomy	Moderate
Do an annual Pap smear if cervical tissue is present	Not stated
Consider mammograms if mastectomy is not done	Not stated
Assess transgender people treated with hormones for cardiovascular risk factors	Low
Before surgery	
Assess the risks and benefits of inclusion of total hysterectomy and oophorectomy as part of sex reassignment surgery	Very low
Consider genital sex reassignment surgery only after both the physician responsible for endocrine transition therapy and the mental health professional find surgery advisable	Very low
Genital sex reassignment surgery to be recommended only after completion of at least 1 year of consistent and compliant hormone treatment	Very low
The physician responsible for endocrine treatment should medically clear transgender individuals for sex reassignment surgery and collaborate with the surgeon on hormone use during and after surgery	Very low

Table 1: Recommendations from the Endocrine Society's clinical practice guidelines¹¹

Distinguishing the effects of testosterone from those of oestrogen on body composition can be complex because testosterone is converted to oestradiol via aromatisation. To clarify the effects of the different sex steroids, a 16 week study²⁰ was done in healthy young natal men (mean age 33 years) who all received a gonadotropin-releasing hormone agonist to suppress endogenous sex steroids. They were given various doses of testosterone replacement with or without an aromatase inhibitor. Changes in lean mass, thigh-muscle area, and leg-press strength were mostly related to total testosterone concentrations, whereas increased subcutaneous and intra-abdominal fat were related to oestrogen deficiency.

Skin and hair

One of the most important intended effects of testosterone therapy is the development of facial and body hair. However, this hair growth is often accompanied by acne. Androgens interact with pilosebaceous units in the skin to produce these effects and, in transgender men who are genetically predisposed, can cause alopecia. Whereas facial hair and acne develop within months of starting testosterone, androgenetic alopecia is a long-term effect of androgen use. In a study²¹ that included 17 transgender men given intramuscular testosterone esters, investigators noted progressive increases in the median Ferriman-Gallwey hirsutism score from 2 at baseline to 11 at 4 months, to 13 at 8 months, and to 16 at 12 months. Testosterone progressively increased hair density, growth rate, and diameter at the cheek and upper abdomen. Although the hair changes began within 4 months of initiation of therapy, hair diameter did not reach that of natal males by 12 months. Based on the Leeds classification system, the prevalence of physiological acne at baseline was 31% at the face and 19% at the back, increasing to 94% at the face and 88% at the back after 4 months of androgen therapy.

Facial hair, androgenetic alopecia, and acne were also assessed with validated instruments in a prospective study of 20 transgender men who took intramuscular testosterone undecanoate for 1 year and in a cross-sectional study of another 50 transgender men who had been on various testosterone formulations for about 10 years.²² In the prospective study, the median Ferriman-Gallwey score increased from 0.5 at baseline to 12.0 at 1 year, with inter-individual variability from 2 to 25. In the cross-sectional study of long-term treatment, the median Ferriman-Gallwey score was 24, with a range of 6 to 34. One of 20 individuals developed mild frontotemporal hair loss during the prospective study, based on the Norwood-Hamilton classification system for hair loss. By contrast, long-term testosterone therapy resulted in mild frontotemporal hair loss in 33% (16/50) of participants and moderate-to-severe alopecia in 31% (15/50). Based on the Gradual Acne Grading Scale, prevalence of facial acne increased from 35% at baseline to 82% at 1 year, with a corresponding increase in back or

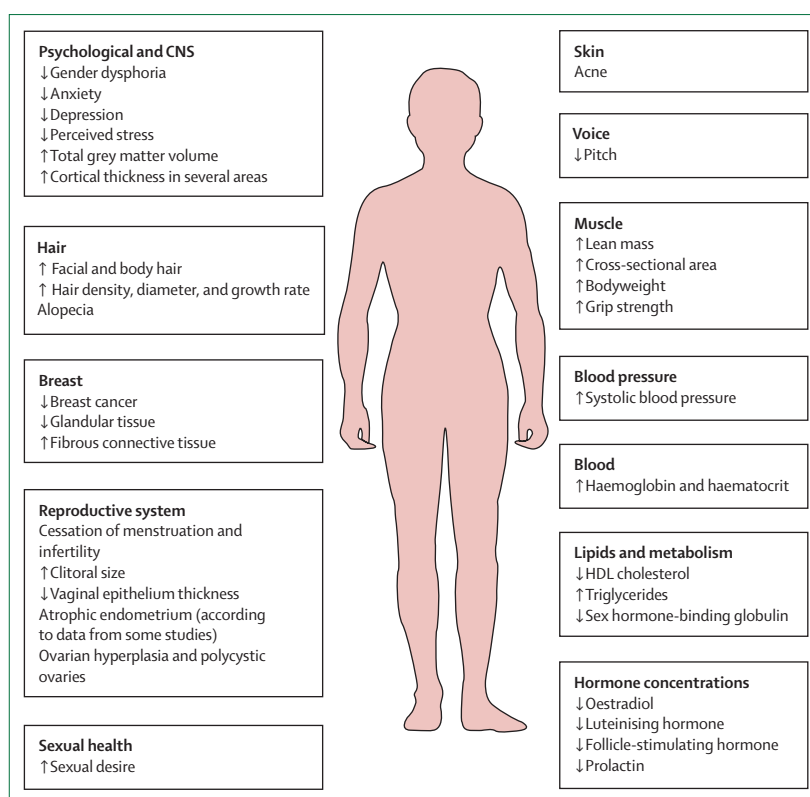


Figure: Effects of testosterone therapy in transgender men

chest acne from 15% to 88%. Despite the high prevalence of acne at 12 months, acne scores peaked at 6 months, with much lower scores seen at 12 months and after long-term testosterone use.

In another prospective study of 53 transgender men who took intramuscular testosterone undecanoate for 1 year,¹⁹ 17% of participants developed androgenetic alopecia, based on the Norwood-Hamilton classification system. In this study, no cases of severe acne were reported and topical or oral acne medications were initiated by 18 (34%) participants. In another study of transgender men who used intramuscular testosterone undecanoate for 24 months,¹⁵ 16% (7/45) of individuals developed so-called troublesome acne.

Although alopecia is an undesirable effect for some transgender men, it can be desirable for others because it is considered a masculine feature. For those at risk or bothered by alopecia, treatment with a 5 α -reductase inhibitor can be used, but potential users should be made aware of evidence showing persistent sexual and other side-effects in otherwise healthy young men and that potential adverse effects on masculinisation in transgender men have not been well studied.^{23,24}

Reproductive system

Testosterone therapy is associated with changes to serum concentrations of reproductive and pituitary

	Route	Dosing	Advantages	Disadvantages
Enanthate or cypionate	Intramuscular	100–200 mg every 2 weeks (or half dose weekly)	Inexpensive Effective at achieving target testosterone concentrations	Peaks and troughs with pharmacokinetics Pain with injections Increased erythrocytosis compared with other formulations
Gels (1%)	Topical	25–100 mg per day	Consistent testosterone concentrations	Expensive Potential transference to women or children on personal contact
Patch	Topical	2.5–10 mg per day	Consistent testosterone concentrations	Expensive Skin irritation Inadequate testosterone concentrations
Axillary solution	Topical	30–120 mg per day	Consistent testosterone concentrations	Expensive
Undecanoate	Intramuscular	750–1000 mg every ten to 14 weeks	Consistent testosterone concentrations Infrequent dosing	Expensive Large injection volume Risk of pulmonary oil microembolus (rare)
Undecanoate	Oral	40–80 mg, 2–3 times per day with meals	..	Variable testosterone concentrations
Pellets	Subcutaneous implants	150–450 mg every 3–6 months	Consistent testosterone concentrations Infrequent dosing	Expensive Invasive (incision with scalpel) Bleeding Infection Inflexible dosing
Buccal	Buccal	30 mg twice per day	..	Expensive Gum irritation Taste alterations Fall off
Nasal spray	Nasal	11 mg three times per day	..	Expensive Frequent dosing Inadequate testosterone concentrations

Availability of certain formulations varies by country.

Table 2: Testosterone formulations

hormones. In addition to an expected rise in testosterone, oestrogen concentrations often decrease to 70–301 pmol/L (19–82 pg/mL), with an accompanying decrease in sex hormone-binding globulin.^{15,16,19} The magnitude of the reduction in sex hormone-binding globulin is similar between the various modes of testosterone delivery. Most large studies have shown testosterone therapy to be associated with reduced, but not totally suppressed, gonadotropins (luteinising hormone and follicle-stimulating hormone) and reduced prolactin concentrations.^{15,16,19}

As with facial hair, one of the most sought-after effects of testosterone therapy is the cessation of menstruation, which can be an unpleasant reminder of the presence of female body parts. In a study²⁷ of 138 transgender men who took three different doses of intramuscular testosterone enanthate ranging from 125 mg every 2 weeks to 250 mg every 2 weeks, cessation of menstruation was noted by 86–97% of participants by 6 months. In a study of 45 transgender men randomly assigned either intramuscular testosterone esters, testosterone gel, or intramuscular testosterone undecanoate,¹⁶ time to amenorrhoea ranged from 30 to 41 weeks, with all participants reporting amenorrhoea by 1 year.

Another desired early physical sign of testosterone therapy is clitoral enlargement, which can be accompanied

by pain. In a 1 year prospective study of transgender men given intramuscular testosterone undecanoate,¹⁹ clitoral pain was noted by 20% (5/25) of participants and peaked at 6 months of therapy. In another study,²⁸ a mean maximal clitoral length of 4.6 cm was recorded after 1 year of testosterone cypionate treatment.

Testosterone therapy typically induces changes to the vagina, endometrium, and ovaries. In one study, transgender men taking intramuscular testosterone esters had thinner vaginal epithelia in which a loss of the intermediate and superficial layers had occurred, compared with premenopausal and postmenopausal women.²⁹ Other findings include loss of intracytoplasmic glycogen, reduced expression of oestrogen receptor α and oestrogen receptor β , and reduced cellular proliferation as measured by Ki-67 immunostaining. Two studies^{30,31} examining the effects of testosterone on the endometrium had inconsistent results. One of the studies,³⁰ of 104 patients given testosterone enanthate for 2–9 years, showed two distinct patterns: half of the participants had proliferative endometrium and half had atrophic endometrium. One case of endometrial adenocarcinoma was identified. In the other study,³¹ which included 27 transgender men who received intramuscular testosterone esters for 1–6 years, all participants had inactive endometrium similar to that of postmenopausal

women. With respect to the ovaries, testosterone therapy results in stromal hyperplasia and mean volumes of 10–11 mL, which is significantly larger than that of natal women not on testosterone. 80% of patients had histological characteristics of polycystic ovary syndrome, if a definition of more than 12 antral follicles per ovary was used.³⁰

Some transgender men wish to have children and therefore to remain fertile. In one study³² of 50 transgender men who had all undergone sexual reassignment surgery (also called gender-affirming surgery), 27 (54%) wanted to have children, although not necessarily biological children. In some countries, many transgender men choose to undergo hysterectomy and bilateral oophorectomy, whereas in other countries many do not undergo any sexual reassignment surgery. Fertility options also depend on the sexual orientation of the individual, since a male partner can potentially provide sperm and a female partner can potentially become pregnant with donor sperm. Transgender men who have not had sexual reassignment surgery might be able to become pregnant after discontinuing testosterone therapy. A web-based study³¹ of 25 transgender men, mostly from the USA, assessed participants who experienced pregnancy and delivered a neonate after female-to-male gender transition. 24 (96%) participants resumed having menstruation within 4 months of stopping testosterone treatment. 5 (20%) actually had no menses before pregnancy. A major limitation of this study was that one of the inclusion criteria was a successful birth, so the results cannot be generalised to all transgender men who discontinue testosterone, because some will not be fertile. For transgender men who undergo sexual reassignment surgery, fertility options should be discussed before any surgery is done. In theory, patients who choose surgery can have cryopreservation of oocytes or ovarian tissue for future use, but there has been little published about this approach. Notably, pregnancy improved gender dysphoria for some transgender men, but worsened it for others.^{32,33}

Breasts

Testosterone therapy alters the composition of breast tissue in transgender men. Using tissue obtained from mastectomies as part of the surgical management of transgender men, investigators of two studies of intramuscular testosterone esters^{30,34} showed a substantial reduction of glandular tissue and an increase in fibrous connective tissue. A reduced amount of adipose tissue was noted compared with menopausal women.³⁴

In addition to mastectomies that are routinely done in many countries, testosterone therapy in transgender men also reduces the incidence of breast cancer. No cases of atypical hyperplasia or carcinoma were seen in two studies of transgender men given long-term testosterone

therapy, of which one included 100 participants treated for 2–9 years³⁰ and the other included 23 participants treated for 18–24 months.³⁴ No cases of breast cancer were seen in a Dutch retrospective study³⁵ of 365 transgender men who received testosterone therapy for a mean of 19 years. The same Dutch research group later reported one case of breast cancer among 795 transgender men (mean age 23 years at start of hormone therapy) who received testosterone for a mean of 20 years.³⁶ The estimated incidence rate for breast cancer was 5.9 cases per 100 000 person-years in transgender men taking testosterone, compared with 154.7 cases per 100 000 person-years in natal women.

Likewise, incidence of breast cancer was significantly lower in premenopausal and postmenopausal women given subcutaneous testosterone pellet implants for various symptoms (mean age 52 years).³⁷ The serum concentrations of testosterone achieved³⁷ were supra-physiological for women and close to the lower end of the reference range for natal men.

Sexual health

Testosterone therapy is associated with increased sexual desire in both transgender men and postmenopausal women with low libido who receive lower doses of testosterone.^{25,38,39} This effect is probably biological because it is seen in blinded randomised controlled trials.⁴⁰ Results of a prospective study of 50 transgender men without psychiatric disorders who were given various types of testosterone for 1 year showed increased frequencies of desire, sexual fantasies, arousal, and masturbation.²⁵ However, no changes were seen in frequency of sexual activity with a partner or with relationship satisfaction. In a retrospective study of 138 transgender men who received testosterone therapy for a mean of 7 years,⁴¹ 71% reported an increase in sexual desire, whereas 12% had a decrease and 17% had no change. Although most of these participants underwent hysterectomy, oophorectomy, and phalloplasty, no difference was reported in sexual desire between those with or without phalloplasties. In another retrospective study of 45 transgender men who had undergone sexual reassignment surgery at least 1 year before the study,³⁸ 32 (74%) had increased scores for sexual desire and 11 (25%) had no change while on testosterone therapy.

Data from most observational studies and testosterone trials have shown a link between testosterone concentrations and female sexual function.⁴² In a randomised controlled trial of 814 postmenopausal women with low libido, those who received a testosterone patch (300 µg per day) without oestrogen therapy had a small increase in the number of satisfying sexual episodes per month, increased desire, and decreased distress.³⁹ Nonetheless, a few studies (including unpublished ones) of transdermal testosterone gels have not shown a benefit for sexual function or desire.⁴⁰

Voice

Similar to changes that occur in boys going through puberty, the increased levels of testosterone in transgender men on testosterone therapy are associated with a lowering of the pitch of the voice. A longitudinal retrospective study⁴³ collected voice data on 50 transgender men, of whom 36 had data from baseline to 12 months on testosterone therapy. The largest drop in mean fundamental frequency occurred during the first 2–5 months of testosterone therapy. Nonetheless, 24% of transgender men received vocal therapy due to symptoms of vocal fatigue, vocal instability, strained voice quality, insufficiency lowering of pitch, voice projection difficulties, and problems with the voice sounding younger than the subjects' chronological age.⁴³ In one cross-sectional study,⁴⁴ voice parameters were compared between 40 transgender men who had been on long-term testosterone therapy (mean >10 years) and a control group of natal men. Acoustically, 90% of transgender men had voices indistinguishable from those of natal men. Nonetheless, 10% of transgender men had either a gender ambiguous fundamental frequency between 150 and 185 Hz when reading or had undergone voice therapy or surgery.

Psychological and cognitive effects

Androgen and oestrogen receptors are distributed throughout the central nervous system, and testosterone therapy is generally associated with improved overall wellbeing in transgender men. Although some of the improvements to mental health could be related to the effects of testosterone, a more likely explanation is the reduction in gender dysphoria associated with hormone therapy, since both transgender men and transgender women experience beneficial effects irrespective of the differences in hormone therapy.⁴⁵ In a prospective study, the psychological functioning of transgender men before starting hormone therapy was worse than that of non-transgender male and female control groups. After 3 months of testosterone therapy, transgender men showed improvements on several scales (depression, hypochondria, hysteria, and paranoia) of the validated Minnesota Multiphasic Personality Inventory compared with the control groups.⁴⁶

In another prospective study,⁴⁵ investigators assessed depression, anxiety, and psychological symptoms of 29 transgender men using three validated instruments (Zung Self-Rating Depression Scale, Zung Self-Rating Anxiety Scale, and Symptom Checklist 90-Revised) before and after 1 year of treatment with intramuscular testosterone esters. In both transgender men and transgender women, treatment was associated with a reduction prevalence of anxiety (from 53 [50%] individuals to 18 [17%]), depression (from 45 [42%] individuals to 24 [23%]), and various symptoms on several scales on the Symptom Checklist 90-Revised. The same research group reported that 1 year of therapy with intramuscular testosterone esters was associated with

reduced levels of perceived stress and a decrease in mean morning serum cortisol concentrations from 772 nmol/L to 413 nmol/L (28 µg/dL to 15 µg/dL).⁴⁷ In another study,⁴⁸ investigators measured the prevalence of anxiety, depression, and social distress using validated instruments (Hospital Anxiety and Depression Scale and Social Anxiety and Distress Scale), comparing 38 transgender men (and 29 transgender women) who had not begun hormone therapy and 36 transgender men (and 84 transgender women) who had been taking various formulations of testosterone for an average of 5 years. Compared with individuals (the study combined the results for both transgender men and transgender women) who had not begun hormone therapy, those receiving hormone therapy had lower prevalence of anxiety symptoms (33% [39/120] vs 61% [41/67]), depression symptoms (8% [10/120] vs 31% [21/67]), and social distress. By contrast with the previous studies, investigators of a prospective study²⁵ of 50 transgender men without psychiatric disorders who were given various types of testosterone for 1 year noted no changes to mood, depression, happiness, temper, or anger, based on a non-validated questionnaire.

The effects of testosterone therapy on cognition in transgender men have been poorly studied. Some data for premenopausal and postmenopausal women suggest that low doses of testosterone therapy result in improvements in various cognitive functions. For example, in a double-blind, placebo-controlled trial⁴⁹ of a single dose of sublingual testosterone in young women, (age range 20–32 years) visuospatial ability was improved 4–5 h after they had ingested the testosterone. Similarly, in a 26 week randomised controlled trial⁵⁰ of transdermal testosterone gel in postmenopausal women (age range 55–65 years) not on oestrogen, the results showed improvements in verbal learning and memory. The testosterone concentrations achieved in the trial⁵⁰ were at the upper limit of normal for premenopausal women.

Concordant with changes in cognition and behaviour seen with testosterone therapy, imaging has revealed physical changes in the size of various brain structures and areas during testosterone therapy. In one such study,⁵¹ researchers used MRI to compare the brain structure of 15 transgender men before and after at least 6 months of cross-sex hormone therapy. Testosterone treatment was associated with increased total grey matter volume and bilateral increased cortical thickness in the postcentral gyrus, in the cuneus and rostral middle frontal areas on the right lobe, and in the inferior parietal, lingual, pericalcarine, and supramarginal regions on the left lobe.

Bone

Both oestrogen and testosterone have important roles in bone health. Although testosterone therapy often results in a decrease in mean oestradiol concentrations in transgender men compared with natal women, testosterone is also converted into oestradiol by

aromatase in several tissues, including bone.^{15,16,18,19,21,22,25,26} Oestrogen is needed to maintain adequate bone health and to prevent the rapid bone loss that would otherwise occur after menopause.

Compared with age-matched natal women, 50 transgender men receiving testosterone therapy for an average of 10 years were reported to have increased radial cortical bone size and decreased cortical volumetric bone mineral density at the radius and tibia.⁵² In a 1 year prospective study of 23 transgender men given intramuscular testosterone undecanoate,¹⁸ areal and volumetric bone parameters remained largely unchanged, apart from small increases in trabecular volumetric bone mineral density at the distal radius and bone mineral density at the total hip. A potential explanation is that increased muscle mass induces an increased mechanical load on the bone, which might stimulate bone formation. In another study,⁵³ transgender men taking testosterone had reduced bone mineral density after oophorectomy, with the decrease inversely associated with serum concentrations of luteinising hormone and follicle-stimulating hormone.

In addition to the positive effects on bone mineral density seen with oestrogen use by postmenopausal women, evidence suggests that androgens provide further bone support. In a randomised controlled trial of various combinations of oral conjugated equine oestrogen with or without methyltestosterone,⁵⁴ the oestrogen and androgen combination increased bone mineral density at the spine and hip more than did oestrogen alone.

However, it is important to note that bone mineral density is a surrogate marker for fracture, which is the endpoint of real clinical interest. Trials showing a benefit of testosterone therapy with respect to fracture rates are lacking not only in transgender men, but also in hypogonadal men and postmenopausal women.

Potential risks of testosterone therapy

Cardiometabolic risk factors

To provide some context, the cardiovascular benefits and risks of testosterone therapy for natal men with low or low-normal testosterone concentrations are poorly understood and controversial. The cardiovascular effects of testosterone might be mediated via several mechanisms, including changes to insulin sensitivity, lipid profiles, inflammatory cytokines, salt retention, polycythaemia, and platelet aggregation.⁵⁵ In a 3 year randomised controlled trial that included 308 older men (mean age 68 years) with low or low-normal testosterone concentrations,⁵⁶ topical testosterone therapy did not affect the rate of change in common carotid artery intima-media thickness or coronary artery calcium deposition. In a large retrospective study of more than 83 000 male US veterans (mean age 64 years) with low testosterone concentrations⁵⁷ reduced incidences of myocardial infarction, stroke, and all-cause mortality

were seen in men who achieved normal testosterone levels on therapy compared with untreated men and men who were treated but did not have normalisation of testosterone levels. Conversely, data from two studies have shown an increase in cardiovascular events associated with testosterone therapy. In a randomised controlled trial of 209 community-dwelling older men (mean age 74 years) with mobility limitations and total testosterone concentrations of 100–350 ng/dL (3.5–12.1 nmol/L), free testosterone concentrations of less than 50 pg/mL (173 pmol/L), or both,⁵⁸ men given topical testosterone had more than five times as many cardiovascular-related events, which were broadly defined to include events such as raised blood pressure, oedema, and electrocardiogram changes. In the second study,⁵⁵ investigators examined the association between testosterone prescriptions and incidence of acute myocardial infarction in a large health-care database. Irrespective of baseline testosterone concentrations, which were not known, men aged 65 years and older who received testosterone prescriptions had a doubling of acute myocardial infarction in the 90 days after receiving the prescription, compared with the period before receiving the prescription. In view of the controversy surrounding cardiovascular risk associated with testosterone treatment in natal men, there is concern that this potential risk might also apply to transgender men given testosterone formulations.

The lipid parameter most consistently affected by testosterone therapy in transgender men is HDL cholesterol, which is reported to decrease by 0.10–0.34 mmol/L (4–13 mg/dL) during 1 year of testosterone therapy, irrespective of formulation.^{14–17,19} Findings from some studies^{15,17,19} have also shown an increase in triglycerides of 0.07–0.36 mmol/L (6–32 mg/dL) during 1 or 2 years with topical testosterone and intramuscular testosterone undecanoate. The evidence is inconsistent with respect to total cholesterol and LDL cholesterol. In one study of intramuscular testosterone esters,¹⁴ substantial increases in both total cholesterol (0.62 mmol/L [24 mg/dL] at 1 year and 1.04 mmol/L [40 mg/dL] at 2 years) and LDL cholesterol (0.28 mmol/L [11 mg/dL] at 1 year and 0.93 mmol/L [36 mg/dL] at 2 years) were reported after 1 and 2 years. Hypogonadal men given testosterone therapy might also develop reduced HDL cholesterol concentrations, but triglycerides are not usually affected.³⁹

None of the testosterone formulations seem to have an effect on fasting serum glucose or insulin sensitivity, as measured by homeostatic model assessment–insulin resistance.^{13,14,16,19,60} By contrast, decreased insulin sensitivity has been reported in hypogonadal men not receiving testosterone therapy and in women with polycystic ovarian syndrome who have increased endogenous androgen levels.^{61,62} The evidence is inconsistent with respect to fasting serum insulin concentrations, with separate studies showing increases, decreases, or no change.^{14,16,19}

Investigators of one case-control study⁶³ noted that testosterone therapy in transgender men was associated with increased incidence of type 2 diabetes, although no effect on obesity was seen. Results of a study of 12 patients who took intramuscular testosterone esters for 6 months showed reduced serum concentrations of leptin and adiponectin at the end of the study.¹³

Findings from some studies^{14,15,19} have shown that, in transgender men, testosterone therapy for 1 year is associated with an increase in systolic blood pressure of 4–12 mm Hg, but no significant change in diastolic blood pressure. In one study of 97 patients using either topical testosterone or intramuscular testosterone undecanoate¹⁷ no changes were seen in either systolic or diastolic blood pressure during a 2 year period. Although rates of cardiovascular events do not seem to be increased in the short term, the implication of increased systolic blood pressure is unknown in the long term. The main challenge in establishing whether raised systolic blood pressure is associated with an increased incidence of cardiovascular events is the age of transgender men studied as most begin testosterone therapy before the age of 30 years, when the risk of such events is exceedingly low. Long-term data about transgender men who started testosterone in early adulthood are scarce, as are short-term data about transgender men who started testosterone when they were older than 50 years. Notably, increased blood pressure is not a major concern for hypogonadal men on testosterone replacement. The results of a systematic review and meta-analysis⁵⁹ showed that testosterone therapy in hypogonadal men was not associated with changes in blood pressure. Likewise, the Endocrine Society guidelines on treatment of androgen deficiency⁶⁴ do not mention increased blood pressure as a potential adverse effect in this population.

In a retrospective study of 50 transgender men who received testosterone for an average of 10 years,⁶⁵ no cardiovascular events such as myocardial infarction or stroke occurred. In the same study, in which an increased prevalence of type 2 diabetes among transgender men was reported,⁶³ the investigators also compared the prevalence of cardiovascular disease between 138 transgender men, who had been on testosterone for an average of 9 years, and age-matched natal women, showing no differences in myocardial infarction or cerebrovascular disease. It is important to note that 86% of transgender men had hysterectomy or oophorectomy in addition to mastectomy. In a systematic review and meta-analysis of hormone therapy in transgender populations,⁶⁶ very few reported cardiovascular events (deaths, strokes, myocardial infarctions, or venous thromboembolism) were identified, but the quality of the evidence was very low and the data were inconclusive. Ultimately, because of the potential for testosterone to increase cardiovascular events in transgender men, research needs to be done in older transgender men rather than in younger individuals who are at low risk of cardiovascular events.

All formulations of testosterone therapy increase the haemoglobin concentration and hematocrit but rarely to levels consistent with erythrocytosis. Greater increases are seen with intramuscular esters than with other formulations, consistent with studies in hypogonadal men given testosterone replacement.⁶⁷ Topical testosterone for 1 year resulted in a mean rise in haemoglobin of 6 g/L (0.6 g/dL) and a mean rise in haematocrit of 2%.¹⁶ Intramuscular testosterone esters resulted in a mean rise in haemoglobin of 17 g/L (1.7 g/dL) and a mean rise in haematocrit of 4.7% in 1 year.¹⁶ Intramuscular testosterone undecanoate for 1 year resulted in a mean rise in haemoglobin of 12–13 g/L (1.2–1.3 g/dL) and a mean rise in haematocrit of 3.3–5.0%.^{15,16,19,23} No further increases were seen after 1 year.¹⁵

Testosterone therapy does not seem to be associated with increased incidence of venous thromboembolism in transgender men, but studies have not been sufficiently powered to address this issue. Results from one study⁶⁸ showed testosterone to be antithrombotic with lower activated protein C resistance in transgender men given testosterone. In a group of 89 transgender men with a mean age of 27 years and 62 (70%) of whom smoked, who were given intramuscular testosterone undecanoate and lynestrenol, with a mean follow-up of 47 months, no cases of venous thromboembolism occurred.⁶⁹ Results from a study of premenopausal women with premenstrual symptoms who were given low doses of testosterone via subcutaneous implants for at least 2 years⁷⁰ showed no effects on clotting factors. Nonetheless, in 2014, on the basis of post-marketing reports, the US Food and Drug Administration required manufacturers of testosterone products for men to include a general warning about the risk of venous blood clots unrelated to polycythaemia.⁷¹ A retrospective study⁶⁵ of 50 transgender men who received testosterone for an average of 10 years showed no deep vein thrombosis events.

Mortality

No prospective studies have been done to investigate mortality rates in transgender men, and the studies that have been reported have had inconsistent results. In one study done in the Netherlands,³⁵ researchers compared standardised mortality rates between 365 transgender men who were all on testosterone therapy and the general population and noted no differences. The transgender group started testosterone therapy at a mean age of 26 years and had a mean follow-up of 19 years on hormone therapy. In a Swedish population-based registry study,⁷² investigators used data from a national death registry between 1973 and 2003 to compare mortality rates between 133 transgender men (who had received both hormone therapy and gender reassignment surgery) and 1330 random population controls matched by age and birth sex. Mortality rates seemed to be similar during the first 10 years after gender reassignment surgery, but the curves diverged

Search strategy and selection criteria

References for this Review were identified through searches of PubMed and Scopus for articles published in English and Spanish from Jan 1, 2000, to April 5, 2016. The search terms used were “transgender”, “transsexual”, or “gender dysphoria” in combination with the terms “testosterone” or “androgen”. Abstracts of articles resulting from these searches and relevant references cited in those articles were reviewed. Case reports and small case series of less than ten individuals were only included if the findings were deemed very important. Selected older publications were also included based on importance.

after 10 years, with transgender men having increased mortality rates. The adjusted hazard ratio for suicide was 19.1 (95% CI 5.8–62.9) for transgender men and transgender women combined as mortality data were not broken down by gender.

Conclusions

Within several months of starting testosterone therapy, transgender men begin to notice many desired effects, including increased facial and body hair, increased lean mass and strength, decreased fat mass, deepened voice, increased sexual desire, cessation of menstruation, clitoral enlargement, and reductions in gender dysphoria, perceived stress, anxiety, and depression. The most common undesired effect is acne, for which many patients take topical or oral medications. The main physical feature that testosterone therapy does not address is the presence of breast tissue, although some atrophy might occur. Many transgender men elect to undergo so-called top surgery to remove their breasts or wear a binder to flatten their chests. Many of the effects of testosterone therapy have also been noted in natal hypogonadal men and postmenopausal women with low libido who are given testosterone. Nonetheless, the effects in transgender men should not be generalised to other populations because of the different anatomical and hormonal background of natal men and the lower testosterone doses used for natal women. For example, the dose of testosterone used for postmenopausal symptoms is not associated with clitoromegaly, increased muscle mass, or deepening of the voice.⁷³

Testosterone therapy seems to be quite safe in the short term, based on results from many studies. Nonetheless, testosterone decreases HDL cholesterol, increases triglycerides, might increase systolic blood pressure, and might increase the incidence of diabetes and metabolic syndrome. The long-term consequences of these changes are not known. In view of the substantial reduction in the risk of breast cancer associated with testosterone therapy, there is no clear evidence to guide the interval of screening mammography. The few studies that compare mortality rates of transgender men with those of the general population have yielded inconsistent results. Since

transgender medicine is a fairly new field, more research is needed, especially in the form of larger and longer prospective studies that include diverse populations.

Declaration of interests

I declare no competing interests.

Acknowledgments

I thank librarian Laura Abate (George Washington University, Washington, DC, USA) for doing the search of the scientific literature.

References

- Gooren LJ, Sungkaew T, Giltay EJ, Guadamuz TE. Cross-sex hormone use, functional health and mental well-being among transgender men (Toms) and transgender women (Kathoeys) in Thailand. *Cult Health Sex* 2015; **17**: 92–103.
- Irwig MS. Transgender care by endocrinologists in the United States. *Endocr Pract* 2016. Published online Feb 26. DOI:10.4158/EP151185.OR.
- van Kesteren PJ, Gooren LJ, Megens JA. An epidemiological and demographic study of transsexuals in the Netherlands. *Arch Sex Behav* 1996; **25**: 589–600.
- Conron KJ, Scott G, Stowell GS, Landers SJ. Transgender health in Massachusetts: results from a household probability sample of adults. *Am J Public Health* 2012; **102**: 118–22.
- Zhou JN, Hofman MA, Gooren LJ, Swaab DF. A sex difference in the human brain and its relation to transsexuality. *Nature* 1995; **378**: 68–70.
- Heylens G, De Cuypere G, Zucker KJ, et al. Gender identity disorder in twins: a review of the case report literature. *J Sex Med* 2012; **9**: 751–57.
- Hare L, Bernard P, Sánchez FJ, et al. Androgen receptor repeat length polymorphism associated with male-to-female transsexualism. *Biol Psychiatry* 2009; **65**: 93–96.
- Henningsson S, Westberg L, Nilsson S, et al. Sex steroid-related genes and male-to-female transsexualism. *Psychoneuroendocrinology* 2005; **30**: 657–64.
- Ujike H, Otani K, Nakatsuka M, et al. Association study of gender identity disorder and sex hormone-related genes. *Prog Neuropsychopharmacol Biol Psychiatry* 2009; **33**: 1241–44.
- Coleman E, Bockting W, Botzer M, et al. Standards of care for the health of transsexual, transgender, and gender-nonconforming people. *Int J Transgend* 2011; **13**: 165–232.
- Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, et al, and the Endocrine Society. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2009; **94**: 3132–54.
- Wylie K, Barrett J, Besser M, et al. Good practice guidelines for the assessment and treatment of adults with gender dysphoria. *Sex Relationship Ther* 2014; **29**: 154–214.
- Berra M, Armillotta F, D’Emidio L, et al. Testosterone decreases adiponectin levels in female to male transsexuals. *Asian J Androl* 2006; **8**: 725–29.
- Colizzi M, Costa R, Scaramuzzi F, et al. Concomitant psychiatric problems and hormonal treatment induced metabolic syndrome in gender dysphoria individuals: a 2 year follow-up study. *J Psychosom Res* 2015; **78**: 399–406.
- Mueller A, Haerberle L, Zollver H, et al. Effects of intramuscular testosterone undecanoate on body composition and bone mineral density in female-to-male transsexuals. *J Sex Med* 2010; **7**: 3190–98.
- Pelusi C, Costantino A, Martelli V, et al. Effects of three different testosterone formulations in female-to-male transsexual persons. *J Sex Med* 2014; **11**: 3002–11.
- Quirós C, Patrascioiu I, Mora M, et al. Effect of cross-sex hormone treatment on cardiovascular risk factors in transsexual individuals. Experience in a specialized unit in Catalonia. *Endocrinol Nutr* 2015; **62**: 210–16.
- Van Caenegem E, Wierckx K, Taes Y, et al. Body composition, bone turnover, and bone mass in trans men during testosterone treatment: 1-year follow-up data from a prospective case-controlled study (ENIGI). *Eur J Endocrinol* 2015; **172**: 163–71.
- Wierckx K, Van Caenegem E, Schreiner T, et al. Cross-sex hormone therapy in trans persons is safe and effective at short-time follow-up: results from the European network for the investigation of gender incongruence. *J Sex Med* 2014; **11**: 1999–2011.

- 20 Finkelstein JS, Lee H, Burnett-Bowie SA, et al. Gonadal steroids and body composition, strength, and sexual function in men. *N Engl J Med* 2013; **369**: 1011–22.
- 21 Giltay EJ, Gooren LJ. Effects of sex steroid deprivation/administration on hair growth and skin sebum production in transsexual males and females. *J Clin Endocrinol Metab* 2000; **85**: 2913–21.
- 22 Wierckx K, Van de Peer F, Verhaeghe E, et al. Short- and long-term clinical skin effects of testosterone treatment in trans men. *J Sex Med* 2014; **11**: 222–29.
- 23 Irwig MS, Kolukula S. Persistent sexual side effects of finasteride for male pattern hair loss. *J Sex Med* 2011; **8**: 1747–53.
- 24 Irwig MS. Depressive symptoms and suicidal thoughts among former users of finasteride with persistent sexual side effects. *J Clin Psychiatry* 2012; **73**: 1220–23.
- 25 Costantino A, Cerpolini S, Alvisi S, Morselli PG, Venturoli S, Meriggiola MC. A prospective study on sexual function and mood in female-to-male transsexuals during testosterone administration and after sex reassignment surgery. *J Sex Marital Ther* 2013; **39**: 321–35.
- 26 Jacobeit JW, Gooren LJ, Schulte HM. Long-acting intramuscular testosterone undecanoate for treatment of female-to-male transgender individuals. *J Sex Med* 2007; **4**: 1479–84.
- 27 Nakamura A, Watanabe M, Sugimoto M, et al. Dose-response analysis of testosterone replacement therapy in patients with female to male gender identity disorder. *Endocr J* 2013; **60**: 275–81.
- 28 Meyer WJ 3rd, Webb A, Stuart CA, Finkelstein JW, Lawrence B, Walker PA. Physical and hormonal evaluation of transsexual patients: a longitudinal study. *Arch Sex Behav* 1986; **15**: 121–38.
- 29 Baldassarre M, Giannone FA, Foschini MP, et al. Effects of long-term high dose testosterone administration on vaginal epithelium structure and estrogen receptor- α and - β expression of young women. *Int J Impot Res* 2013; **25**: 172–77.
- 30 Grynberg M, Fanchin R, Dubost G, et al. Histology of genital tract and breast tissue after long-term testosterone administration in a female-to-male transsexual population. *Reprod Biomed Online* 2010; **20**: 553–58.
- 31 Perrone AM, Cerpolini S, Maria Salfi NC, et al. Effect of long-term testosterone administration on the endometrium of female-to-male (FtM) transsexuals. *J Sex Med* 2009; **6**: 3193–200.
- 32 Wierckx K, Van Caenegem E, Pennings G, et al. Reproductive wish in transsexual men. *Hum Reprod* 2012; **27**: 483–87.
- 33 Light AD, Obedin-Maliver J, Sevelius JM, Kerns JL. Transgender men who experienced pregnancy after female-to-male gender transitioning. *Obstet Gynecol* 2014; **124**: 1120–27.
- 34 Slagter MH, Gooren LJ, Scorilas A, Petraki CD, Diamandis EP. Effects of long-term androgen administration on breast tissue of female-to-male transsexuals. *J Histochem Cytochem* 2006; **54**: 905–10.
- 35 Asscheman H, Giltay EJ, Megens JA, de Ronde WP, van Trotsenburg MA, Gooren LJ. A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. *Eur J Endocrinol* 2011; **164**: 635–42.
- 36 Gooren LJ, van Trotsenburg MA, Giltay EJ, van Diest PJ. Breast cancer development in transsexual subjects receiving cross-sex hormone treatment. *J Sex Med* 2013; **10**: 3129–34.
- 37 Glaser RL, Dimitrakakis C. Reduced breast cancer incidence in women treated with subcutaneous testosterone, or testosterone with anastrozole: a prospective, observational study. *Maturitas* 2013; **76**: 342–49.
- 38 Wierckx K, Elaut E, Van Caenegem E, et al. Sexual desire in female-to-male transsexual persons: exploration of the role of testosterone administration. *Eur J Endocrinol* 2011; **165**: 331–37.
- 39 Davis SR, Moreau M, Kroll R, et al, and the APHRODITE Study Team. Testosterone for low libido in postmenopausal women not taking estrogen. *N Engl J Med* 2008; **359**: 2005–17.
- 40 Wierman ME, Arlt W, Basson R, et al. Androgen therapy in women: a reappraisal: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2014; **99**: 3489–510.
- 41 Wierckx K, Elaut E, Van Hoorde B, et al. Sexual desire in trans persons: associations with sex reassignment treatment. *J Sex Med* 2014; **11**: 107–18.
- 42 Davis SR, Wahlin-Jacobsen S. Testosterone in women—the clinical significance. *Lancet Diabetes Endocrinol* 2015; **3**: 980–92.
- 43 Nygren U, Nordenskjöld A, Arver S, Södersten M. Effects on voice fundamental frequency and satisfaction with voice in trans men during testosterone treatment—a longitudinal study. *J Voice* 2015; published online Dec 8. DOI:10.1016/j.jvoice.2015.10.016.
- 44 Cosyns M, Van Borsel J, Wierckx K, et al. Voice in female-to-male transsexual persons after long-term androgen therapy. *Laryngoscope* 2014; **124**: 1409–14.
- 45 Colizzi M, Costa R, Todarello O. Transsexual patients' psychiatric comorbidity and positive effect of cross-sex hormonal treatment on mental health: results from a longitudinal study. *Psychoneuroendocrinology* 2014; **39**: 65–73.
- 46 Keo-Meier CL, Herman LI, Reisner SL, Pardo ST, Sharp C, Babcock JC. Testosterone treatment and MMPI-2 improvement in transgender men: a prospective controlled study. *J Consult Clin Psychol* 2015; **83**: 143–56.
- 47 Colizzi M, Costa R, Pace V, Todarello O. Hormonal treatment reduces psychobiological distress in gender identity disorder, independently of the attachment style. *J Sex Med* 2013; **10**: 3049–58.
- 48 Gómez-Gil E, Zubiaurre-Elorza L, Esteva I, et al. Hormone-treated transsexuals report less social distress, anxiety and depression. *Psychoneuroendocrinology* 2012; **37**: 662–70.
- 49 Aleman A, Bronk E, Kessels RP, Koppeschaar HP, van Honk J. A single administration of testosterone improves visuospatial ability in young women. *Psychoneuroendocrinology* 2004; **29**: 612–17.
- 50 Davis SR, Jane F, Robinson PJ, et al. Transdermal testosterone improves verbal learning and memory in postmenopausal women not on oestrogen therapy. *Clin Endocrinol (Oxf)* 2014; **81**: 621–28.
- 51 Zubiaurre-Elorza L, Junque C, Gómez-Gil E, Guillaumon A. Effects of cross-sex hormone treatment on cortical thickness in transsexual individuals. *J Sex Med* 2014; **11**: 1248–61.
- 52 Van Caenegem E, Wierckx K, Taes Y, et al. Bone mass, bone geometry, and body composition in female-to-male transsexual persons after long-term cross-sex hormonal therapy. *J Clin Endocrinol Metab* 2012; **97**: 2503–11.
- 53 van Kesteren P, Lips P, Gooren LJ, Asscheman H, Megens J. Long-term follow-up of bone mineral density and bone metabolism in transsexuals treated with cross-sex hormones. *Clin Endocrinol (Oxf)* 1998; **48**: 347–54.
- 54 Barrett-Connor E, Young R, Notelovitz M, et al. A two-year, double-blind comparison of estrogen-androgen and conjugated estrogens in surgically menopausal women. Effects on bone mineral density, symptoms and lipid profiles. *J Reprod Med* 1999; **44**: 1012–20.
- 55 Finkle WD, Greenland S, Ridgeway GK, et al. Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men. *PLoS One* 2014; **9**: e85805.
- 56 Basaria S, Harman SM, Travison TG, et al. Effects of testosterone administration for 3 years on subclinical atherosclerosis progression in older men with low or low-normal testosterone levels: a randomized clinical trial. *JAMA* 2015; **314**: 570–81.
- 57 Sharma R, Oni OA, Gupta K, et al. Normalization of testosterone level is associated with reduced incidence of myocardial infarction and mortality in men. *Eur Heart J* 2015; **36**: 2706–15.
- 58 Basaria S, Coviello AD, Travison TG, et al. Adverse events associated with testosterone administration. *N Engl J Med* 2010; **363**: 109–22.
- 59 Fernández-Balsells MM, Murad MH, Lane M, et al. Clinical review 1: Adverse effects of testosterone therapy in adult men: a systematic review and meta-analysis. *J Clin Endocrinol Metab* 2010; **95**: 2560–75.
- 60 Elbers JM, Giltay EJ, Teerlink T, et al. Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. *Clin Endocrinol (Oxf)* 2003; **58**: 562–71.
- 61 Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. *Diabetes* 1989; **38**: 1165–74.
- 62 Pitteloud N, Mootha VK, Dwyer AA, et al. Relationship between testosterone levels, insulin sensitivity, and mitochondrial function in men. *Diabetes Care* 2005; **28**: 1636–42.
- 63 Wierckx K, Elaut E, Declercq E, et al. Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: a case-control study. *Eur J Endocrinol* 2013; **169**: 471–78.

- 64 Bhasin S, Cunningham GR, Hayes FJ, et al, and the Task Force, Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2010; **95**: 2536–59.
- 65 Wierckx K, Mueller S, Weyers S, et al. Long-term evaluation of cross-sex hormone treatment in transsexual persons. *J Sex Med* 2012; **9**: 2641–51.
- 66 Elamin MB, Garcia MZ, Murad MH, Erwin PJ, Montori VM. Effect of sex steroid use on cardiovascular risk in transsexual individuals: a systematic review and meta-analyses. *Clin Endocrinol (Oxf)* 2010; **72**: 1–10.
- 67 Dobs AS, Meikle AW, Arver S, Sanders SW, Caramelli KE, Mazer NA. Pharmacokinetics, efficacy, and safety of a permeation-enhanced testosterone transdermal system in comparison with bi-weekly injections of testosterone enanthate for the treatment of hypogonadal men. *J Clin Endocrinol Metab* 1999; **84**: 3469–78.
- 68 Toorians AW, Thomassen MC, Zweegman S, et al. Venous thrombosis and changes of hemostatic variables during cross-sex hormone treatment in transsexual people. *J Clin Endocrinol Metab* 2003; **88**: 5723–29.
- 69 Ott J, Kaufmann U, Bentz EK, Huber JC, Tempfer CB. Incidence of thrombophilia and venous thrombosis in transsexuals under cross-sex hormone therapy. *Fertil Steril* 2010; **93**: 1267–72.
- 70 Buckler HM, McElhone K, Durrington PN, Mackness MI, Ludlam CA, Wu FC. The effects of low-dose testosterone treatment on lipid metabolism, clotting factors and ultrasonographic ovarian morphology in women. *Clin Endocrinol (Oxf)* 1998; **49**: 173–78.
- 71 US Food and Drug Administration. FDA adding general warning to testosterone products about potential for venous blood clots. June 19, 2014. <http://www.fda.gov/Drugs/DrugSafety/ucm401746.htm> (accessed Oct 10, 2015).
- 72 Dhejne C, Lichtenstein P, Boman M, Johansson AL, Långström N, Landén M. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. *PLoS One* 2011; **6**: e16885.
- 73 Davis SR, Braunstein GD. Efficacy and safety of testosterone in the management of hypoactive sexual desire disorder in postmenopausal women. *J Sex Med* 2012; **9**: 1134–48.

Sport and Transgender People: A Systematic Review of the Literature Relating to Sport Participation and Competitive Sport Policies

Bethany Alice Jones^{1,2} · Jon Arcelus^{1,3} · Walter Pierre Bouman¹ · Emma Haycraft² 

Published online: 3 October 2016

© The Author(s) 2016. This article is published with open access at Springerlink.com

Abstract

Background Whether transgender people should be able to compete in sport in accordance with their gender identity is a widely contested question within the literature and among sport organisations, fellow competitors and spectators. Owing to concerns surrounding transgender people (especially transgender female individuals) having an athletic advantage, several sport organisations place restrictions on transgender competitors (e.g. must have undergone gender-confirming surgery). In addition, some transgender people who engage in sport, both competitively and for leisure, report discrimination and victimisation.

Objective To the authors' knowledge, there has been no systematic review of the literature pertaining to sport participation or competitive sport policies in transgender people. Therefore, this review aimed to address this gap in the literature.

Method Eight research articles and 31 sport policies were reviewed.

Results In relation to sport-related physical activity, this review found the lack of inclusive and comfortable environments to be the primary barrier to participation for transgender people. This review also found transgender people had a mostly negative experience in competitive sports because of the restrictions the sport's policy placed on them. The majority of transgender competitive sport policies that were reviewed were not evidence based.

Conclusion Currently, there is no direct or consistent research suggesting transgender female individuals (or male individuals) have an athletic advantage at any stage of their transition (e.g. cross-sex hormones, gender-confirming surgery) and, therefore, competitive sport policies that place restrictions on transgender people need to be considered and potentially revised.

Key points

The majority of transgender people have a negative experience when engaging in competitive sports and sport-related physical activity.

There is no direct and consistent research to suggest that transgender female individuals (and transgender male individuals) have an athletic advantage in sport and, therefore, the majority of competitive sport policies are discriminatory against this population.

There are several areas of future research required to significantly improve our knowledge of transgender people's experiences in sport, inform the development of more inclusive sport policies, and, most importantly, enhance the lives of transgender people, both physically and psychosocially.

✉ Jon Arcelus
J.Arcelus@nottingham.ac.uk

¹ Nottingham Centre for Gender Dysphoria, 3 Oxford Street, Nottingham NG1 5BH, UK

² School of Sport, Exercise, and Health Sciences, Loughborough University, Loughborough, UK

³ Division of Psychiatry and Applied Psychology, Faculty of Medicine and Health Sciences, University of Nottingham, Nottingham, UK

1 Introduction

Transgender people are those who experience incongruence between the gender that they were assigned at birth (based on the appearance of their genitals) and their gender identity/experienced gender. Gender identity, or experienced gender, can be defined as a person's internal sense of gender, whether this be male, female, neither or somewhere along the gender continuum. Some transgender people, but not all, will choose to affirm their gender identity by socially transitioning (i.e. living as their experienced gender socially, at work or at an educational institution, with friends and family, outside the home) and some, in addition, will choose to medically transition with cross-sex hormones and gender-confirming surgeries [1, 2]. Although over time various different terms have been used, the term 'transgender female individual' will be used to describe individuals assigned male at birth, based on their genital appearance, but who later identify as female. 'Transgender male individual' will be used to describe people who are assigned female at birth, based on their genital appearance, but later identify as male. 'Cisgender' will be used to describe people who do not experience incongruence between their gender assigned at birth and their gender identity.

Recent reports indicate that the number of transgender individuals who attend transgender health services has increased substantially over the years in many European countries [3–5]. There has also been a significant increase in the number of people who self-identify as transgender and do not necessarily attend transgender health services [6]. For example, Kuyper and Wijzen [6] found that 4.6 % of people who were assigned male at birth and 3.2 % of people who were assigned female at birth in their Dutch population sample reported an ambivalent gender identity (equal identification with the other gender as with the gender they were assigned at birth). The authors also reported that 1.1 % of the people who were assigned male at birth and 0.8 % of the people who were assigned female at birth identified as transgender. It remains unknown how many of these people will seek treatment through a transgender health service. The increase in people who identify as transgender may be at least partly explained by the increase in visibility of transgender people within Western society [4, 5]. For example, Caitlin Jenner, a former athlete and current television personality, recently came out as transgender during a television interview that was viewed all over the world [7]. Increases in visibility may have prompted some people to reflect and question their gender identity [8].

Some transgender people experience stigma, transphobia, prejudice, discrimination and violence as a consequence of their gender identity [9–11]. Ellis et al. [12]

found that transgender people were more likely to avoid situations when they were afraid of being harassed, identified as transgender or 'outed', such as in clothes shops, public toilets and gyms. Gyms are a popular outlet to engage in sport-related physical activities (i.e. gym fitness exercises) and therefore it is important to create an inclusive environment given the established mental and physical health benefits of physical activity and sport [13, 14]. This is particularly important for transgender people as they have been found to report a high prevalence of depression and anxiety [15, 16], which could be managed with physical activity. Furthermore, physical activity and sport can also contribute towards maintaining the appropriate weight necessary to undergo gender-confirming surgery, acknowledging that not every transgender person will wish to do so [1, 2, 17].

The premise of competitive sport is fairness (i.e. inclusion in the absence of advantage) and, owing to fears surrounding the perceived athletic advantage of transgender people, the question of whether transgender people should be permitted to compete in accordance with their gender identity has been raised and greatly contested within the literature, among sport organisations, fellow competitors and spectators. It is a commonly held belief that androgenic hormones (especially testosterone) confer an athletic advantage in competitive sport. Therefore transgender female individuals, because of high endogenous testosterone levels, are perceived to hold an advantage in sport (when testosterone has not been blocked to a cisgender female level). Transgender men are not thought to possess an athletic advantage, despite being injected with testosterone if they chose to medically transition with cross-sex hormones. However, there has been a paucity of research that has directly explored how androgenic hormone levels are associated with athletic competence in both cisgender and transgender populations (e.g. running time).

To facilitate the inclusion of transgender competitors, in 2004, the International Olympic Committee (IOC) [18] announced that transgender people could participate in all future Olympic games providing they had fully medically transitioned (i.e. had been prescribed cross-sex hormone treatment for 2 years and undergone gender-confirming surgery). Although the requirements of this policy appear to concur with the commonly held belief that transgender people hold an athletic advantage, they have been criticised for not being underpinned by an evidence-based rationale [19]. The IOC [20] has recently updated its policy to be more inclusive of transgender athletes (i.e. fewer restrictions); however, the 2004 policy has been extremely influential on other sport organisations' policy development. The new (2016) IOC policy will be considered in Sect. 3.

In an attempt to draw a consensus as to whether transgender people should be able to compete in accordance with their gender identity, in 2005 Reeser [21] conducted a review of the literature pertaining to gender identity issues in competitive (elite) sport. Reeser paid particular attention to the evolution of gender verification in competitive sport and whether current competitive sport policies for transgender people are fair. He concluded that, while gender verification has made significant advances, there is a lack of physiological performance-related data in transgender people. This is preventing an overall consensus from being made as to whether transgender sport policies are fair or not (i.e. fairness in the absence of advantage). Reeser's review, although important, has some limitations. He did not adopt a systematic methodology and therefore did not include the majority of transgender sport policies. Additionally, Reeser only considered the implications of such policies in relation to elite competitive sport and did not consider the experiences of transgender people who engage in sport or sport-related physical activity for leisure or fitness (e.g. gym fitness activities, jogging).

With the intention of addressing the limitations of the previous literature review, this systematic review has two aims. First, to systematically analyse and critically review the available literature regarding transgender people's experiences in relation to competitive sport (elite and recreational) and sport-related physical activity participation (e.g. jogging, gym fitness activities). Second, to systematically review the available transgender competitive sport policies with regard to their fairness (i.e. competition in the absence of advantage). It is hoped that this systematic review will further enhance the understanding of sport participation and competition amongst transgender people. It may be expected that as more people define themselves as transgender, the issues that transgender people experience in competitive sport and sport-related physical activity will become more pronounced. It is therefore important that those who work to facilitate and promote sport and develop policies for their own sport organisations (e.g. sport medicine specialists, sport policymakers) are informed about the issues that this vulnerable population face. This will allow for a non-discriminatory atmosphere in sport, whilst ensuring a fair system for all participants and competitors (regardless of their gender identity).

2 Methods

2.1 Search Strategy

Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed to undertake this systematic review [22]. To obtain relevant peer-reviewed

articles, an electronic search of literature published between January 1966 and August 2015 was conducted using the following search engines: ScienceDirect, Web of Science, Scopus and PubMed. Within each search engine, the following search terms were entered: gender dysphoria, gender identity disorder, trans people, trans individual, transgender and transsexual. These terms were combined with three terms relating to sport (physical activity, exercise and sport) using the "AND" operator. The reference lists of eligible papers were searched for potentially relevant publications. Sport policies were obtained through a Google search using the above search terms with the addition of "policy" at the end of all sport-related terms.

2.2 Inclusion and Exclusion Criteria

To address the first aim, articles that were selected were concerned with the experiences and issues surrounding physical activity and sport participation for transgender people. This systematic review only considered articles eligible if they were research articles, as opposed to discussion papers. Case studies were also considered eligible, as research articles were limited. Peer-reviewed articles that were written in English only were included. For the second aim, all available national and international policies on competitive sport in transgender people were selected and reviewed.

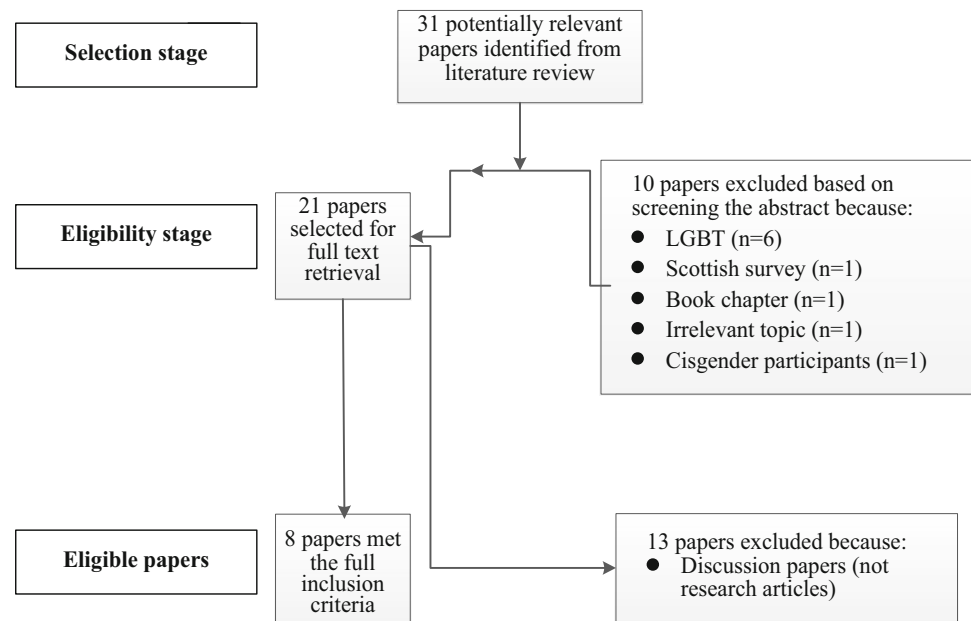
2.3 Study Selection

Thirty-one research articles were considered potentially relevant to the remit of this review. The search also identified 31 competitive sport policies for transgender people. After screening the abstracts, ten research articles were excluded as six were concerned with lesbian, gay, bisexual and transgender sport, one was a Scottish non-academic survey, one was a book chapter, one was concerned with an irrelevant topic and another focused on cisgender participants. The remaining 21 articles were downloaded for full-text review and 13 papers were excluded as they were discussion papers, as opposed to research articles. Therefore, eight research articles fulfilled the inclusion criteria and were consequently included within this systematic review (Fig. 1). All 31 competitive sport policies for transgender people were reviewed and included within this systematic review.

3 Results

This section presents the findings from the research articles and sport policies included within this systematic review. First, the findings from the research articles that explored

Fig. 1 Process of identifying eligible research articles. *LGBT*: lesbian, gay, bisexual, transgender



participation in sports (both elite and recreational standards) and sport-related physical activities (i.e. gym fitness activities, jogging) are provided. Second, findings from the reviewed competitive sport policies relating to transgender inclusion are given.

3.1 Transgender People and Sport Participation

3.1.1 Characteristics of the Eligible Research Studies

The oldest research article included was published in 2004 [23] and the most recent publication was from 2015 [24]. The majority of the studies were qualitative in nature, all of which employed interviews [24–29]. The remaining two research articles included an experimental study [23] and a cross-sectional survey [30]. Most of the studies were concerned with transgender people who participated in sport competitively, at an elite or recreational level [21, 23, 25–29]. Some authors focused on a specific sport; ice hockey, netball and softball [26, 28, 29] while others were concerned with transgender people engaging in any sport [25, 27, 29]. Broadly, across all sports, Gooren and Bunck [23] explored whether transgender athletes have a physiological advantage in competitive sport. One study explored participation in competitive sports and sport-related physical activity [24] and another study discussed participation in sport-related physical activity only [30]. Details of all of the research articles included within this systematic review can be found in Table 1.

3.1.2 Review of Transgender People and Competitive Sport Participation (Elite and Recreational): Research Articles

The same data were extracted from all research articles reviewed (Table 1). Below, we provide the most prominent findings in relation to competitive sport participation from each of these articles. Six research articles were concerned with competitive sport participation within this systematic review [23, 25–29]. The only experimental study was by Gooren and Bunck [23] who aimed to explore whether transgender people taking cross-sex hormone treatment can fairly compete in sport. The authors measured transgender people's muscle mass (via magnetic resonance imaging) and hormone levels (via urine and blood analyses) before and 1 year after cross-sex hormone treatment. They found that 1 year after transgender male individuals had been administered cross-sex hormone treatment, testosterone levels significantly increased and these levels were within a cisgender male range. They also found that 1 year after cross-sex hormone treatment, transgender male individuals' muscle mass had increased and was within the same range as transgender female individuals (assigned male at birth) who had not been prescribed cross-sex hormone treatment. In relation to transgender female individuals, Gooren and Bunck found testosterone levels had significantly reduced to castration levels after 1 year of cross-sex hormone treatment. Muscle mass had also reduced after 1 year of cross-sex hormone treatment. However, muscle mass remained significantly greater than in transgender

Table 1 Study characteristics of research articles included within the review

References	Year	Country	Aim(s)	Sample size (<i>n</i>)	Study design	Main finding(s)
Caudwell [25]	2012	UK	To explore two transgender male individuals' experiences of sport in an educational and recreational environment	2	Qualitative (semi-structured interviews) and a narrative review	Four themes: school sport, their embodied subjectivities, transitioning and sport participation
Cohen and Semerjian [26]	2008	USA	To explore the experience of a transgender female participating in women's national ice hockey tournaments	1	Qualitative (four open-ended interviews)	Five main themes: policed identity, internal conflict, taint of masculinity, affirmation and creating gender norms
Gooren and Bunck [23]	2004	Netherlands	To explore androgen deprivation and androgen administration in transgender people	36	Retrospective	Androgen deprivation in transgender female individuals increases the overlap in muscle mass with women but does not reverse it
Hargie et al. [24]	2015	UK	To explore transgender people's experiences of sport in relation to social exclusion and minority stress theory	10	Qualitative (semi-structured interviews)	Four themes: intimidating nature of locker rooms, the impact of alienating sport experiences at school, fear of public space, and being denied the social, health and well-being aspects of sport
Muchicko et al. [30]	2014	USA	To explore the relationship between gender identity and physical activity	80	Cross-sectional survey	Transgender people reported less physical activity and reported lower social support and physical self-perception than the cisgender participants
Semerjian and Cohen [27]	2006	USA	To explore the experiences of transgender athletes, paying particular attention to whether gender identity or performance was related to participation	4	Qualitative (semi-structured interviews)	Athletes discussed a number of barriers and challenges in relation to their sport participation (i.e. incorrect pronoun use, discomfort in changing rooms)
Tagg [28]	2012	Australia and New Zealand	To understand the issues surrounding transgender athletes' sport participation, specifically in relation to men's netball in New Zealand	2	Qualitative (semi-structured interview) and a narrative review	Transgender-inclusive policies have medicalised gender. Instead of being protective they have done little to make sport fair for transgender participants. Transgender people who are undergoing physical transition have no place to openly participate in netball in New Zealand
Travers and Deri [29]	2011	Canada	To examine the re-negotiation of sex-based boundaries within the context of transgender inclusion in North American lesbian softball leagues	12	Qualitative (semi-structured interviews)	Positive experiences were more often reported by transgender women than transgender men in relation to inclusion despite the re-negotiation of sex boundaries. Several participants perceived testosterone as an athletic advantage in transgender male individuals (when injected) and female individuals (endogenous)

male individuals (assigned female at birth) who had not been prescribed cross-sex hormone treatment.

Therefore, Gooren and Bunck concluded that transgender male individuals are likely to be able to compete without an athletic advantage 1-year post-cross-sex hormone treatment. To a certain extent this also applies to transgender female individuals; however, there still remains a level of uncertainty owing to a large muscle mass 1-year post-cross-sex hormones. While this study was the first to explore, experimentally, whether transgender people can compete fairly, the sample size was relatively small ($n = 36$). Additionally, they did not explore the role of testosterone blockers and did not directly measure the effect cross-sex hormones had on athletic performance (e.g. running time). Many, but not all, transgender female individuals are prescribed testosterone blockers to help them to reach cisgender female testosterone levels, when administration of oestrogen alone is not enough to reduce testosterone levels. This is particularly important if the person aims to undergo gender-confirming surgery, as 6 months of testosterone suppression is a requirement for such procedures. However, if a transgender woman does not wish to undergo surgery or does not wish to have their testosterone blocked to cisgender female levels (e.g. as they wish to use their penis), their testosterone levels will be above cisgender female levels. Differentiating not only between those taking cross-sex hormones and not taking cross-sex hormones, but also transgender female individuals taking testosterone blockers, may be necessary when discussing an athletic advantage.

The remaining studies considered within this section are qualitative, and although they have provided insight into the experiences of transgender people participating in competitive sport, the findings cannot be generalised. Semerjian and Cohen's [27] narrative account provides a good overview of how diverse and individual the issues and experiences of transgender people participating in competitive sport can be. Some participants felt anxious when engaging in sport because they felt their genitals may be revealed (e.g. when changing). In contrast, one participant used sport as a safe space to escape from the harassment he received at school. It must be considered though, that participants within the study engaged in different sports and their experiences could therefore be associated with the specific sport (i.e. some sports could be more inclusive than others).

Three qualitative studies described the implications that sport policies had on the experiences of transgender people who engaged in sport [26, 28, 29]. Cohen and Semerjian [26] published a case study about a transgender woman (pre-gender-confirming surgery) who was playing in the women's national ice hockey tournament, but who was eventually banned from playing in the tournament because it was felt she had an athletic advantage. She described

how she felt under constant surveillance when she was playing and at times felt ambivalent about what gendered team she should play on. It was apparent that although teammates were supportive, the issues she experienced in relation to inclusion in the tournament were primarily related to constraints put in place by competitive sport policies. Similarly, the discussions held by two former New Zealand transgender female netball players in Tagg's [28] study gave the impression that although transgender sport policies were supposedly implemented to increase the inclusivity of transgender people, this was not always the case. They discussed how policy would allow a pre-gender-confirming surgery transgender woman to compete in a male or mixed-gender netball team only and they must obey male dress codes. However, the participants in this study were former netball players and therefore their discussions may not have been based on the current state of netball in relation to transgender participation. In contrast to the previously mentioned studies, the majority of participants ($n = 12$) in Travers and Deri's [29] study discussed the positive experiences they had in relation to transgender participation in competitive sport. However, some of the transgender men did discuss how they had hostile experiences (e.g. incorrect pronoun use). Several of the participants in this study also felt that testosterone gave transgender women (endogenous) and men (when injected) an athletic advantage.

For the two young transgender male individuals in Caudwell's [25] study, the stage of transition appeared to be instrumental in disengagement from participation in competitive sport. The discussion held by the participants highlighted how accessing sport during their transitional period was difficult as they would not be accepted or feel comfortable on either a male or female team during this period. However, this study again discussed sport very broadly and therefore it is unknown whether the participants' experiences were associated with specific sports or whether they are generalisable across other sports.

In summary, there is limited research from which to draw any conclusion about whether transgender people have an athletic advantage in competitive sport or not. The limited physiological research conducted to date has informed the development of transgender sport policies that are implemented by sporting organisations all over the world. It is these sport policies that appear to be instrumental in transgender people's experiences with competitive sport, most of which are negative.

3.1.3 Review of Transgender People and Sport-Related Physical Activities: Research Articles

Within this systematic review, only two studies explored sport-related physical activities [24, 30]. Muchicko et al.

[30] set out to quantitatively explore the relationship between gender identity and physical activity. They compared levels of physical activity between cisgender and transgender people. The study found that self-identified transgender participants ($n = 33$) reported engaging in less physical activity than cisgender participants ($n = 47$). Social support and self-perception were found to mediate the relationship between gender identity and physical activity. The authors suggested that their study highlights how leisure centres need to be more inclusive, and transgender people need to be given more social support to encourage physical activity. However, this study was limited by the sampling methods employed. The cisgender participants were recruited from a university campus where they potentially had more opportunity to walk around campus, and opportunity for discounted gym memberships, whereas the transgender participants were recruited from a support group for transgender people and were not associated with the university.

As with transgender people who engage in sport at a competitive level, transgender people who engage in sport-related physical activity also appear to experience a range of different barriers. Hargie et al. [24] found in their qualitative study that transgender people prefer to engage in individual, as opposed to group, sport-related physical activities. This was reportedly owing to their fear of being ‘outed’. Regardless of whether sport-related physical activities are engaged in individually or in a group, changing rooms appeared to be a significant barrier. Being excluded from sport-related physical activities was distressing for participants, as they could not maintain physical fitness, which they felt was important in preparation for gender-confirming surgery. Despite these interesting findings, the study is limited by the lack of sociodemographic information provided about participants. Within qualitative research, because of the small sample size, it is often desirable to provide a large amount of sociodemographic detail about participants so that the findings can be interpreted in relation to this information. For instance, in the context of sport-related physical activities, the stage of transition may be an important factor when interpreting the individuals’ current experiences of sport-related physical activities.

The limited research studies concerned with sport-related physical activities suggest that inclusive environments are not created for transgender people engaging in such activities, which may deter engagement.

3.2 Transgender-Inclusive Sport Policies

3.2.1 Characteristics of the Eligible Sport Policies

Of the 31 transgender inclusive policies reviewed, 13 were from the USA [31–43]. Ten of the policies reviewed were

from the UK [44–53]. One policy was from Australia [54]. The rest of the policies ($n = 7$) were international [18, 20, 55–59]. Details of all of the sport policies included within this review can be found in Table 2.

3.2.2 Review of the Sport Policies

Policies within this section were systematically reviewed in relation to their inclusiveness of transgender competitors (i.e. maintaining fairness in the absence of advantage for all competitors). The fairness of the policy requirements was judged against the available physiological research that has explored athletic advantage. The time restrictions associated with each requirement were also reviewed (e.g. cross-sex hormones must have been administered for at least 2 years prior to competition). The requirements from each policy are summarised within Table 2 and the most salient points of these policies are then presented in the section that follows.

In 2004, the IOC [18] announced that transgender people who transition after puberty are permitted to compete in sport in line with their experienced gender identity providing they have had gender-confirming surgery, can provide legal recognition of their gender, have been prescribed cross-sex hormone treatment for at least 2 years and have lived in their experienced gender for the same amount of time [18]. Additionally, transgender people who had undergone gender-confirming surgery pre-puberty are eligible to compete in sport in line with their experienced gender identity [18]. This is an international policy and has been adopted by sport organisations all over the world.

While the 2004 IOC [18] policy has been praised for its efforts to address the inclusion of transgender athletes [61], several flaws have been identified [61]. First, the policy excludes transgender people who choose not to have gender-confirming surgery owing to a lack of genital dysphoria (distress), medical reasons, fears about risk during operations, and/or because of other personal reasons [28, 62, 63]. The 2004 IOC [18] policy also excludes transgender people who are in the process of transitioning. For instance, a transgender athlete may be prescribed cross-sex hormone treatment, but be yet to undergo gender-confirming surgery. The 2004 IOC policy [18] therefore adopts a very narrow definition and excludes a large proportion of transgender people [19]. In addition to this, the policy appears to have been developed with only transgender female individuals in mind, possibly as transgender male individuals are not thought to possess athletic advantages in the majority of sports, and therefore the policy discriminates against transgender male individuals [21]. Moreover, the 2004 IOC [18] policy fails to take into consideration the regional, national and international differences in accessing cross-sex hormone treatment and

Table 2 Transgender-inclusive sport policies included within this systematic review

Organisation	Pre-puberty	Post-puberty
IOC (2004) [18]	If had GCS, then may complete in line with gender identity	Provide legal recognition of their gender Had GCS Been on CHT for at least 2 years Lived in their newly assigned gender for at least 2 years Transgender male individuals: no restrictions Transgender female individuals: declared gender as female for at least 4 years and have testosterone levels below 10 nmol/L for at least 12 months prior to competition IOC 2004 policy is adopted
IOC (2016) [20]	Transgender male individuals: no restrictions Transgender female individuals: declared gender as female for at least 4 years and have testosterone levels below 10 nmol/L for at least 12 months prior to competition IOC 2004 policy is adopted	Transsexual female individuals must comply with the IOC Transsexual male individuals must provide legal evidence of their gender and be prescribed CHT Transgender female individuals taking a testosterone suppressant must compete as a male individual until 2 years of medical treatment has been prescribed Transgender male individuals must be being prescribed CHT IOC 2004 policy is adopted A transgender male individual may compete as a male individual or in mixed competition Transgender female individuals may compete as female individuals or in mixed competitions providing testosterone levels are within the normal range for a female individual or they have had a gonadectomy If a transgender female individual has not started treatment then they may compete as a male individual or in mixed competition Recommended that when transgender issues arise, then the policy of each national governing body for that sport should be adopted Encourages participation in line with experienced gender but suggests completion of a TUE form if necessary Gender must be confirmed via birth certificate Female players may be required to submit a gender certificate and/or undergo a medical examination IOC 2004 policy is adopted Allows players to self-identify
Amateur Swimming Association (UK; 2015) [48]	Allowed to complete in line with gender identity providing they have had GCS	
Association of Boxing Commissions (2012) [31]		
Badminton England (UK; 2013) [46]	IOC 2004 policy is adopted	
British Rowing (UK; 2013) [50]	If hormone treatment has not been started, a transgender female individual may compete as a male individual A transgender girl pre-puberty may compete as a girl or in mixed competition	
British Universities and Colleges Sport (UK; 2012) [47]	Not applicable	
Disability Sport Australia (2014) [54]	Encourages participation in line with experienced gender but suggests completion of a TUE form if necessary Gender must be confirmed via birth certificate Female players may be required to submit a gender certificate and/or medical examination	
Fédération Internationale de Volleyball (2014) [58]	IOC 2004 policy is adopted Allows players to self-identify	
International Tennis Federation (n.d.) [57]		
International Quidditch Association (2015) [59]		
International Gay and Lesbian Football Association (2014) [56]	Provide legal recognition of their gender Undergo uninterrupted hormone treatment for at least 1 year prior to competition	Provide legal recognition of their gender Undergo uninterrupted hormone treatment for at least 1 year prior to competition

Table 2 continued

Organisation	Pre-puberty	Post-puberty
International Association of Athletics Federations (2011) [55]	Endocrine assessment Evidence of GCS Details of post-surgery treatment and monitoring to date A transgender female individual may compete as a female individual if they have undergone GCS	Endocrine assessment Evidence of GCS Details of post-surgery treatment and monitoring to date A transgender female individual may compete as a female if they have undergone GCS
Ladies Professional Golf Association (USA; 2010) [43]	Or, a transgender female individual who is treated with testosterone suppression must compete as a man until they have completed hormone treatment for 1 year. After this time they may compete as a woman A transgender male individual who is treated with testosterone may compete in a men's event but not in a women's event	Or, a transgender female who is treated with testosterone suppression must compete as a man until they have completed hormone treatment for 1 year. After this time they may compete as a woman. A transgender male individual who is treated with testosterone may compete in a men's event but not in a women's event
Lawn Tennis Association (UK; n.d.) [45]	Allowed to play in line with gender identity providing they have undergone GCS	Surgical anatomical changes have been completed, including external genitalia changes and gonadectomy (removal of ovaries or testes). Legal recognition of their assigned sex has been conferred by the appropriate official authorities CHT has been administered for a sufficient length of time to minimise gender-related advantages in sport competitions Eligibility should begin no sooner than 2 years after gonadectomy
National Collegiate Athletic Association (2011) [32]	To compete on a men's team, a transgender male individual must be taking CHT and have a diagnosis of gender dysphoria ^a . They are not allowed to play on a women's team Transgender female individuals must be taking CHT and have a diagnosis of gender dysphoria. They are not allowed to play on a men's team until they have completed 1 year of CHT A transgender male individual who is not taking CHT may participate on a women's or men's team A transgender female individual who is not taking CHT may not compete on a women's team	To compete on a men's team, a transgender male individual must be taking CHT and have a diagnosis of gender dysphoria. They are not allowed to play on a women's team Transgender female individuals must be taking CHT and have a diagnosis of gender dysphoria. They are not allowed to play on a men's team until they have completed 1 year of CHT A transgender male individual who is not taking CHT may participate on a women's or men's team A transgender female individual who is not taking CHT may not compete on a women's team
Rugby Football Union (UK; n.d.) [51]	IOC 2004 policy is adopted	IOC 2004 policy is adopted
Scottish Football Association (UK; 2008) [49]	IOC 2004 policy is adopted	IOC 2004 policy is adopted
The Football Association (UK; 2014) [44]	Under the age of 16 years, players may play with boys and girls (no GCS required)	Transgender male individuals: must have hormone results within a cisgender male range Undergone CHT for a sufficient amount of time Legal recognition of gender Transgender female individuals: undergone CHT or gonadectomy (removal of testes) Blood results must be within a cisgender female range Legal recognition of gender

Table 2 continued

Organisation	Pre-puberty	Post-puberty
UK Roller Derby Association (2014) [53]	No evidence of gender identity or hormone levels is required to participate Must be living full time as their chosen gender	No evidence of gender identity or hormone levels is required to participate Must be living full time as their chosen gender
US Rowing (2015) [35]	All rowers in men's events are male and all rowers in women's events are female	All rowers in men's events are male and all rowers in women's events are female
US Soccer Federation (2013) [34]	Gender is determined by legal recognition of gender Transgender people are asked to provide legal or another form of documentation to reflect that the athlete's gender identity is sincerely held and part of their core identity	Gender is determined by legal recognition of gender Transgender people are asked to provide legal or another form of documentation to reflect that the athlete's gender identity is sincerely held and part of their core identity
USA Gymnastics (2015) [33]	IOC 2004 policy is adopted	IOC 2004 policy is adopted
USA Senior Softball (2014) [36]	IOC 2004 policy is adopted	IOC 2004 policy is adopted
USA Triathlon (n.d.) [37]	Follows the US Anti-Doping Agency rules regarding the use of testosterone, which is a banned substance requiring a TUE to avoid violating policy	Follows the US Anti-Doping Agency rules regarding the use of testosterone, which is a banned substance requiring a TUE to avoid violating policy
USA Boxing (2013) [38]	IOC 2004 policy is adopted	IOC 2004 policy is adopted
USA Sailing (2013) [39]	IOC 2004 policy is adopted	IOC 2004 policy is adopted
USA Track and Field (2005) [40]	IOC 2004 policy is adopted	IOC 2004 policy is adopted
USA Swimming (2013) [41]	Discrimination against any member or participant on the basis of gender, sexual orientation and gender expression is prohibited	Discrimination against any member or participant on the basis of gender, sexual orientation and gender expression is prohibited
Women's Flat Track Derby Association (UK; n.d.) [52]	Transgender women are allowed to compete as a woman as long as their hormone levels are within a typical female range Information about healthcare provided must be submitted.	Transgender women are allowed to compete as a woman as long as their hormone levels are within a typical female range Information about healthcare provided must be submitted
World Outgames (USA; 2015) [42]	Transgender male individuals may not participate Transgender people are asked to provide legal or another form of documentation to reflect that the athlete's gender identity is sincerely held and part of their core identity	Transgender male individuals may not participate Transgender people are asked to provide legal or another form of documentation to reflect that the athlete's gender identity is sincerely held and part of their core identity

GCS gender-confirming surgery, CHT cross-sex hormone therapy, IOC International Olympic Committee, TUE therapeutic use exemption, n.d. no date

^a Gender dysphoria is the diagnostic name included within the *Diagnostic and Statistical Manual for Mental Disorders*, Fifth Edition, for people who experience an incongruence between their gender assigned at birth and gender identity [60]

gender-confirming surgery [18, 63–65]. Within this policy, there also appears a lack of an evidence-based rationale as to why a period of 2 years was chosen as the length of time cross-sex hormone treatment must be administered prior to sport competition and why individual differences in blood hormone levels are not considered [66]. As mentioned previously, the role of testosterone blockers in transgender women is also not considered. Although the rationale for the 2-year time period is not made explicit, it may be related to the fact that this time period was imposed by the IOC in 2004, when banning athletes from competitive sport to discipline them for doping violations. The evidence-based rationale for gender-confirming surgery is also not clear [61]; whether an athlete has a penis or vagina appears irrelevant, as this will not change the physiology of the body or the physiological advantage of the person [63].

Approximately 200 days before the 2016 Rio Olympic Games, the IOC announced changes to their competitive sport policy for transgender people. The new 2016 IOC [20] policy suggests that transgender male athletes are able to compete in a male category without any restrictions. Transgender female athletes may compete in a female category if they have declared their gender as female for at least 4 years and their blood testosterone levels are below 10 nmol/L for at least 12 months prior to competition. However, the latter requirement is a general guideline, and each case will be reviewed individually to determine whether 12 months is a sufficient amount of time to suppress testosterone levels to an appropriate level. If transgender female athletes do not meet these requirements, they will be able to compete in a male category. This is a great improvement in sport policy, which considers gender assigned at birth and individual difference in relation to bloody hormone levels and moves away from the requirement of surgery to compete in their experienced gender category. However, we could not find any evidence to support the requirement for testosterone levels to be below 10 nmol/L for at least 12 months.

Despite its flaws, the 2004 IOC policy [18] has been adopted by several other sport organisations. Within this systematic review, 11 sport organisations adopted the policy outlined by the IOC in 2004 [33, 36, 38–40, 45, 46, 48, 49, 51, 57]. All but one (the International Tennis Federation) of these sport organisation policies are employed at a national level. Not only is it problematic that other sport organisations adopted the 2004 IOC policy, but elements of the 2004 IOC policy concerning children pre-puberty are not applicable to sport organisations in the UK and many other countries. Within the UK (and many other countries), children presenting with gender incongruence cannot undergo gender-confirming surgery before the age of 18 years, by which time puberty has usually started.

Three policies stated that it is only necessary to provide legal recognition of gender and to be prescribed cross-sex hormone treatment for a ‘sufficient amount of time’ (international policy) [56] or so that hormone blood levels are within cisgender female or male ranges (national policy) [44, 52]. Policies from the National Collegiate Athletic Association [32] and British Rowing [50] also state that only cross-sex hormone treatment is required; however, the specifics of this requirement differ for both transgender male and female individuals. With both of these policies, transgender female individuals have to provide more evidence of cross-sex hormone treatment and their blood hormone levels in comparison to transgender male individuals. Similarly, the Association of Boxing Commissions [31] in its national policy has different cross-sex hormone treatment requirements depending on gender assigned at birth and how the athlete identifies themselves (transgender or transsexual). The language used within the Association of Boxing Commissions’ policy [31] may be seen as offensive by some transgender people and the difference between “transsexuals” and “transgender” people remains unclear. Policies held by the Ladies Professional Golf Association (international policy) [43] and the International Association of Athletics Federations [55] differ dramatically in relation to gender and gender-confirming surgery as a requirement. In both cases, it is necessary for transgender female individuals to have undergone this procedure, but not for transgender male individuals. Although some of the requirements of these policies are unreasonable and not evidence based (e.g. gender-confirming surgery), the gender difference in relation to the amount of evidence that is required about their gender change seems acceptable considering that only transgender female individuals (and not transgender male individuals) are currently seen to potentially have an athletic advantage [23].

The more inclusive sport policies reviewed here only required legal or medical recognition or do not ask for any evidence of gender; thus they encourage competition in line with the experienced gender (five were national policies and two were international) [34, 35, 41, 42, 53, 54, 59]. The Fédération Internationale de Volleyball [58] had the most invasive policy considered within this systematic review; they ask players to provide a birth certificate to verify gender. Additionally, female players may be asked to provide a gender certificate or submit themselves to a medical examination if the medical evidence is not sufficient. Both British Universities & Colleges Sport [47] and USA Triathlon [37] do not have their own policies, but suggest the adoption of other policies (i.e. those relevant to the sport in question or guidelines of the US Anti-Doping Agency, respectively).

Currently, the majority of sport policies unfairly exclude transgender people from competitive sport, as the

requirements they place on them are not underpinned by evidence-based medicine. Until (and if) there is consistent and direct evidence to demonstrate transgender people have an athletic advantage, it seems unreasonable to exclude them on any basis.

4 Discussion

The first aim of this systematic review was to explore the experiences of transgender people in relation to competitive sport participation (elite and recreational) and sport-related physical activity. The majority of the studies within this body of literature are qualitative in nature, which may be at least partly a reflection of the low numbers of transgender people in the general population. It is therefore difficult to draw any definite conclusions because of the lack of quantitative research. By its very nature, the findings from qualitative research cannot be generalised but the findings can be used to form a platform from which generalisations can be made. The research articles reviewed here described a generally negative experience of sport participation and sport-related physical activity for transgender individuals. It was evident from these studies that transgender people are facing barriers when engaging in competitive sport and sport-related physical activity. In relation to sport-related physical activity, lack of accessibility to an inclusive and comfortable environment appeared to be the primary barrier to participation. Charities and support organisations working with transgender people should consider developing campaigns to raise awareness about different gender identities. Leisure centres should also be made more aware of potential gender differences (i.e. via training and greater information provision) and be given advice on how to make such environments more inclusive of transgender people (e.g. gender neutral changing facilities with cubicles). In relation to competitive sport participation, the findings from this systematic review suggest that the requirements that transgender competitive sport policies place on competitors were instrumental in transgender athletes' negative experiences.

While a distinction needs to be made between the issues and experiences transgender people have with regard to participation in sport and competitive sport, it also needs to be acknowledged that there is an overlap. Transgender male and female individuals have anecdotally discussed that access to sport participation (such as becoming part of the local football team) is restricted as even community and local sport organisations who play at a recreational level implement transgender competitive sport policies.

The second aim was to review the available sport policies regarding the fairness for transgender people in

competitive sport (i.e. fairness in the absence of advantage). Owing to overinterpretation and fear of the athletic advantage in transgender athletes, the majority of the policies reviewed were discriminatory against transgender people, especially transgender male individuals (i.e. exclusion in the absence of advantage). Although the updated IOC policy may be perceived as more inclusive than the 2004 version, there are still flaws. The requirement for a transgender female individual to have declared their gender as female for at least 4 years is excessive. In the UK and many other countries, once a transgender person has accessed a transgender health service, it is likely to be less than 4 years before a person legally changes their name, undergoes irreversible treatments and, hence, fully commits to their experienced gender. There appears to be a lack of rationale regarding the 4-year time period for transgender athletes, although this time restriction is consistent with the current disciplinary action for cisgender athletes when a doping incident occurs [67]. The 2016 IOC policy [20] also states that to avoid discrimination against transgender female individuals, they are allowed to compete in a male category if they do not meet the requirements for transgender female athletes. For most transgender female individuals, competing in a male category, when their experienced gender is female, would be distressing and may deter engagement in competitive sport altogether. This particular requirement may be promoting exclusion of transgender female individuals in competitive sport, rather than avoiding discrimination.

Several sport policies, including the recently updated IOC 2016 [20] policy, have based their requirements for transgender competitors on indirect, inconsistent and unambiguous evidence. Physiological research involving cisgender people has shown that testosterone deficiency in young men is associated with a decrease in muscle strength [68] and testosterone injections in cisgender men are associated with an increase in some aspects of muscle strength [69]. However, this research did not determine whether these decreases and increases in muscle mass are within ranges for cisgender female and male individuals and the time required to reach cisgender male or female levels. Elbers et al. [70] expanded on this research by exploring the effects of oestrogen supplements and androgen deprivation on fat distribution and thigh muscle mass (by using magnetic resonance imaging) in 20 transgender female individuals. They found that 12 months after cross-sex hormone treatment, transgender female individuals had a more feminine pattern of adiposity and their thigh muscles had decreased. Other research has found that transgender female athletes who have hormonally and surgically transitioned have reported feeling weaker and their testosterone levels tend to be lower than average compared with cisgender women [19, 71]. However, this

research does not tell us anything about the relationship between androgenic hormones and athletic ability.

To date, Harper's study [72] is the only one to directly explore androgenic hormones and athletic ability. The aim of the study was to explore the long-distance (5–42 km) running times of eight transgender female individuals pre- and post-testosterone suppression. It was found that post-testosterone suppression running times were significantly slower in comparison to pre-testosterone suppression. Harper stated that owing to reductions in testosterone and haemoglobin, transgender female individuals post-transition would have the same endurance capabilities as a cisgender female individual. However, the sample size was very small ($n = 8$) and participants were asked to self-report their race times, which might have been subject to recall or social desirability bias.

On average, men perform better than women in sport; however, no empirical research has identified the specific reason(s) why. Based mainly on indirect research with cisgender people, it is commonly believed that androgenic hormones (specifically high testosterone levels) confer an advantage in competitive sports (i.e. enhance endurance, increase muscle mass) and, while this belief has informed several sporting policies, testosterone may not be the primary, or even a helpful, marker in determining athletic advantage [73]. Karkazis et al. [73] have argued that there is no evidence to suggest that endogenous testosterone levels are predictive of athletic performance (apart from doping), as there is variation in how bodies make and respond to the hormone. Testosterone is only one part of a person's physiology and there are other important factors (both biological and environmental) that should be considered if fairness (the absence of advantage) is the aim in competitive sport. For instance, having large hands is key for manipulation in some sports (e.g. basketball), but this is not seen as an unfair advantage. Establishing what an athletic advantage is in competitive sport would facilitate inclusion of all athletes (regardless of their gender identity) on the premise of fairness.

The Canadian Centre for Ethics in Sport [74] recently released a document offering guidance to sport organisations on how to develop inclusive competitive sport policies for transgender people. An expert panel maintained the viewpoint that everyone has the right to compete in accordance with their gender identity at a recreational and elite level. Cross-sex hormones and gender-confirming surgeries should not be a requirement at any level of sport. If any sport organisation requires transgender competitors to take cross-sex hormones for a specified time, they will have to provide evidence to support that this is reasonable. The panel suggests that when sporting organisations are concerned about safety, based on the size or strength of

competitors, such organisations should develop skill and size categories, such as in wrestling.

The issues and challenges that transgender people experience when engaging in competitive sport and sport-related physical activity will undoubtedly become more prominent as the visibility and prevalence of transgender people become more pronounced. Consequently, health professionals working in sport will need to become more familiar with the specific issues and challenges that a transgender person may experience when engaging in sport. By doing this, these professionals will be able to ensure transgender people can start or continue to engage in sport in a safe and inclusive manner. The most common question of people working within the sport domain will likely be: When it is safe and fair to permit a transgender person to compete in sport in line with their experienced gender? At the current time, this is a difficult issue to address considering that there is a lack of direct and consistent physiological performance-related data with transgender people, which is preventing a consensus from being made as to whether transgender people (especially transgender female individuals) do or do not have an athletic advantage. It may be sensible to suggest that until there are direct and consistent scientific data to suggest that transgender competitors have an advantage, transgender people should be allowed to compete in accordance with their gender identity with no restrictions (e.g. no requirement to have cross-sex hormones, gender-confirming surgery). The athletic advantage transgender female individuals are perceived to have (based on indirect and ambiguous evidence) may be no greater than widely accepted physiological (e.g. large hands) and financial (e.g. training opportunities) advantages that some cisgender people possess in competitive sport. Sport organisations wanting to exclude a transgender person from competing in their experienced gender category would need to demonstrate that the sport is gender affected and that exclusion is necessary for fair and safe competition [74, 75]. At the current time, this would be difficult considering there is no evidence to suggest that androgenic hormone levels consistently confer a competitive advantage [74, 75].

4.1 Limitations of the Area and Directions for Future Research

Within the area of sport, physical activity and transgender individuals, research is limited and mainly qualitative. More quantitative research needs to be conducted to increase the applicability and generalisability of the research findings and so that conclusions about transgender people and sport can be drawn. At a medical level, more physiological research is needed with the transgender

population to accurately determine whether transgender people have an advantage in competitive sport or not. Future studies should investigate when a person can be considered physiologically as their experienced gender. This in turn should aid more inclusive (i.e. inclusion in the absence of advantage) sport policies for transgender individuals and a fair system for all. To date, the few studies exploring the experiences of transgender people have mainly been concerned with exploring experiences in relation to competitive sport. This research now needs to be extended to those who participate in sport-related physical activity for leisure and fitness. It is also important to understand transgender people's experiences in the context of different sports. The barriers to, and facilitators of, football participation, for example, may greatly differ to those experienced when engaging in gymnastics, athletics, swimming or aquatic activities. For the latter four sports, clothing may be revealing and an indication of one's gender. For example, feeling comfortable in swimwear may be an issue for transgender people, especially when they are in the process of transitioning, as the body is often more exposed than in other sportswear (e.g. a football kit) and swimwear is heavily gendered (i.e. swimming trunks are worn by male individuals and swimming costumes by female individuals). In light of this, it would be interesting to explore the experiences of transgender people who have previously participated, or are currently participating, in aquatic activities, gymnastics and/or athletics.

5 Conclusion

Overall, it appears that the majority of transgender people have a negative experience of competitive sport and sport-related physical activities. Accessibility to sport-related physical activity needs to be improved. Within competitive sport, the athletic advantage transgender athletes are perceived to have appears to have been overinterpreted by many sport organisations around the world, which has had a negative effect on the experiences of this population. When the indirect and ambiguous physiological evidence is dissected, it is only transgender female individuals who are perceived to potentially have an advantage as a result of androgenic hormones. Within the literature, it has been questioned as to whether androgenic hormones should be the only marker of athletic advantage or, indeed, if they are even a useful marker of athletic advantage. Given the established mental and physical health benefits of engaging in physical activity and sport [13, 14], the barriers transgender people experience are a significant limitation to the promotion of healthy behaviours in transgender individuals. There are several areas of future research required to significantly improve our knowledge of transgender people's experiences in sport,

inform the development of more inclusive sport policies, and most importantly, enhance the lives of transgender people, both physically and psychosocially.

Acknowledgments We sincerely thank Prof. Barrie Houlihan for his helpful advice and feedback on an early draft of this systematic review.

Compliance with Ethical Standards

Funding Bethany Jones was supported by a PhD studentship co-funded by Leicestershire Partnership NHS Trust and Loughborough University. No other sources of funding were used to assist in the preparation of this article.

Conflict of interest Bethany Jones, Jon Arcelus, Walter Bouman and Emma Haycraft declare that they have no conflicts of interest relevant to the content of this review.

Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

References

1. Coleman E, Bockting W, Botzer M, et al. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, version 7. *Int J Transgend*. 2012;13:165–232.
2. Wylie K, Barrett J, Besser M, et al. Good practice guidelines for the assessment and treatment of adults with gender dysphoria. *Sex Relatsh Ther*. 2012;29:154–214.
3. Arcelus J, Bouman WP, Van De Noortgate W, et al. Systematic review and meta-analysis of prevalence studies in transsexualism. *Eur Psychiatry*. 2015;30(6):807–15.
4. Aitken M, Steensma TD, Blanchard R, et al. Evidence for an altered sex ratio in clinic-referred adolescents with gender dysphoria. *J Sex Med*. 2015;12(3):756–63.
5. De Vries ALC, Kreukels BPC, T'Sjoen G, et al. Increase of referrals to gender identity clinics: a European trend? In: *Transgender healthcare in Europe. Book of abstracts*. Ghent: European Professional Association of Transgender Health (EPATH); p. 10. Available from: <http://epath.eu/wp-content/uploads/2014/07/EPATH-2015-Book-of-Abstracts.pdf>. Accessed 6 Aug 2015.
6. Kuypers L, Wijzen C. Gender identities and gender dysphoria in the Netherlands. *Arch Sex Behav*. 2014;43(2):377–85.
7. Dooley S, Dawson M, Zak L, et al. "Bruce Jenner: 'I'm a woman'". 20/20/ABC News. Available from: <http://abcnews.go.com/Entertainment/bruce-jenner-im-woman/story?id=30570350>. Accessed 10 Jan 2016.
8. Bouman WP, de Vries AL, T'Sjoen G. Gender dysphoria and gender incongruence: an evolving inter-disciplinary field. *Int Rev Psychiatry*. 2016;28(1):1–4.
9. Claes L, Bouman WP, Witcomb GL, et al. Non-suicidal self-injury in trans people: associations with psychological symptoms, victimization, interpersonal functioning and perceived social support. *J Sex Med*. 2015;12(1):168–79.
10. Hill D, Willoughby B. The development and validation of the genderism and transphobia scale. *Sex Roles*. 2005;53(7):534–44.
11. Mizock L, Mueser KT. Employment, mental health, internalized stigma, and coping with transphobia among transgender individuals. *Psychol Sex Orientat Gend Divers*. 2014;1(2):146–58.

12. Ellis SJ, McNeil J, Bailey L. Gender, stage of transition and situational avoidance: a UK study of trans people's experiences. *Sex Relatsh Ther*. 2014;29(3):351–64.
13. De Moor MHM, Beem AL, Stubbe JH, et al. Regular exercise, anxiety, depression and personality: a population-based study. *Prev Med*. 2006;42(4):273–9.
14. Maltby J, Day L. The relationship between exercise motives and psychological well-being. *J Psychol*. 2001;135(6):651–60.
15. Dhejne C, Lichtenstein P, Boman M, et al. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. *PLoS One*. 2011;6(2):e16885.
16. Hepp U, Kraemer B, Schnyder U, et al. Psychiatric comorbidity in gender identity disorder. *J Psychosom Res*. 2005;58(3):259–61.
17. Beek TF, Kreukels BPC, Cohen-Kettenis PT, et al. Partial gender request and underlying motives of applicants for gender affirming interventions. *J Sex Med*. 2015;12(11):2201–5.
18. International Olympic Committee. IOC approves consensus with regard to athletes who have changed sex. Available from: <http://www.olympic.org/content/news/media-resources/manual-news/1999-2009/2004/05/17/ioc-approves-consensus-with-regard-to-athletes-who-have-changed-sex/>. Accessed 15 Aug 2015.
19. Cavanagh S, Sykes H. Transsexual bodies at the Olympics: the International Olympic Committee's policy on transsexual athletes at the 2004 Athens summer games. *Body Soc*. 2006;12(3):75–102.
20. International Olympic Committee. IOC consensus meeting on sex reassignment and hyperandrogenism. Available from: http://www.olympic.org/Documents/Commissions_PDFfiles/Medical_commission/2015-11_ioc_consensus_meeting_on_sex_reassignment_and_hyperandrogenism-en.pdf. Accessed 1 Feb 2016.
21. Reeser JC. Gender identity and sport: is the playing field level? *Br J Sports Med*. 2005;39(10):695–9.
22. Moher D, Liberati A, Tetzlaff J, et al. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2006;6(7):e1000097.
23. Gooren L, Bunck M. Transsexuals and competitive sports. *Eur J Endocrinol*. 2005;151(4):425–9.
24. Hargie OD, Mitchell DH, Somerville IJ. "People have a knack of making you feel excluded if they catch on to your difference": transgender experiences of exclusion in sport. *Int Rev Sociol Sport*. 2015. doi:10.1177/1012690215583283 (Epub Apr 22 2015).
25. Caudwell J. [Transgender] young men: gendered subjectivities and the physically active body. *Sport Educ Soc*. 2012;19(4):1–17.
26. Cohen J, Semerjian T. The collision of trans-experience and the politics of women's ice hockey. *Int J Transgend*. 2008;10(3):133–45.
27. Semerjian TZ, Cohen JH. "FTM means female to me": transgender athletes performing gender. *Women Sport Phys Act J*. 2006;15(2):28.
28. Tagg B. Transgender netballers: ethical issues and lived realities. *Sociol Sport J*. 2012;29(2):151–67.
29. Travers A, Deri J. Transgender inclusion and the changing face of lesbian softball leagues. *Int Rev Social Sport*. 2011;46(4):488–507.
30. Muchicko MM, Lepp A, Barkley JE. Peer victimization, social support and leisure-time physical activity in transgender and cisgender individuals. *Leisure*. 2014;38(3–4):295–308.
31. The Association of Boxing Commissions. Health and safety of combat sports participants. Available from: http://media.wix.com/ugd/2bc3fc_a78ffb4eca2e4f07a122c990005f77dd.pdf. Accessed 16 Aug 2015.
32. National Collegiate Athletic Association. NCAA inclusion of transgender athletes handbook. Available from: http://www.ncaa.org/sites/default/files/Transgender_Handbook_2011_Final.pdf. Accessed 15 Aug 2015.
33. USA Gymnastics. USA gymnastic policy for transgender inclusion. Available from: http://media.wix.com/ugd/2bc3fc_2a79ff51fb2f40a6ac0c1ad4a2493543.pdf. Accessed 16 Aug 2015.
34. US Soccer Federation. USSF policy amendments change. Available from: http://media.wix.com/ugd/2bc3fc_d4601f281da449648ca4c60d0d81a526.pdf. Accessed 15 Aug 2015.
35. US Rowing. The rules of rowing. Available from: http://media.wix.com/ugd/2bc3fc_63894095ad33464bb3a00fdbaf7cc0a7.pdf. Accessed 16 Aug 2015.
36. USA Senior Softball. SSUSA official rulebook. Available from: http://media.wix.com/ugd/2bc3fc_ac2d2cc75887442cb8f310be9e987fc1.pdf. Accessed 16 Aug 2015.
37. USA Triathlon. Employs the United States Anti-Doping Agency policy. Available from: <http://www.usada.org/>. Accessed 16 Aug 2015.
38. USA Boxing. Medical handbook and medical rules of AIBA open boxing. Available from: http://media.wix.com/ugd/2bc3fc_097c27dfc6784e9eb89d7c5ab44dd399.pdf. Accessed 15 Aug 2015.
39. USA Sailing. USA Sailing bylaws. Available from: http://media.wix.com/ugd/2bc3fc_495cfbb7bb0240029f5aa1851b0e99a1.pdf. Accessed 16 Aug 2015.
40. USA Track and Field. Adopted the IOC policy. Available from: <http://www.olympic.org/news>. Accessed 15 Aug 2015.
41. USA Swimming. USA anti-discrimination policy. Available from: <http://www.swimmingworldmagazine.com/news/usa-swimmings-anti-discrimination-policies-include-sexual-orientation-gender-expression/>. Accessed 15 Aug 2015.
42. World Outgames. World Outgames Miami 2017 gender identification policy. Available from: http://media.wix.com/ugd/2bc3fc_7b1ae1602497400397ff125e25aa7036.pdf. Accessed 23 Jan 2016.
43. Ladies Professional Golf Association. Policy on transgender golfer participants. Available from: <http://www.lpga.com/>. Accessed 16 Aug 2015.
44. The Football Association. Policy on trans people in football: policy document. Available from: <http://www.thefa.com/football-rules-governance/equality/lgbt-football>. Accessed 16 Aug 2015.
45. The Lawn Tennis Association. Transgender policy. Available from: <http://www.lta.org.uk/about-the-lta/policies-and-rules/transgender-policy/>. Accessed 16 Aug 2015.
46. Badminton England. Policy and procedures on transsexual people playing in Badminton competitions. Available from: http://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCQQFjAA&url=http%3A%2F%2Fwww.badmintonengland.co.uk%2Fcore%2Fcore_picker%2Fdownload.asp%3Ffid%3D14949&ei=7sqSVbHKO-b67AaI_ZCIAQ&usq=AFQjCNGLaRfFodpT2mkeVsKBclhg8e7P-g. Accessed 15 Aug 2015.
47. British Universities & Colleges Sport. Transgender policy. Available from: http://c1593.r93.cf3.rackcdn.com/BUCS_Transgender_Policy.pdf. Accessed 16 Aug 2015.
48. Amateur Swimming Association. Trans competitors. Available from: <http://www.swimming.org/asa/about-us/policy-documents/swimming-policy1/9479>. Accessed 15 Aug 2015.
49. Scottish Football Association. Transgender and transsexual policy. Available from: <http://www.scottishfa.co.uk/scottish-football.cfm?page=3325>. Accessed 15 Aug 2015.
50. British Rowing. Transgender and transsexual policy. Available from: http://media.wix.com/ugd/2bc3fc_067aff13c7444fd4b223035aa4f82e0d.pdf. Accessed 15 Aug 2015.
51. Rugby Football Union. RFU transgender and transsexual policy. Available from: http://media.wix.com/ugd/2bc3fc_2c8d17994bdb4da897d36c77415935cb.pdf. Accessed 16 Aug 2015.
52. Women's Flat Track Derby Association. Gender policy. Available from: <https://wftda.com/wftda-gender-statement>. Accessed 15 Aug 2015.

53. UK Roller Derby Association. UKRDA transgender policy. Available from: <http://ukrda.org.uk/2014/04/ukrda-transgender-policy/>. Accessed 15 Aug 2015.
54. Disability Sport Australia. Member protection policy. Available from: http://media.wix.com/ugd/2bc3fc_63bb33953f554b7ab0fabfdde502d83d.pdf. Accessed 16 Aug 2015.
55. International Association of Athletics Federations. IAAF regulations governing eligibility of athletes who have undergone sex reassignment to compete in women's competition. Available from: http://media.wix.com/ugd/2bc3fc_476cfbfe00df48c3aa5322a29d5e11b2.pdf. Accessed 15 Aug 2015.
56. International Gay and Lesbian Football Association. IGALF transgender policy. Available from: http://media.wix.com/ugd/2bc3fc_76b96547c2904a27a928165800a11698.pdf. Accessed 15 Aug 2015.
57. International Tennis Federation. Transgender policy. Available from: http://media.wix.com/ugd/2bc3fc_cd8f3b2a4e134a5f96ddab8361570add.pdf. Accessed 16 Aug 2015.
58. Fédération Internationale de Volleyball. Sports regulations. Available from: http://media.wix.com/ugd/2bc3fc_d72b0af75a4840ac8e27a424e7e94691.pdf. Accessed 15 Aug 2015.
59. International Quidditch Association. US Quidditch Association rule book, ninth edition. Available from: https://www.usquidditch.org/files/USQ_Rulebook_9.pdf. Published 2015. Accessed 15 Aug 2015.
60. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013.
61. Carroll JH. The inclusion of transgender students in United States school-based athletics. In: Hargreaves J, Anderson E, editors. Routledge handbook of sport, gender and sexuality. London and New York: Routledge; 2014. p. 367–75.
62. Teetzel S. On transgendered athletes, fairness and doping: an international challenge. *Sport Soc.* 2006;9(2):227–51.
63. Lucas-Carr BC, Krane V. What is the T in LGBT? Supporting transgender athletes through sport psychology. *Sport Psychol.* 2011;25(4):532–48.
64. Pieper LP. Gender regulation: Renée Richards revisited. *Int J Hist Sport.* 2012;29(5):675–90.
65. Sykes H. Transsexual and transgender policies in sport. *Women Sport Phys Act J.* 2006;15(1):3–13.
66. Sullivan CF. Gender verification and gender policies in elite sport: eligibility and “fair play”. *J Sport Social Iss.* 2011;35(4):400–19.
67. The International Olympic Committee. Anti-doping rules applicable to the Games of the XXXI Olympiad, in Rio de Janeiro, in 2016. Available from: <https://www.wada-ama.org/en/resources/world-anti-doping-program/ioc-anti-doping-rules-rio-2016-olympic-games>. Accessed 17 June 2016.
68. Mauras N, Hayes V, Welch S, et al. Testosterone deficiency in young men: marked alterations in whole body protein kinetics, strength, and adiposity. *J Clin Endocrinol Metab.* 1998;83(6):1886–92.
69. Storer TW, Magliano L, Woodhouse L, et al. Testosterone dose-dependently increases maximal voluntary strength and leg power, but does not affect fatigability or specific tension. *J Clin Endocrinol Metab.* 2003;88(4):1478–85.
70. Elbers JMH, Asscheman H, Seidell JC, et al. Effects of sex steroid hormones on regional fat depots as assessed by magnetic resonance imaging in transsexuals. *Am J Physiol Endocrinol Metab.* 1999;276(2):317–25.
71. Schultz J. Caster Semenya and the “question of too”: sex testing in elite women's sport and the issue of advantage. *Quest.* 2011;63(2):228–43.
72. Harper J. Race time for transgender athletes. *J Sporting Cult Identities.* 2015;6:1–9.
73. Karkazis K, Jordan-Young R, Davis G, Camporesi S. Out of bounds? A critique of the new policies on hyperandrogenism in elite female athletes. *Am J Bioeth.* 2012;12(7):3–16.
74. Canadian Centre for Ethics in Sport. Creating inclusive environments for trans participants in Canadian sport. Available from: <http://cces.ca/sites/default/files/content/docs/pdf/cces-transinclusion-policyguidance-e.pdf>. Accessed 15 June 2016.
75. House of Commons. Transgender Equality Inquiry: first report of session 2015–16. London: The Stationery Office Limited. Available from: <http://www.publications.parliament.uk/pa/cm201516/cmselect/cmwomeq/390/39002.htm>. Accessed 1 Jan 2016.

ENDOCRINE PRACTICE Rapid Electronic Article in Press

Rapid Electronic Articles in Press are preprinted manuscripts that have been reviewed and accepted for publication, but have yet to be edited, typeset and finalized. This version of the manuscript will be replaced with the final, published version after it has been published in the print edition of the journal.

The final, published version may differ from this proof.

DOI:10.4158/EP161727.OR

© 2017 AACE.

Original Article

EP161727.OR

**PREVALENCE AND TYPES OF GENDER-AFFIRMING SURGERY AMONG A SAMPLE OF
TRANSGENDER ENDOCRINOLOGY PATIENTS PRIOR TO STATE EXPANSION OF INSURANCE
COVERAGE**

Maya Kailas, BA¹; Hsun Ming Simon Lu, MD¹; Emily F. Rothman, ScD²

Joshua D. Safer, MD, FACP¹

Running title: Prevalence of Gender-Affirming Surgery

From: ¹ Center for Transgender Medicine and Surgery, Boston Medical Center and Section of Endocrinology, Diabetes, and Nutrition, Boston University School of Medicine, Boston, MA, USA; ² Boston University School of Public Health, Department of Community Health Sciences

Corresponding author: Joshua D. Safer

Boston University School of Medicine

Section of Endocrinology, Diabetes, and Nutrition,

715 Albany Street, Room M-1016

Boston MA 02118.

E-mail: jsafer@bu.edu

DOI:10.4158/EP161727.OR

© 2017 AACE.

Word count: 3207

Keywords: Transgender, Hormone Therapy, Gender Confirmation Surgery, Gender Affirmation Surgery

Acknowledgements and Disclosures: Nothing to declare

Abstract

Objective: Transgender individuals now have many options for medical intervention, including gender affirmation surgeries. However, it is unknown how common it is for transgender individuals to undergo these surgeries. The purpose of this cross-sectional study was to assess the prevalence of gender affirming surgeries among transgender patients in 2015, which was immediately prior to insurance changes that made gender affirming surgery more affordable for Massachusetts residents.

Design: A retrospective chart review of 99 transgender patients was performed at the Endocrinology Clinic at Boston Medical Center, an urban safety net hospital.

Patients: 99 transgender subjects who received treatment between 2004-2015, including 28 transmen and 71 transwomen.

Measurements: The outcome measures were the types of medical interventions chosen by transgender patients, which included hormone therapy, chest surgery, gonadectomy, genital surgery, and facial surgery.

Results: 35% of subjects had undergone at least one gender affirming surgery. Transmen were more likely to have had surgery than transwomen (54% vs. 28%). 25% of patients had chest surgery, 13% had genital surgery or gonadectomy, and 8% had facial surgery.

Conclusions: In 2015 a majority of transgender endocrinology clinic patients had not undergone any type of gender affirmation surgery. Among those who did elect to have a surgery, genital surgery or gonadectomy were uncommon. The low rate of surgery among this sample of transgender patients may be attributable to the financial cost, lack of interest in surgery, or that genital surgery is not a high priority for transgender individuals relative to surgery to change visible features such as face and chest.

Abbreviations:

HT = Hormone Therapy, **BMC** = Boston Medical Center, **TAH-BSO** = total hysterectomy and bilateral salpingo-oophorectomy, **U.S.** = United States, **SD** = Standard Deviation.

Introduction

Transgender individuals are those with gender identity different from external sexual anatomy at birth. Studies show that 0.6% of the adult population in the United States identify as transgender.¹ Many transgender individuals wish to undergo hormone therapy (HT) and/or gender affirmation surgery to make their bodies match their gender identities. Gender affirmation surgeries include chest reconstruction (*i.e.*, mammoplasty, mastectomy, breast augmentation),

external genital surgeries and gonadectomies (*i.e.*, hysterectomy, oophorectomy, orchidectomy, penectomy, vaginoplasty, clitoroplasty, labioplasty, phalloplasty, penile-scrotal reconstruction), facial surgeries (*i.e.*, facial feminization), and variations on them.^{2,3}

Although gender affirmation surgeries are not new, accessibility to these surgeries, particularly genital surgeries, have increased over the last 10 years and the average age at which transgender people seek genital surgery has fallen.⁴⁻⁶ However, there are limited data regarding the prevalence of surgical procedures among transgender individuals in the United States and there are presently no nationally-representative datasets from well-defined cohorts that would permit inferences about the proportions of U.S. transmen or transwomen* who elect to have gender-affirming surgery.

The US Transgender Survey is the nation's largest survey on transgender health, and it includes data on prevalence of surgery.⁷ A weakness of the US Transgender Survey despite the large sample size (about 28,000 transgender and gender non-binary informants) is that the percentage of transgender individuals who choose to participate in the survey is unknown, making it difficult to determine the representativeness of the survey and the generalizability of the results.

In the absence a large-scale defined cohort to provide representative data, clinic-based data can provide the field with benchmark data about the commonality of gender-affirming surgery in defined population of transgender patients.

Estimating the proportion of transgender patients who elected to get gender-affirming surgery in Massachusetts prior to 2015 is important because as of January 2015 the state issued

* The terms "transmen" and "transwomen" are used instead of the terms "Female-to-male" and "Male-to-female" in order to be consistent with the most recently published transgender medicine research studies.

guidance for private insurers that advised them that the denial of coverage for medically necessary care related to gender transition would be unlawful, and the Massachusetts Medicaid program also instituted a new policy that made clear that gender-affirming surgeries will be covered if determined to be medically necessary.⁸ We speculate that there may now be an increase in gender-affirming surgeries in Massachusetts as a result of the insurance policy change. Establishing the prevalence of surgery prior to the policy change could be important for other states considering similar policy changes and attempting to forecast transgender healthcare service delivery needs.

Methods

Study Design.

This was a retrospective medical chart review study. Data were abstracted from the electronic medical records of 99 patients of the Endocrinology Clinic at Boston Medical Center who received outpatient transgender medical care between 2004-2015. All patients were seen by one male physician, who is a primary provider of transgender healthcare at Boston Medical Center, in addition to various endocrinology fellows who trained at BMC throughout the years of the study, (fellows' gender breakdown: approximately 80% female, 20% male). The study was approved by the Institutional Review Board for the Boston University Medical Campus.

Procedures.

All transgender patients in the Endocrinology Clinic are routinely asked for their consent for their de-identified medical records to be analyzed for research purposes. Of the 104 patients approached in 2015, 95% (99) provided consent. Data was abstracted by a trained research

assistant who had access to the patients' de-identified medical records. Data were analyzed in Excel.

Sample.

The analytic sample included 99 patients, 28% transmen (female-to-male) and 71% transwomen (male-to-female). Patients' mean age was 42 years old, and patients' ages ranged from 20 to 73 years old. Of the 99 patients, all but three were on hormone therapy (HT); reasons why patients were not on HT were that one transmen was trying to get pregnant, one transwoman was still contemplating HT, and one patient required further medical evaluation before hormones could be prescribed.

Results

Surgery prevalence

Overall, 35% of all transgender patients had had at least one gender affirming surgical intervention in their lifetimes. Twenty-five percent (n=25) had one or more surgical interventions in the chest area, and 13% (n=13) had surgical interventions in the genital area. Eight percent (n=8) had facial plastic surgery, and all of these were transwomen who had facial feminization surgery.

Surgery prevalence among transmen

Of the 28 transmen subjects, 54% had a transgender surgical intervention, and 28% had surgery in both chest and genital areas (Table 1). Fifty percent (n=14) of transmen had had chest reconstruction surgery. All of the chest surgeries were reductive mammoplasty of some sort.

These surgeries included bilateral mastectomies and bilateral breast reductions. Fourteen percent (n=4) of transmen had surgery in the genital area. Among the four transmen who had genital surgeries, two had total hysterectomies and bilateral salpingo-oophorectomies (TAH-BSO), one had a penile implant with urethral lengthening and implanted clitoral stimulator, and one had an unspecified type of genital surgery. There were two additional transmen who had hysterectomies for endometriosis prior to other transgender medical intervention, but these were not included in our calculation of gender affirming surgery prevalence. Zero transgender men had facial plastic surgery of any kind. Transmen were almost twice as likely as transwomen to have had any gender affirming surgery (Table 1). The average age at first surgery for transmen was 33.6 years (range 20-70). The median year of chest surgery was 2012, and the median year for genital surgery or gonadectomy was 2007.

Surgery prevalence among transwomen

Of the 71 transwomen in this study, 27% had transgender surgical intervention (Table 1). Four had surgeries in both the chest and genital area. Among transwomen 17% (n=12) had chest reconstruction surgery. All of the chest reconstruction surgeries were breast augmentations with implants, except for one transwoman who preferred her chest to be male-appearing and pursued a bilateral breast reduction due to gynecomastia from her HT. Thirteen percent (n=9) of transwomen had at least one surgical intervention in the genitourinary tract. Among these nine transwomen, four of them had bilateral orchiectomy without further reconstruction. One individual had both an orchiectomy and a penectomy without further reconstruction. Two had documented vaginoplasties. Two had unspecified genital surgery. Eleven percent (n=8) of transwomen had facial plastic surgery. Transwomen were almost three times less likely to have

had chest or top surgery as compared to transmen, and were significantly older than transmen when they had their first procedure (34 years vs. 45 years) (Table 1). The average age at first surgery for transwomen was 44.7 years (range 27-60). The median year of chest surgery was 2015, genital surgery or gonadectomy was 2006, and the median year of facial surgery was 2014.

Desire for Surgery

24% of patients in this sample (24 patients) desired surgery/additional surgery and were either in pursuit of it or were unable to receive it for various reasons. Of these 24, 5 were transmen and 19 were transwomen. Four patients reported that they were unable to receive surgery due to cost or lack of insurance coverage. Of the five transmen who wanted surgery but had not had it, all five wanted chest surgery. Two explicitly said they did not want genital surgery or gonadectomy. Of the 19 transwomen, 4 wanted chest reconstruction, 15 wanted surgery in the genital area, and 3 wanted facial surgery. We do not know the exact types of chest, genital, or facial surgeries that the patients desired.

Discussion

To our knowledge, this is the first paper to calculate the percentage of hormone treated patients who had ever had a gender affirming surgery in a U.S. clinic-based sample of transgender individuals, and to characterize the nature of those surgeries by gender. Only a minority of transgender patients receiving HT ever had gender affirming surgery (35%), and of these a small minority had undergone any type of surgery in the genital area as opposed to chest or facial surgery. These data are useful to the field for two reasons. First, estimates of the

percentage of transgender patients who have had surgery from clinical samples provide helpful benchmark prevalence rates until nationally-representative data are available, and permit comparisons with other characterizations of transgender patients from similar clinical samples elsewhere.⁶ Second, this study analyzed medical records that accumulated over an eleven-year period, with a study endpoint that coincided with a major change in state policy increasing insurance coverage for gender affirming surgery. Documenting the rates and types of surgeries that transgender patients had undergone up to the point of the policy change can be used for comparisons in the future. Additionally, with the current changing political climate, there may be further changes in health insurance in the coming years. Although it is unclear what impact this may have on transgender care, it will be interesting to see if and how rates of transgender surgery change with the coming policy changes.

Our results align with the 2015 US Transgender Survey. They similarly found that more transmen had undergone surgery than transwomen (42% and 28% respectively). Additionally, they similarly found that in transmen genital surgery or gonadectomy was less prevalent than chest surgery (36% chest surgery, 14% hysterectomy, and 3% phalloplasty). They also found that among transwomen, rates of chest surgery and genital surgery or gonadectomy were more similar (11% chest, 11% orchiectomy, and 12% vaginoplasty), which is also consistent with our findings.⁷

In addition, our results are in concordance with those of one prior endocrinology clinic study of transgender patients from Northern Ireland, which found that 73% of their patient population were transwomen and 27% were transmen, and that fewer than 10% of patients had ever had genital gender affirmation surgery.⁶

Our findings are also quite similar to those from a non-representative self-report survey among a convenience sample of Canadian and U.S. transmen conducted in 2005 that found that 43% had chest surgery and 18% had genital surgery.⁹ Finally, a 2010 non-representative self-report survey of French and Belgian transgender advocacy organization members or healthcare patients, of which 85% were HT patients, found that 30% had ever had genital surgery.² The relatively narrow range in findings across these studies bolsters confidence in the potential generalizability of our results to transgender HT patients in U.S. urban areas.

Our study found that the majority of transgender patients who elected to have surgery had breast surgery (71%) and that relatively few had genital surgery, gonadectomy, or facial surgery. The medical literature has tended to focus predominantly on the effects of genital gender affirmation surgery as an important (and at some periods in history, necessary) element of transgender medical intervention. However, our findings that few patients have opted for genital surgery are consistent with prior studies of body dissatisfaction in transgender individuals, which have found that transwomen may care most about their outward appearance, including the appearance of their hair and sound of their voice, and that transmen prioritize altering muscularity and posture.^{10, 11} Further, although facial feminization surgery is often neglected as a consideration by other studies, by policy makers and by medical providers, our study found interest in facial feminization surgery among transwomen to be similar to interest in genital surgery.

Further, all of the transmen in our sample who desired surgery but had not had it wanted chest surgery only, and two explicitly stated that they were not interested in genital surgery. This also supports the idea that public appearance may be the main priority. The higher rate of chest

surgery among transmen may be partly attributable to the fact that there are continued complications and revisions necessary for the neo-phallus relative to the fewer concerns for orchiectomy and vaginoplasty for trans women. Also, more surgeons may be comfortable performing chest surgeries than the more complex genital reconstruction surgeries. If this is the case, perhaps the rates of genital surgery among transmen would increase with improvements in this procedure. In addition, our study found that transmen were more likely to have undergone surgery than transwomen (54% vs. 28%). There are data to show that transmen may have a better quality of life following gender affirming surgery than transwomen.¹² This idea might push more transmen towards surgery than transwomen.

Cost may be another factor pushing people more toward chest surgery. Although specific costs vary, the surgeries alone can cost \$30,000 for genital reconstruction surgery for transgender women, double that or more for transgender men, and a third or less for chest reconstruction surgeries. However, it is interesting to note that of the transwomen who desired surgery but had not received it, the majority wanted genital surgery or gonadectomy (80%). It would be interesting to explore the reasons for this. It may be because many of them already had chest surgery and felt that genital surgery or gonadectomy is the next step, or there may be more barriers to getting genital surgery than chest surgery.

One potential implication of our findings is that physicians training in transgender medicine should not focus exclusively or disproportionately on genital affirmation surgery-related issues, but should be provided comprehensive education about the unique needs of transgender patients who may opt for HT or chest surgery alone.

It is noteworthy that in an era with poor insurance coverage, even among transgender patients who sought out medical treatment, only one-third had gender affirmation surgery. It remains to be seen if the relative cost of surgical intervention versus medical intervention was a significant factor in the low rate of surgery. We know that 24 patients in this sample desired a surgery that they had not yet received for various reasons. At least four of these were due to cost or lack of insurance coverage, however we do not know if there were more with similar issues. If cost of surgery was, in fact, a large factor contributing to the low rate of surgery, a major increase in transgender individuals opting for surgical interventions may take place in the immediate future because of the new financial access created by better insurance coverage.

Alternatively, if the surgical rate does not increase, it might confirm that surgery in the genitourinary tract is not as much of a priority to transgender medicine patients as members of the public or medical workforce might imagine. Boston Medical Center provides care to a largely underserved population, with approximately 59% of patients receiving Medicaid, Medicare, and other assisted or subsidized health insurance plans. At the time of this data collection, government-funded insurance plans were not required to cover gender-affirming surgeries.^{13, 14} Therefore, the effect of changes in insurance coverage of gender-affirming surgeries may be particularly evident in this population.

Recent advances in the social acceptance of transgender people may have had two competing effects on the rates of gender affirmation surgery. On the one hand, because there are an increasing number of transgender medicine providers, improving insurance coverage, and less social stigma, more individuals may opt to get surgery. On the other hand, because there is more social awareness of gender diversity and better social acceptance of individuals with non-

conforming bodies and identities, transgender people may not feel that it is essential for their bodies to match their gender identities in order to be socially integrated and supported.

The reason why none of the transmen in the sample had any facial plastic surgeries, but 11% of the transwomen did could be that testosterone has a virilizing effect, producing more masculine facial features and making the need for facial surgery less important. Moreover, it is difficult to reverse the already virilized facial features of transwomen presenting for HT. Additionally, there tends to be more societal acceptance of feminine-appearing men as opposed to masculine-appearing women.^{15, 16} Transmen may be so well passing, that they may not even seek hormone therapy in the first place, especially if there are additional barriers (cost, access, etc.). The fact that, in general, transmen may experience easier and smoother transitions because feminine-appearing men are more likely to be socially accepted than masculine-appearing women could also explain the 3:1 ratio of transwomen to transmen seeking medical intervention from the clinic. Another reason for this could be that transmen are more comfortable seeking a female doctor as opposed to male, as the primary provider in this study was male.

The average age for transwomen undergoing gender affirming surgery was past mid-life: 54 years of age. This finding could be explained by increased financial security later in life that allowed these individuals to undergo surgery. It could also be explained by the advent of safer and less drastic procedures in more recent years.³

There are many reasons transgender people may not undergo gender affirmation surgery, including barriers such as access to care, mistrust of the medical system which historically has been discriminatory towards transgender people, fears about the risks of surgery, limitations on time and energy, concern about a loss of sexual function, lack of knowledge about surgery, and a

degree of satisfaction in one's own body.¹⁷⁻²¹ Above all, the cost of gender affirmation surgery has been prohibitive for many individuals.²² As of January 2015 Massachusetts interpreted the reversal of the Medicare ban on transgender care, in combination with existing Massachusetts law protecting transgender individuals, to mean that transgender care is obligatory for all payers.²³ Further, under the Affordable Care Act of 2012, US insurance companies cannot exclude transition-related care altogether from their coverage plans.²³ We may expect to see the number of such surgeries increase in the wake of the insurance policy changes. However, because our ideas about why people may or may not elect to undergo gender affirmation surgery are conjecture, further research into the specific factors that drive people to seek surgery itself and the specific surgeries they choose is needed.²⁴

This study is subject to at least two limitations. First, it utilized a convenience sample and is therefore not representative of all transgender HT patients. The patients at this particular endocrinology clinic may have been more likely to be underinsured than transgender medicine patients in general, because the hospital is an urban safety net hospital, and therefore less likely than average to seek surgical procedures. On the other hand, patients at this clinic may have been more motivated to engage in gender affirmation surgery than transgender people in some other parts of the United States because there is a relatively well-established and visible transgender community in Boston. Second, there were several patients for whom data on previous surgeries were unclear. This highlights the importance of healthcare providers asking about past medical and surgical histories and documenting it in medical records, even when the subject matter can be sensitive. It should also be noted that this sample contained more data from transwomen than transmen, in a ratio of approximately 3:1. The ratio of transwomen to

transmen in our sample is comparable to that found in other clinical studies,²⁵ but future research should investigate if transwomen are disproportionately likely to seek medical care for transgender health issues.

Additionally as we have noted, although the US Transgender Survey is the nation's largest survey on transgender health and it includes data on prevalence of surgery, the percentage of transgender individuals who choose to participate in the survey is unknown, making it difficult to determine the representativeness of the survey and the generalizability of the results. An advantage of our more defined cohort is that the results can be generalized to patients who seek services from a large, metropolitan hospital endocrinology clinic.

In conclusion, we show that in 2015 the majority of transgender patients seeking gender-affirming care had not undergone any type of gender affirmation surgery. Furthermore, among those who did undergo surgery, only a small minority elected to undergo any type of surgery in the genital area. Reasons for this may include cost, lack of interest, or prioritizing outward appearance. With the advent of both better insurance coverage and greater acceptance in society, it will be interesting to see how the prevalence of gender-affirming surgery may change in the future.

Table 1. Descriptive characteristics of transgender medicine patients, by gender

	All patients	Transmen	Transwomen
Total	100% (99)	28% (28)	72% (71)
<u>Age (mean, SD)</u>			
Mean, SD	42.3, 14.7	35.9, 14.0	44.9, 14.4
Range	20-73 years	20-73 years old	21-69 years old
<u>Current Hormone Treatment (HT)</u>			
Yes	97% (96)	96% (27)	97% (69)
No	3% (3)	4% (1)	3% (2)
<u>History of gender affirming surgery[†]</u>			
Yes	35% (35)	54% (15)	28% (20)
No	65% (65)	46% (13)	72% (51)
<u>Type of surgery</u>			
<u>Chest or top surgery (n=25)</u>	<u>25% (25)</u>	<u>50% (14)</u>	<u>17% (12)</u>
Breast augmentation	40% (10)	0% (0)	91% (10)
Breast reduction	8% (2)	7% (1)	9% (1)
Mastectomy	48% (12)	86% (12)	0% (0)
Unspecified type	8% (2)	7% (1)	9% (1)
<u>Genital or bottom surgery (n=13)</u>	<u>13% (13)</u>	<u>14% (4)</u>	<u>13% (9)</u>
Orchiectomy	33% (5)	0% (0)	56% (5)
Vaginoplasty	13% (2)	0% (0)	22% (2)
Penectomy	7% (1)	0% (0)	11% (1)
Unspecified type	20% (3)	25% (1)	22% (2)
Penile implant	7% (1)	25% (1)	0% (0)
TAH SBO*	13% (2)	50% (2)	0% (0)
<u>Facial surgery</u>	8% (8)	0% (0)	11% (8)
<u>Age at first procedure</u>			
Mean	38.7	33.6	44.7
Range	20-70 yrs.	20-70 yrs.	27-60 yrs.
<u>Year of procedure (median)</u>			
Chest or top surgery	2012	2012	2015
Genital or bottom surgery	2007	2007	2006
Facial surgery	2014	N/A	2014
<u>Desire for (more) surgery (n=24)</u>			
Total	24% (24)	18% (5)	27% (19)
Chest or top surgery	83% (20)	100% (5)	21% (4)
Genital or bottom surgery	17% (4)	0% (0)	80% (15)
Facial surgery	13% (3)	0% (0)	16% (3)

*total abdominal hysterectomy with salpingo-oophorectomy; † some patients had more than one surgery so counts do not sum

References

1. **Flores AR, Herman JL, Gates GJ, Brown TNT.** (2016). How Many Adults Identify as Transgender in the United States? Los Angeles, CA: The Williams Institute.
2. **Giami A, Beaubatie E.** Gender identification and sex reassignment surgery in the trans population: A survey study in France. *Archives of sexual behavior*. 2014;1;4:1491-501.
3. **Wroblewski P, Gustafsson J, Selvaggi G.** Sex reassignment surgery for transsexuals. *Current Opinion in Endocrinology, Diabetes and Obesity*. 2013;1;20:570-4.
4. **Milrod C.** How young is too young: ethical concerns in genital surgery of the transgender MTF adolescent. *The journal of sexual medicine*. 2014. 11:338-46.
5. **Raigosa M, Avvedimento S, Yoon TS, Cruz-Gimeno J, Rodriguez G, Fontdevila J.** Male-to-Female Genital Reassignment Surgery: A Retrospective Review of Surgical Technique and Complications in 60 Patients. *The journal of sexual medicine*. 2015. 12:1837-45.
6. **Judge C, O'Donovan C, Callaghan G, Gaoatswe G, O'Shea D.** Gender dysphoria—prevalence and co-morbidities in an Irish adult population. *Neurological and Psychiatric Disorders in Endocrine Diseases*. 2015;17:24.
7. **James SE, Herman JL, Rankin S, Keisling M, Mottet L, Ana M.** (2016). *The Report of the 2015 U.S. Transgender Survey*. Washington, DC: National Center for Transgender Equality.
8. Guidance regarding prohibited discrimination on the basis of gender identity or gender dysphoria including medically necessary transgender surgery and related health care

services. Office of Consumer Affairs and Business Regulation, Division of Insurance, 2014. (Accessed September 1, 2016, at

<http://www.masstpc.org/pubs/3party/DOI%20Bulletin%202014-03.pdf>.)

9. **Forshee AS.** Transgender men: A demographic snapshot. *Journal of Gay & Lesbian Social Services*. 2008;20:221-36.
10. **van de Grift TC, Cohen-Kettenis PT, Elaut E, et al.** A network analysis of body satisfaction of people with gender dysphoria. *Body image*. 2016;17:184-90.
11. **Ainsworth TA, Spiegel JH.** Quality of life of individuals with and without facial feminization surgery or gender reassignment surgery. *Quality of Life Research*. 2010;19:1019-24.
12. **De Cuypere, Griet, et al.** Long-term follow-up: psychosocial outcome of Belgian transsexuals after sex reassignment surgery. *Sexologies* . 2006: 126-133.
13. "Commitment to Our Community." Boston Medical Center. N.p., 20 Sept. 2016. Web. 13 Jan. 2017.
14. **Stroumsa, D.** The state of transgender health care: policy, law, and medical frameworks. *American journal of public health* 104.3:e31-e38.
15. **Gerhardstein KR, Anderson VN.** There's more than meets the eye: Facial appearance and evaluations of transsexual people. *Sex roles*. 2010;62:361-73.
16. **Winter S, Webster B, Cheung PK.** Measuring Hong Kong undergraduate students' attitudes towards transpeople. *Sex Roles*. 2008;59:670-83.
17. **Safer JD, Coleman E, Feldman J, et al.** Barriers to healthcare for transgender individuals. *Current Opinion in Endocrinology, Diabetes and Obesity*. 2016;23:168-71.

18. **Snelgrove JW, Jasudavicius AM, Rowe BW, Head EM, Bauer GR.** Completely out-at-sea” with “two-gender medicine: A qualitative analysis of physician-side barriers to providing healthcare for transgender patients. *BMC health services research*. 2012;12:1.
19. **Grant JM, Mottet LA, Tanis J, Herman JL, Harrison J, Keisling M.** National transgender discrimination survey report on health and health care. Washington, DC: National Center for Transgender Equality and the National Gay and Lesbian Task Force. 2010 Oct.
20. **Cruz TM.** Assessing access to care for transgender and gender nonconforming people: A consideration of diversity in combating discrimination. *Social science & medicine*. 2014 ;110:65-73.
21. **Cohen-Kettenis PT, Pfäfflin F.** The DSM diagnostic criteria for gender identity disorder in adolescents and adults. *Archives of sexual behavior*. 2010;39:499-513.
22. **Padula WV, Heru S, Campbell JD.** Societal implications of health insurance coverage for medically necessary services in the US transgender population: A cost-effectiveness analysis. *Journal of general internal medicine*. 2016;31:394-401.
23. Know your rights: Medicare. 2016. (Accessed September 5, 2016, at <http://www.transequality.org/know-your-rights/medicare>.)
24. **Feldman J, Brown GR, Deutsch MB, et al.** Priorities for transgender medical and healthcare research. *Current Opinion in Endocrinology, Diabetes and Obesity*. 2016 ;23:180-7.
25. **De Cuypere G, Van Hemelrijck M, Michel A, et al.** Prevalence and demography of transsexualism in Belgium. *European psychiatry*. 2007;22:137-41.

Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline

Wylie C. Hembree,¹ Peggy T. Cohen-Kettenis,² Louis Gooren,³ Sabine E. Hannema,⁴ Walter J. Meyer,⁵ M. Hassan Murad,⁶ Stephen M. Rosenthal,⁷ Joshua D. Safer,⁸ Vin Tangpricha,⁹ and Guy G. T'Sjoen,¹⁰

¹New York Presbyterian Hospital, Columbia University Medical Center, New York, New York 10032 (Retired); ²VU University Medical Center, 1007 MB Amsterdam, Netherlands (Retired); ³VU University Medical Center, 1007 MB Amsterdam, Netherlands (Retired); ⁴Leiden University Medical Center, 2300 RC Leiden, Netherlands; ⁵University of Texas Medical Branch, Galveston, Texas 77555; ⁶Mayo Clinic Evidence-Based Practice Center, Rochester, Minnesota 55905; ⁷University of California San Francisco, Benioff Children's Hospital, San Francisco, California 94143; ⁸Boston University School of Medicine, Boston, Massachusetts 02118; ⁹Emory University School of Medicine and the Atlanta VA Medical Center, Atlanta, Georgia 30322; and ¹⁰Ghent University Hospital, 9000 Ghent, Belgium

***Cosponsoring Associations:** American Association of Clinical Endocrinologists, American Society of Andrology, European Society for Pediatric Endocrinology, European Society of Endocrinology, Pediatric Endocrine Society, and World Professional Association for Transgender Health.

Objective: To update the "Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline," published by the Endocrine Society in 2009.

Participants: The participants include an Endocrine Society-appointed task force of nine experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation approach to describe the strength of recommendations and the quality of evidence. The task force commissioned two systematic reviews and used the best available evidence from other published systematic reviews and individual studies.

Consensus Process: Group meetings, conference calls, and e-mail communications enabled consensus. Endocrine Society committees, members and cosponsoring organizations reviewed and commented on preliminary drafts of the guidelines.

Conclusion: Gender affirmation is multidisciplinary treatment in which endocrinologists play an important role. Gender-dysphoric/gender-incongruent persons seek and/or are referred to endocrinologists to develop the physical characteristics of the affirmed gender. They require a safe and effective hormone regimen that will (1) suppress endogenous sex hormone secretion determined by the person's genetic/gonadal sex and (2) maintain sex hormone levels within the normal range for the person's affirmed gender. Hormone treatment is not recommended for prepubertal gender-dysphoric/gender-incongruent persons. Those clinicians who recommend gender-affirming endocrine treatments—appropriately trained diagnosing clinicians (required), a mental health provider for adolescents (required) and mental health

professional for adults (recommended)—should be knowledgeable about the diagnostic criteria and criteria for gender-affirming treatment, have sufficient training and experience in assessing psychopathology, and be willing to participate in the ongoing care throughout the endocrine transition. We recommend treating gender-dysphoric/gender-incongruent adolescents who have entered puberty at Tanner Stage G2/B2 by suppression with gonadotropin-releasing hormone agonists. Clinicians may add gender-affirming hormones after a multidisciplinary team has confirmed the persistence of gender dysphoria/gender incongruence and sufficient mental capacity to give informed consent to this partially irreversible treatment. Most adolescents have this capacity by age 16 years old. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to age 16 years, although there is minimal published experience treating prior to 13.5 to 14 years of age. For the care of peripubertal youths and older adolescents, we recommend that an expert multidisciplinary team comprised of medical professionals and mental health professionals manage this treatment. The treating physician must confirm the criteria for treatment used by the referring mental health practitioner and collaborate with them in decisions about gender-affirming surgery in older adolescents. For adult gender-dysphoric/gender-incongruent persons, the treating clinicians (collectively) should have expertise in transgender-specific diagnostic criteria, mental health, primary care, hormone treatment, and surgery, as needed by the patient. We suggest maintaining physiologic levels of gender-appropriate hormones and monitoring for known risks and complications. When high doses of sex steroids are required to suppress endogenous sex steroids and/or in advanced age, clinicians may consider surgically removing natal gonads along with reducing sex steroid treatment. Clinicians should monitor both transgender males (female to male) and transgender females (male to female) for reproductive organ cancer risk when surgical removal is incomplete. Additionally, clinicians should persistently monitor adverse effects of sex steroids. For gender-affirming surgeries in adults, the treating physician must collaborate with and confirm the criteria for treatment used by the referring physician. Clinicians should avoid harming individuals (via hormone treatment) who have conditions other than gender dysphoria/gender incongruence and who may not benefit from the physical changes associated with this treatment. (*J Clin Endocrinol Metab* 102: 1–35, 2017)

Summary of Recommendations

1.0 Evaluation of youth and adults

- 1.1. We advise that only trained mental health professionals (MHPs) who meet the following criteria should diagnose gender dysphoria (GD)/gender incongruence in adults: (1) competence in using the Diagnostic and Statistical Manual of Mental Disorders (DSM) and/or the International Statistical Classification of Diseases and Related Health Problems (ICD) for diagnostic purposes, (2) the ability to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) training in diagnosing psychiatric conditions, (4) the ability to undertake or refer for appropriate treatment, (5) the ability to psychosocially assess the person's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) a practice of regularly attending relevant professional meetings. (Ungraded Good Practice Statement)

- 1.2. We advise that only MHPs who meet the following criteria should diagnose GD/gender incongruence in children and adolescents: (1) training in child and adolescent developmental psychology and psychopathology, (2) competence in using the DSM and/or the ICD for diagnostic purposes, (3) the ability to make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (4) training in diagnosing psychiatric conditions, (5) the ability to undertake or refer for appropriate treatment, (6) the ability to psychosocially assess the person's understanding and social conditions that can impact gender-affirming hormone therapy, (7) a practice of regularly attending relevant professional meetings, and (8) knowledge of the criteria for puberty blocking and gender-affirming hormone treatment in adolescents. (Ungraded Good Practice Statement)
- 1.3. We advise that decisions regarding the social transition of prepubertal youths with GD/gender incongruence are made with the assistance of an MHP or another experienced professional. (Ungraded Good Practice Statement).

- 1.4. We recommend against puberty blocking and gender-affirming hormone treatment in pre-pubertal children with GD/gender incongruence. (1 ⊕⊕○○)
- 1.5. We recommend that clinicians inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression in adolescents and prior to treating with hormonal therapy of the affirmed gender in both adolescents and adults. (1 ⊕⊕⊕○)

2.0 Treatment of adolescents

- 2.1. We suggest that adolescents who meet diagnostic criteria for GD/gender incongruence, fulfill criteria for treatment, and are requesting treatment should initially undergo treatment to suppress pubertal development. (2 ⊕⊕○○)
- 2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty. (2 ⊕⊕○○)
- 2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. (1 ⊕⊕○○)
- 2.4. In adolescents who request sex hormone treatment (given this is a partly irreversible treatment), we recommend initiating treatment using a gradually increasing dose schedule after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years. (1 ⊕⊕○○).
- 2.5. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5 to 14 years. As with the care of adolescents ≥16 years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment. (1 ⊕○○○)
- 2.6. We suggest monitoring clinical pubertal development every 3 to 6 months and laboratory parameters every 6 to 12 months during sex hormone treatment. (2 ⊕⊕○○)

3.0 Hormonal therapy for transgender adults

- 3.1. We recommend that clinicians confirm the diagnostic criteria of GD/gender incongruence and

the criteria for the endocrine phase of gender transition before beginning treatment. (1 ⊕⊕⊕○)

- 3.2. We recommend that clinicians evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment. (1 ⊕⊕⊕○)
- 3.3. We suggest that clinicians measure hormone levels during treatment to ensure that endogenous sex steroids are suppressed and administered sex steroids are maintained in the normal physiologic range for the affirmed gender. (2 ⊕⊕○○)
- 3.4. We suggest that endocrinologists provide education to transgender individuals undergoing treatment about the onset and time course of physical changes induced by sex hormone treatment. (2 ⊕○○○)

4.0 Adverse outcome prevention and long-term care

- 4.1. We suggest regular clinical evaluation for physical changes and potential adverse changes in response to sex steroid hormones and laboratory monitoring of sex steroid hormone levels every 3 months during the first year of hormone therapy for transgender males and females and then once or twice yearly. (2 ⊕⊕○○)
- 4.2. We suggest periodically monitoring prolactin levels in transgender females treated with estrogens. (2 ⊕⊕○○)
- 4.3. We suggest that clinicians evaluate transgender persons treated with hormones for cardiovascular risk factors using fasting lipid profiles, diabetes screening, and/or other diagnostic tools. (2 ⊕⊕○○)
- 4.4. We recommend that clinicians obtain bone mineral density (BMD) measurements when risk factors for osteoporosis exist, specifically in those who stop sex hormone therapy after gonadectomy. (1 ⊕⊕○○)
- 4.5. We suggest that transgender females with no known increased risk of breast cancer follow breast-screening guidelines recommended for non-transgender females. (2 ⊕⊕○○)
- 4.6. We suggest that transgender females treated with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 ⊕○○○)
- 4.7. We advise that clinicians determine the medical necessity of including a total hysterectomy and oophorectomy as part of gender-affirming surgery. (Ungraded Good Practice Statement)

5.0 Surgery for sex reassignment and gender confirmation

- 5.1. We recommend that a patient pursue genital gender-affirming surgery only after the MHP and the clinician responsible for endocrine transition therapy both agree that surgery is medically necessary and would benefit the patient's overall health and/or well-being. (1 ⊕⊕○○)
- 5.2. We advise that clinicians approve genital gender-affirming surgery only after completion of at least 1 year of consistent and compliant hormone treatment, unless hormone therapy is not desired or medically contraindicated. (Ungraded Good Practice Statement)
- 5.3. We advise that the clinician responsible for endocrine treatment and the primary care provider ensure appropriate medical clearance of transgender individuals for genital gender-affirming surgery and collaborate with the surgeon regarding hormone use during and after surgery. (Ungraded Good Practice Statement)
- 5.4. We recommend that clinicians refer hormone-treated transgender individuals for genital surgery when: (1) the individual has had a satisfactory social role change, (2) the individual is satisfied about the hormonal effects, and (3) the individual desires definitive surgical changes. (1 ⊕○○○)
- 5.5. We suggest that clinicians delay gender-affirming genital surgery involving gonadectomy and/or hysterectomy until the patient is at least 18 years old or legal age of majority in his or her country. (2 ⊕⊕○○)
- 5.6. We suggest that clinicians determine the timing of breast surgery for transgender males based upon the physical and mental health status of the individual. There is insufficient evidence to recommend a specific age requirement. (2 ⊕○○○)

Changes Since the Previous Guideline

Both the current guideline and the one published in 2009 contain similar sections. Listed here are the sections contained in the current guideline and the corresponding number of recommendations: Introduction, Evaluation of Youth and Adults (5), Treatment of Adolescents (6), Hormonal Therapy for Transgender Adults (4), Adverse Outcomes Prevention and Long-term Care (7), and Surgery for Sex Reassignment and Gender Confirmation (6). The current introduction updates the diagnostic classification of “gender dysphoria/gender incongruence.” It also reviews the development of “gender identity” and summarizes its natural development. The section on

clinical evaluation of both youth and adults, defines in detail the professional qualifications required of those who diagnose and treat both adolescents and adults. We advise that decisions regarding the social transition of prepubertal youth are made with the assistance of a mental health professional or similarly experienced professional. We recommend against puberty blocking followed by gender-affirming hormone treatment of prepubertal children. Clinicians should inform pubertal children, adolescents, and adults seeking gender-confirming treatment of their options for fertility preservation. Prior to treatment, clinicians should evaluate the presence of medical conditions that may be worsened by hormone depletion and/or treatment. A multidisciplinary team, preferably composed of medical and mental health professionals, should monitor treatments. Clinicians evaluating transgender adults for endocrine treatment should confirm the diagnosis of persistent gender dysphoria/gender incongruence. Physicians should educate transgender persons regarding the time course of steroid-induced physical changes. Treatment should include periodic monitoring of hormone levels and metabolic parameters, as well as assessments of bone density and the impact upon prostate, gonads, and uterus. We also make recommendations for transgender persons who plan genital gender-affirming surgery.

Method of Development of Evidence-Based Clinical Practice Guidelines

The Clinical Guidelines Subcommittee (CGS) of the Endocrine Society deemed the diagnosis and treatment of individuals with GD/gender incongruence a priority area for revision and appointed a task force to formulate evidence-based recommendations. The task force followed the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation group, an international group with expertise in the development and implementation of evidence-based guidelines (1). A detailed description of the grading scheme has been published elsewhere (2). The task force used the best available research evidence to develop the recommendations. The task force also used consistent language and graphical descriptions of both the strength of a recommendation and the quality of evidence. In terms of the strength of the recommendation, strong recommendations use the phrase “we recommend” and the number 1, and weak recommendations use the phrase “we suggest” and the number 2. Cross-filled circles indicate the quality of the evidence, such that ⊕○○○ denotes very low-quality evidence; ⊕⊕○○, low quality; ⊕⊕⊕○, moderate quality; and ⊕⊕⊕⊕, high quality. The task force has confidence that persons who receive care according to the strong recommendations will derive, on average, more benefit than harm. Weak recommendations require more careful consideration of the person's circumstances, values, and preferences to determine the best course of action. Linked to each recommendation is a description of the evidence and the

values that the task force considered in making the recommendation. In some instances, there are remarks in which the task force offers technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical person being treated. Often this evidence comes from the unsystematic observations of the task force and their preferences; therefore, one should consider these remarks as suggestions.

In this guideline, the task force made several statements to emphasize the importance of shared decision-making, general preventive care measures, and basic principles of the treatment of transgender persons. They labeled these “Ungraded Good Practice Statement.” Direct evidence for these statements was either unavailable or not systematically appraised and considered out of the scope of this guideline. The intention of these statements is to draw attention to these principles.

The Endocrine Society maintains a rigorous conflict-of-interest review process for developing clinical practice guidelines. All task force members must declare any potential conflicts of interest by completing a conflict-of-interest form. The CGS reviews all conflicts of interest before the Society’s Council approves the members to participate on the task force and periodically during the development of the guideline. All others participating in the guideline’s development must also disclose any conflicts of interest in the matter under study, and most of these participants must be without any conflicts of interest. The CGS and the task force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined as remuneration in any amount from commercial interests; grants; research support; consulting fees; salary; ownership interests [e.g., stocks and stock options (excluding diversified mutual funds)]; honoraria and other payments for participation in speakers’ bureaus, advisory boards, or boards of directors; and all other financial benefits. Completed forms are available through the Endocrine Society office.

The Endocrine Society provided the funding for this guideline; the task force received no funding or remuneration from commercial or other entities.

Commissioned Systematic Review

The task force commissioned two systematic reviews to support this guideline. The first one aimed to summarize the available evidence on the effect of sex steroid use in transgender individuals on lipids and cardiovascular outcomes. The review identified 29 eligible studies at moderate risk of bias. In transgender males (female to male), sex steroid therapy was associated with a statistically significant increase in serum triglycerides and low-density lipoprotein cholesterol levels. High-density lipoprotein cholesterol levels decreased significantly across all follow-up time periods. In transgender females (male to female), serum triglycerides were significantly higher without any changes in other parameters. Few myocardial infarction, stroke, venous thromboembolism (VTE), and death events were reported. These events were more frequent in transgender females. However, the

quality of the evidence was low. The second review summarized the available evidence regarding the effect of sex steroids on bone health in transgender individuals and identified 13 studies. In transgender males, there was no statistically significant difference in the lumbar spine, femoral neck, or total hip BMD at 12 and 24 months compared with baseline values before initiating masculinizing hormone therapy. In transgender females, there was a statistically significant increase in lumbar spine BMD at 12 months and 24 months compared with baseline values before initiation of feminizing hormone therapy. There was minimal information on fracture rates. The quality of evidence was also low.

Introduction

Throughout recorded history (in the absence of an endocrine disorder) some men and women have experienced confusion and anguish resulting from rigid, forced conformity to sexual dimorphism. In modern history, there have been numerous ongoing biological, psychological, cultural, political, and sociological debates over various aspects of gender variance. The 20th century marked the emergence of a social awakening for men and women with the belief that they are “trapped” in the wrong body (3). Magnus Hirschfeld and Harry Benjamin, among others, pioneered the medical responses to those who sought relief from and a resolution to their profound discomfort. Although the term transsexual became widely known after Benjamin wrote “The Transsexual Phenomenon” (4), it was Hirschfeld who coined the term “transsexual” in 1923 to describe people who want to live a life that corresponds with their experienced gender vs their designated gender (5). Magnus Hirschfeld (6) and others (4, 7) have described other types of trans phenomena besides transsexualism. These early researchers proposed that the gender identity of these people was located somewhere along a unidimensional continuum. This continuum ranged from all male through “something in between” to all female. Yet such a classification does not take into account that people may have gender identities outside this continuum. For instance, some experience themselves as having both a male and female gender identity, whereas others completely renounce any gender classification (8, 9). There are also reports of individuals experiencing a continuous and rapid involuntary alternation between a male and female identity (10) or men who do not experience themselves as men but do not want to live as women (11, 12). In some countries, (e.g., Nepal, Bangladesh, and Australia), these nonmale or nonfemale genders are officially recognized (13). Specific treatment protocols, however, have not yet been developed for these groups.

Instead of the term transsexualism, the current classification system of the American Psychiatric Association uses the term gender dysphoria in its diagnosis of persons who are not satisfied with their designated gender (14). The current version of the World Health Organization's ICD-10 still uses the term transsexualism when diagnosing adolescents and adults. However, for the ICD-11, the World Health Organization has proposed using the term "gender incongruence" (15).

Treating persons with GD/gender incongruence (15) was previously limited to relatively ineffective elixirs or creams. However, more effective endocrinology-based treatments became possible with the availability of testosterone in 1935 and diethylstilbestrol in 1938. Reports of individuals with GD/gender incongruence who were treated with hormones and gender-affirming surgery appeared in the press during the second half of the 20th century. The Harry Benjamin International Gender Dysphoria Association was founded in September 1979 and is now called the World Professional Association for Transgender Health (WPATH). WPATH published its first Standards of Care in 1979. These standards have since been regularly updated, providing guidance for treating persons with GD/gender incongruence (16).

Prior to 1975, few peer-reviewed articles were published concerning endocrine treatment of transgender persons. Since then, more than two thousand articles about various aspects of transgender care have appeared.

It is the purpose of this guideline to make detailed recommendations and suggestions, based on existing medical literature and clinical experience, that will enable treating physicians to maximize benefit and minimize risk when caring for individuals diagnosed with GD/gender incongruence.

In the future, we need more rigorous evaluations of the effectiveness and safety of endocrine and surgical protocols. Specifically, endocrine treatment protocols for GD/gender incongruence should include the careful assessment of the following: (1) the effects of prolonged delay of puberty in adolescents on bone health, gonadal function, and the brain (including effects on cognitive, emotional, social, and sexual development); (2) the effects of treatment in adults on sex hormone levels; (3) the requirement for and the effects of progestins and other agents used to suppress endogenous sex steroids during treatment; and (4) the risks and benefits of gender-affirming hormone treatment in older transgender people.

To successfully establish and enact these protocols, a commitment of mental health and endocrine investigators is required to collaborate in long-term, large-scale

studies across countries that use the same diagnostic and inclusion criteria, medications, assay methods, and response assessment tools (*e.g.*, the European Network for the Investigation of Gender Incongruence) (17, 18).

Terminology and its use vary and continue to evolve. Table 1 contains the definitions of terms as they are used throughout this guideline.

Biological Determinants of Gender Identity Development

One's self-awareness as male or female changes gradually during infant life and childhood. This process of cognitive and affective learning evolves with interactions with parents, peers, and environment. A fairly accurate timetable exists outlining the steps in this process (19). Normative psychological literature, however, does not address if and when gender identity becomes crystallized and what factors contribute to the development of a gender identity that is not congruent with the gender of rearing. Results of studies from a variety of biomedical disciplines—genetic, endocrine, and neuroanatomic—support the concept that gender identity and/or gender expression (20) likely reflect a complex interplay of biological, environmental, and cultural factors (21, 22).

With respect to endocrine considerations, studies have failed to find differences in circulating levels of sex steroids between transgender and nontransgender individuals (23). However, studies in individuals with a disorder/difference of sex development (DSD) have informed our understanding of the role that hormones may play in gender identity outcome, even though most persons with GD/gender incongruence do not have a DSD. For example, although most 46,XX adult individuals with virilizing congenital adrenal hyperplasia caused by mutations in *CYP21A2* reported a female gender identity, the prevalence of GD/gender incongruence was much greater in this group than in the general population without a DSD. This supports the concept that there is a role for prenatal/postnatal androgens in gender development (24–26), although some studies indicate that prenatal androgens are more likely to affect gender behavior and sexual orientation rather than gender identity *per se* (27, 28).

Researchers have made similar observations regarding the potential role of androgens in the development of gender identity in other individuals with DSD. For example, a review of two groups of 46,XY persons, each with androgen synthesis deficiencies and female raised, reported transgender male (female-to-male) gender role changes in 56% to 63% and 39% to 64% of patients, respectively (29). Also, in 46,XY female-raised individuals with cloacal

Table 1. Definitions of Terms Used in This Guideline

<i>Biological sex, biological male or female:</i> These terms refer to physical aspects of maleness and femaleness. As these may not be in line with each other (e.g., a person with XY chromosomes may have female-appearing genitalia), the terms biological sex and biological male or female are imprecise and should be avoided.
<i>Cisgender:</i> This means not transgender. An alternative way to describe individuals who are not transgender is “non-transgender people.”
<i>Gender-affirming (hormone) treatment:</i> See “gender reassignment”
<i>Gender dysphoria:</i> This is the distress and unease experienced if gender identity and designated gender are not completely congruent (see Table 2). In 2013, the American Psychiatric Association released the fifth edition of the DSM-5, which replaced “gender identity disorder” with “gender dysphoria” and changed the criteria for diagnosis.
<i>Gender expression:</i> This refers to external manifestations of gender, expressed through one’s name, pronouns, clothing, haircut, behavior, voice, or body characteristics. Typically, transgender people seek to make their gender expression align with their gender identity, rather than their designated gender.
<i>Gender identity/experienced gender:</i> This refers to one’s internal, deeply held sense of gender. For transgender people, their gender identity does not match their sex designated at birth. Most people have a gender identity of man or woman (or boy or girl). For some people, their gender identity does not fit neatly into one of those two choices. Unlike gender expression (see below), gender identity is not visible to others.
<i>Gender identity disorder:</i> This is the term used for GD/gender incongruence in previous versions of DSM (see “gender dysphoria”). The ICD-10 still uses the term for diagnosing child diagnoses, but the upcoming ICD-11 has proposed using “gender incongruence of childhood.”
<i>Gender incongruence:</i> This is an umbrella term used when the gender identity and/or gender expression differs from what is typically associated with the designated gender. Gender incongruence is also the proposed name of the gender identity–related diagnoses in ICD-11. Not all individuals with gender incongruence have gender dysphoria or seek treatment.
<i>Gender variance:</i> See “gender incongruence”
<i>Gender reassignment:</i> This refers to the treatment procedure for those who want to adapt their bodies to the experienced gender by means of hormones and/or surgery. This is also called gender-confirming or gender-affirming treatment.
<i>Gender-reassignment surgery (gender-confirming/gender-affirming surgery):</i> These terms refer only to the surgical part of gender-confirming/gender-affirming treatment.
<i>Gender role:</i> This refers to behaviors, attitudes, and personality traits that a society (in a given culture and historical period) designates as masculine or feminine and/or that society associates with or considers typical of the social role of men or women.
<i>Sex designated at birth:</i> This refers to sex assigned at birth, usually based on genital anatomy.
<i>Sex:</i> This refers to attributes that characterize biological maleness or femaleness. The best known attributes include the sex-determining genes, the sex chromosomes, the H-Y antigen, the gonads, sex hormones, internal and external genitalia, and secondary sex characteristics.
<i>Sexual orientation:</i> This term describes an individual’s enduring physical and emotional attraction to another person. Gender identity and sexual orientation are not the same. Irrespective of their gender identity, transgender people may be attracted to women (gynephilic), attracted to men (androphilic), bisexual, asexual, or queer.
<i>Transgender:</i> This is an umbrella term for people whose gender identity and/or gender expression differs from what is typically associated with their sex designated at birth. Not all transgender individuals seek treatment.
<i>Transgender male (also: trans man, female-to-male, transgender male):</i> This refers to individuals assigned female at birth but who identify and live as men.
<i>Transgender woman (also: trans woman, male-to-female, transgender female):</i> This refers to individuals assigned male at birth but who identify and live as women.
<i>Transition:</i> This refers to the process during which transgender persons change their physical, social, and/or legal characteristics consistent with the affirmed gender identity. Prepubertal children may choose to transition socially.
<i>Transsexual:</i> This is an older term that originated in the medical and psychological communities to refer to individuals who have permanently transitioned through medical interventions or desired to do so.

exstrophy and penile agenesis, the occurrence of transgender male changes was significantly more prevalent than in the general population (30, 31). However, the fact that a high percentage of individuals with the same conditions did not change gender suggests that cultural factors may play a role as well.

With respect to genetics and gender identity, several studies have suggested heritability of GD/gender incongruence (32, 33). In particular, a study by Heylens *et al.* (33) demonstrated a 39.1% concordance rate for gender identity disorder (based on the DSM-IV criteria) in 23 monozygotic twin pairs but no concordance in 21 same-sex dizygotic or seven opposite-sex twin pairs. Although numerous investigators have sought to identify

specific genes associated with GD/gender incongruence, such studies have been inconsistent and without strong statistical significance (34–38).

Studies focusing on brain structure suggest that the brain phenotypes of people with GD/gender incongruence differ in various ways from control males and females, but that there is not a complete sex reversal in brain structures (39).

In summary, although there is much that is still unknown with respect to gender identity and its expression, compelling studies support the concept that biologic factors, in addition to environmental factors, contribute to this fundamental aspect of human development.

Natural History of Children With GD/Gender Incongruence

With current knowledge, we cannot predict the psychosexual outcome for any specific child. Prospective follow-up studies show that childhood GD/gender incongruence does not invariably persist into adolescence and adulthood (so-called “desisters”). Combining all outcome studies to date, the GD/gender incongruence of a minority of prepubertal children appears to persist in adolescence (20, 40). In adolescence, a significant number of these desisters identify as homosexual or bisexual. It may be that children who only showed some gender nonconforming characteristics have been included in the follow-up studies, because the DSM-IV text revision criteria for a diagnosis were rather broad. However, the persistence of GD/gender incongruence into adolescence is more likely if it had been extreme in childhood (41, 42). With the newer, stricter criteria of the DSM-5 (Table 2), persistence rates may well be different in future studies.

1.0 Evaluation of Youth and Adults

Gender-affirming treatment is a multidisciplinary effort. After evaluation, education, and diagnosis, treatment may include mental health care, hormone therapy, and/or surgical therapy. Together with an MHP, hormone-prescribing clinicians should examine the psychosocial impact of the potential changes on people’s lives, including mental health, friends, family, jobs, and their role in society. Transgender individuals should be encouraged to experience living in the new gender role and assess whether

this improves their quality of life. Although the focus of this guideline is gender-affirming hormone therapy, collaboration with appropriate professionals responsible for each aspect of treatment maximizes a successful outcome.

Diagnostic assessment and mental health care

GD/gender incongruence may be accompanied with psychological or psychiatric problems (43–51). It is therefore necessary that clinicians who prescribe hormones and are involved in diagnosis and psychosocial assessment meet the following criteria: (1) are competent in using the DSM and/or the ICD for diagnostic purposes, (2) are able to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) are trained in diagnosing psychiatric conditions, (4) undertake or refer for appropriate treatment, (5) are able to do a psychosocial assessment of the patient’s understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) regularly attend relevant professional meetings.

Because of the psychological vulnerability of many individuals with GD/gender incongruence, it is important that mental health care is available before, during, and sometimes also after transitioning. For children and adolescents, an MHP who has training/experience in child and adolescent gender development (as well as child and adolescent psychopathology) should make the diagnosis, because assessing GD/gender incongruence in children and adolescents is often extremely complex.

During assessment, the clinician obtains information from the individual seeking gender-affirming treatment. In the case

Table 2. DSM-5 Criteria for Gender Dysphoria in Adolescents and Adults

- A. A marked incongruence between one’s experienced/expressed gender and natal gender of at least 6 mo in duration, as manifested by at least two of the following:
 1. A marked incongruence between one’s experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
 2. A strong desire to be rid of one’s primary and/or secondary sex characteristics because of a marked incongruence with one’s experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
 3. A strong desire for the primary and/or secondary sex characteristics of the other gender
 4. A strong desire to be of the other gender (or some alternative gender different from one’s designated gender)
 5. A strong desire to be treated as the other gender (or some alternative gender different from one’s designated gender)
 6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one’s designated gender)
- B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:

 1. The condition exists with a disorder of sex development.
 2. The condition is posttransitional, in that the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or treatment regimen—namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (*e.g.*, penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

of adolescents, the clinician also obtains information from the parents or guardians regarding various aspects of the child's general and psychosexual development and current functioning. On the basis of this information, the clinician:

- decides whether the individual fulfills criteria for treatment (see Tables 2 and 3) for GD/gender incongruence (DSM-5) or transsexualism (DSM-5 and/or ICD-10);
- informs the individual about the possibilities and limitations of various kinds of treatment (hormonal/surgical and nonhormonal), and if medical treatment is desired, provides correct information to prevent unrealistically high expectations;
- assesses whether medical interventions may result in unfavorable psychological and social outcomes.

In cases in which severe psychopathology, circumstances, or both seriously interfere with the diagnostic work or make satisfactory treatment unlikely, clinicians should assist the adolescent in managing these other issues. Literature on postoperative regret suggests that besides poor quality of surgery, severe psychiatric comorbidity and lack of support may interfere with positive outcomes (52–56).

For adolescents, the diagnostic procedure usually includes a complete psychodiagnostic assessment (57) and an assessment of the decision-making capability of the youth. An evaluation to assess the family's ability to endure stress, give support, and deal with the complexities of the adolescent's situation should be part of the diagnostic phase (58).

Social transitioning

A change in gender expression and role (which may involve living part time or full time in another gender role that is consistent with one's gender identity) may test the person's resolve, the capacity to function in the affirmed gender, and the adequacy of social, economic, and psychological supports. It assists both the individual and the clinician in their judgments about how to proceed (16). During social transitioning, the person's feelings about the social transformation (including coping with the responses of others) is a major focus of the counseling. The optimal timing for social transitioning may differ between individuals. Sometimes people wait until they

start gender-affirming hormone treatment to make social transitioning easier, but individuals increasingly start social transitioning long before they receive medically supervised, gender-affirming hormone treatment.

Criteria

Adolescents and adults seeking gender-affirming hormone treatment and surgery should satisfy certain criteria before proceeding (16). Criteria for gender-affirming hormone therapy for adults are in Table 4, and criteria for gender-affirming hormone therapy for adolescents are in Table 5. Follow-up studies in adults meeting these criteria indicate a high satisfaction rate with treatment (59). However, the quality of evidence is usually low. A few follow-up studies on adolescents who fulfilled these criteria also indicated good treatment results (60–63).

Recommendations for Those Involved in the Gender-Affirming Hormone Treatment of Individuals With GD/Gender Incongruence

- 1.1. We advise that only trained MHPs who meet the following criteria should diagnose GD/gender incongruence in adults: (1) competence in using the DSM and/or the ICD for diagnostic purposes, (2) the ability to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) training in diagnosing psychiatric conditions, (4) the ability to undertake or refer for appropriate treatment, (5) the ability to psychosocially assess the person's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) a practice of regularly attending relevant professional meetings. (Ungraded Good Practice Statement)
- 1.2. We advise that only MHPs who meet the following criteria should diagnose GD/gender incongruence in children and adolescents: (1) training in child and adolescent developmental psychology and psychopathology, (2) competence in using the DSM and/or ICD for diagnostic

Table 3. ICD-10 Criteria for Transsexualism

Transsexualism (F64.0) has three criteria:

1. The desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatments.
2. The transsexual identity has been present persistently for at least 2 y.
3. The disorder is not a symptom of another mental disorder or a genetic, DSD, or chromosomal abnormality.

Table 4. Criteria for Gender-Affirming Hormone Therapy for Adults

1. Persistent, well-documented gender dysphoria/gender incongruence
2. The capacity to make a fully informed decision and to consent for treatment
3. The age of majority in a given country (if younger, follow the criteria for adolescents)
4. Mental health concerns, if present, must be reasonably well controlled

Reproduced from World Professional Association for Transgender Health (16).

purposes, (3) the ability to make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (4) training in diagnosing psychiatric conditions, (5) the ability to undertake or refer for appropriate treatment, (6) the ability to psychosocially assess the person's understanding and social conditions that can impact gender-affirming hormone therapy, (7) a practice of regularly attending relevant professional meetings, and (8) knowledge of the criteria for puberty blocking and gender-affirming hormone treatment in adolescents. (Ungraded Good Practice Statement)

Evidence

Individuals with gender identity issues may have psychological or psychiatric problems (43–48, 50, 51, 64, 65). It is therefore necessary that clinicians making the diagnosis are able to make a distinction between GD/gender incongruence and conditions that have similar features. Examples of conditions with similar features are body dysmorphic disorder, body identity integrity disorder (a condition in which individuals have a sense that their anatomical configuration as an able-bodied person is somehow wrong or inappropriate) (66), or certain forms of eunuchism (in which a person is preoccupied with or engages in castration and/or penectomy for

Table 5. Criteria for Gender-Affirming Hormone Therapy for Adolescents

Adolescents are eligible for GnRH agonist treatment if:

1. A qualified MHP has confirmed that:
 - the adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed),
 - gender dysphoria worsened with the onset of puberty,
 - any coexisting psychological, medical, or social problems that could interfere with treatment (*e.g.*, that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment,
 - the adolescent has sufficient mental capacity to give informed consent to this (reversible) treatment,
2. And the adolescent:
 - has been informed of the effects and side effects of treatment (including potential loss of fertility if the individual subsequently continues with sex hormone treatment) and options to preserve fertility,
 - has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,
3. And a pediatric endocrinologist or other clinician experienced in pubertal assessment
 - agrees with the indication for GnRH agonist treatment,
 - has confirmed that puberty has started in the adolescent (Tanner stage $\geq$ G2/B2),
 - has confirmed that there are no medical contraindications to GnRH agonist treatment.

Adolescents are eligible for subsequent sex hormone treatment if:

1. A qualified MHP has confirmed:
 - the persistence of gender dysphoria,
 - any coexisting psychological, medical, or social problems that could interfere with treatment (*e.g.*, that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start sex hormone treatment,
 - the adolescent has sufficient mental capacity (which most adolescents have by age 16 years) to estimate the consequences of this (partly) irreversible treatment, weigh the benefits and risks, and give informed consent to this (partly) irreversible treatment,
2. And the adolescent:
 - has been informed of the (irreversible) effects and side effects of treatment (including potential loss of fertility and options to preserve fertility),
 - has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,
3. And a pediatric endocrinologist or other clinician experienced in pubertal induction:
 - agrees with the indication for sex hormone treatment,
 - has confirmed that there are no medical contraindications to sex hormone treatment.

Reproduced from World Professional Association for Transgender Health (16).

reasons that are not gender identity related) (11). Clinicians should also be able to diagnose psychiatric conditions accurately and ensure that these conditions are treated appropriately, particularly when the conditions may complicate treatment, affect the outcome of gender-affirming treatment, or be affected by hormone use.

Values and preferences

The task force placed a very high value on avoiding harm from hormone treatment in individuals who have conditions other than GD/gender incongruence and who may not benefit from the physical changes associated with this treatment and placed a low value on any potential benefit these persons believe they may derive from hormone treatment. This justifies the good practice statement.

- 1.3. We advise that decisions regarding the social transition of prepubertal youths with GD/gender incongruence are made with the assistance of an MHP or another experienced professional. (Ungraded Good Practice Statement).
- 1.4. We recommend against puberty blocking and gender-affirming hormone treatment in prepubertal children with GD/gender incongruence. (1 ⊕⊕○○)

Evidence

In most children diagnosed with GD/gender incongruence, it did not persist into adolescence. The percentages differed among studies, probably dependent on which version of the DSM clinicians used, the patient's age, the recruitment criteria, and perhaps cultural factors. However, the large majority (about 85%) of prepubertal children with a childhood diagnosis did not remain GD/gender incongruent in adolescence (20). If children have completely socially transitioned, they may have great difficulty in returning to the original gender role upon entering puberty (40). Social transition is associated with the persistence of GD/gender incongruence as a child progresses into adolescence. It may be that the presence of GD/gender incongruence in prepubertal children is the earliest sign that a child is destined to be transgender as an adolescent/adult (20). However, social transition (in addition to GD/gender incongruence) has been found to contribute to the likelihood of persistence.

This recommendation, however, does not imply that children should be discouraged from showing gender-variant behaviors or should be punished for exhibiting such behaviors. In individual cases, an early complete social transition may result in a more favorable outcome, but there are currently no criteria to identify the

GD/gender-incongruent children to whom this applies. At the present time, clinical experience suggests that persistence of GD/gender incongruence can only be reliably assessed after the first signs of puberty.

Values and preferences

The task force placed a high value on avoiding harm with gender-affirming hormone therapy in prepubertal children with GD/gender incongruence. This justifies the strong recommendation in the face of low-quality evidence.

- 1.5. We recommend that clinicians inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression in adolescents and prior to treating with hormonal therapy of the affirmed gender in both adolescents and adults. (1 ⊕⊕⊕○)

Remarks

Persons considering hormone use for gender affirmation need adequate information about this treatment in general and about fertility effects of hormone treatment in particular to make an informed and balanced decision (67, 68). Because young adolescents may not feel qualified to make decisions about fertility and may not fully understand the potential effects of hormonal interventions, consent and protocol education should include parents, the referring MHP(s), and other members of the adolescent's support group. To our knowledge, there are no formally evaluated decision aids available to assist in the discussion and decision regarding the future fertility of adolescents or adults beginning gender-affirming treatment.

Treating early pubertal youth with GnRH analogs will temporarily impair spermatogenesis and oocyte maturation. Given that an increasing number of transgender youth want to preserve fertility potential, delaying or temporarily discontinuing GnRH analogs to promote gamete maturation is an option. This option is often not preferred, because mature sperm production is associated with later stages of puberty and with the significant development of secondary sex characteristics.

For those designated male at birth with GD/gender incongruence and who are in early puberty, sperm production and the development of the reproductive tract are insufficient for the cryopreservation of sperm. However, prolonged pubertal suppression using GnRH analogs is reversible and clinicians should inform these individuals that sperm production can be initiated following prolonged gonadotropin suppression. This can be accomplished by spontaneous gonadotropin recovery after

cessation of GnRH analogs or by gonadotropin treatment and will probably be associated with physical manifestations of testosterone production, as stated above. Note that there are no data in this population concerning the time required for sufficient spermatogenesis to collect enough sperm for later fertility. In males treated for precocious puberty, spermarche was reported 0.7 to 3 years after cessation of GnRH analogs (69). In adult men with gonadotropin deficiency, sperm are noted in seminal fluid by 6 to 12 months of gonadotropin treatment. However, sperm numbers when partners of these patients conceive are far below the “normal range” (70, 71).

In girls, no studies have reported long-term, adverse effects of pubertal suppression on ovarian function after treatment cessation (72, 73). Clinicians should inform adolescents that no data are available regarding either time to spontaneous ovulation after cessation of GnRH analogs or the response to ovulation induction following prolonged gonadotropin suppression.

In males with GD/gender incongruence, when medical treatment is started in a later phase of puberty or in adulthood, spermatogenesis is sufficient for cryopreservation and storage of sperm. *In vitro* spermatogenesis is currently under investigation. Restoration of spermatogenesis after prolonged estrogen treatment has not been studied.

In females with GD/gender incongruence, the effect of prolonged treatment with exogenous testosterone on ovarian function is uncertain. There have been reports of an increased incidence of polycystic ovaries in transgender males, both prior to and as a result of androgen treatment (74–77), although these reports were not confirmed by others (78). Pregnancy has been reported in transgender males who have had prolonged androgen treatment and have discontinued testosterone but have not had genital surgery (79, 80). A reproductive endocrine gynecologist can counsel patients before gender-affirming hormone treatment or surgery regarding potential fertility options (81). Techniques for cryopreservation of oocytes, embryos, and ovarian tissue continue to improve, and oocyte maturation of immature tissue is being studied (82).

2.0 Treatment of Adolescents

During the past decade, clinicians have progressively acknowledged the suffering of young adolescents with GD/gender incongruence. In some forms of GD/gender incongruence, psychological interventions may be useful and sufficient. However, for many adolescents with GD/gender incongruence, the pubertal physical changes are unbearable. As early medical intervention may prevent

psychological harm, various clinics have decided to start treating young adolescents with GD/gender incongruence with puberty-suppressing medication (a GnRH analog). As compared with starting gender-affirming treatment long after the first phases of puberty, a benefit of pubertal suppression at early puberty may be a better psychological and physical outcome.

In girls, the first physical sign of puberty is the budding of the breasts followed by an increase in breast and fat tissue. Breast development is also associated with the pubertal growth spurt, and menarche occurs ~2 years later. In boys, the first physical change is testicular growth. A testicular volume ≥ 4 mL is seen as consistent with the initiation of physical puberty. At the beginning of puberty, estradiol and testosterone levels are still low and are best measured in the early morning with an ultrasensitive assay. From a testicular volume of 10 mL, daytime testosterone levels increase, leading to virilization (83). Note that pubic hair and/or axillary hair/odor may not reflect the onset of gonadarche; instead, it may reflect adrenarche alone.

- 2.1. We suggest that adolescents who meet diagnostic criteria for GD/gender incongruence, fulfill criteria for treatment (Table 5), and are requesting treatment should initially undergo treatment to suppress pubertal development. (2 $\oplus\oplus\oplus\oplus$)
- 2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty (Tanner stages G2/B2). (2 $\oplus\oplus\oplus\oplus$)

Evidence

Pubertal suppression can expand the diagnostic phase by a long period, giving the subject more time to explore options and to live in the experienced gender before making a decision to proceed with gender-affirming sex hormone treatments and/or surgery, some of which is irreversible (84, 85). Pubertal suppression is fully reversible, enabling full pubertal development in the natal gender, after cessation of treatment, if appropriate. The experience of full endogenous puberty is an undesirable condition for the GD/gender-incongruent individual and may seriously interfere with healthy psychological functioning and well-being. Treating GD/gender-incongruent adolescents entering puberty with GnRH analogs has been shown to improve psychological functioning in several domains (86).

Another reason to start blocking pubertal hormones early in puberty is that the physical outcome is improved compared with initiating physical transition after puberty has been completed (60, 62). Looking like a man or woman when living as the opposite sex creates difficult

barriers with enormous life-long disadvantages. We therefore advise starting suppression in early puberty to prevent the irreversible development of undesirable secondary sex characteristics. However, adolescents with GD/gender incongruence should experience the first changes of their endogenous spontaneous puberty, because their emotional reaction to these first physical changes has diagnostic value in establishing the persistence of GD/gender incongruence (85). Thus, Tanner stage 2 is the optimal time to start pubertal suppression. However, pubertal suppression treatment in early puberty will limit the growth of the penis and scrotum, which will have a potential effect on future surgical treatments (87).

Clinicians can also use pubertal suppression in adolescents in later pubertal stages to stop menses in transgender males and prevent facial hair growth in transgender females. However, in contrast to the effects in early pubertal adolescents, physical sex characteristics (such as more advanced breast development in transgender boys and lowering of the voice and outgrowth of the jaw and brow in transgender girls) are not reversible.

Values and preferences

These recommendations place a high value on avoiding an unsatisfactory physical outcome when secondary sex characteristics have become manifest and irreversible, a higher value on psychological well-being, and a lower value on avoiding potential harm from early pubertal suppression.

Remarks

Table 6 lists the Tanner stages of breast and male genital development. Careful documentation of hallmarks of pubertal development will ensure precise timing when initiating pubertal suppression once puberty has started. Clinicians can use pubertal LH and sex steroid levels to confirm that puberty has progressed sufficiently before starting pubertal suppression (88). Reference

ranges for sex steroids by Tanner stage may vary depending on the assay used. Ultrasensitive sex steroid and gonadotropin assays will help clinicians document early pubertal changes.

Irreversible and, for GD/gender-incongruent adolescents, undesirable sex characteristics in female puberty are breasts, female body habitus, and, in some cases, relative short stature. In male puberty, they are a prominent Adam’s apple; low voice; male bone configuration, such as a large jaw, big feet and hands, and tall stature; and male hair pattern on the face and extremities.

- 2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. (1 ⊕ ⊕ ⊕ ⊕)

Evidence

Clinicians can suppress pubertal development and gonadal function most effectively via gonadotropin suppression using GnRH analogs. GnRH analogs are long-acting agonists that suppress gonadotropins by GnRH receptor desensitization after an initial increase of gonadotropins during ~10 days after the first and (to a lesser degree) the second injection (89). Antagonists immediately suppress pituitary gonadotropin secretion (90, 91). Long-acting GnRH analogs are the currently preferred treatment option. Clinicians may consider long-acting GnRH antagonists when evidence on their safety and efficacy in adolescents becomes available.

During GnRH analog treatment, slight development of secondary sex characteristics may regress, and in a later phase of pubertal development, it will stop. In girls, breast tissue will become atrophic, and menses will stop. In boys, virilization will stop, and testicular volume may decrease (92).

An advantage of using GnRH analogs is the reversibility of the intervention. If, after extensive exploration of his/her transition wish, the individual no longer desires transition, they can discontinue pubertal suppression. In subjects with

Table 6. Tanner Stages of Breast Development and Male External Genitalia

The description of Tanner stages for breast development:

1. Prepubertal
2. Breast and papilla elevated as small mound; areolar diameter increased
3. Breast and areola enlarged, no contour separation
4. Areola and papilla form secondary mound
5. Mature; nipple projects, areola part of general breast contour

For penis and testes:

1. Prepubertal, testicular volume <4 mL
2. Slight enlargement of penis; enlarged scrotum, pink, texture altered, testes 4–6 mL
3. Penis longer, testes larger (8–12 mL)
4. Penis and glans larger, including increase in breadth; testes larger (12–15 mL), scrotum dark
5. Penis adult size; testicular volume > 15 ml

Adapted from Lawrence (56).

precocious puberty, spontaneous pubertal development has been shown to resume after patients discontinue taking GnRH analogs (93).

Recommendations 2.1 to 2.3 are supported by a prospective follow-up study from The Netherlands. This report assessed mental health outcomes in 55 transgender adolescents/young adults (22 transgender females and 33 transgender males) at three time points: (1) before the start of GnRH agonist (average age of 14.8 years at start of treatment), (2) at initiation of gender-affirming hormones (average age of 16.7 years at start of treatment), and (3) 1 year after “gender-reassignment surgery” (average age of 20.7 years) (63). Despite a decrease in depression and an improvement in general mental health functioning, GD/gender incongruence persisted through pubertal suppression, as previously reported (86). However, following sex hormone treatment and gender-reassignment surgery, GD/gender incongruence was resolved and psychological functioning steadily improved (63). Furthermore, well-being was similar to or better than that reported by age-matched young adults from the general population, and none of the study participants regretted treatment. This study represents the first long-term follow-up of individuals managed according to currently existing clinical practice guidelines for transgender youth, and it underscores the benefit of the multidisciplinary approach pioneered in The Netherlands; however, further studies are needed.

Side effects

The primary risks of pubertal suppression in GD/gender-incongruent adolescents may include adverse effects on bone mineralization (which can theoretically be reversed with sex hormone treatment), compromised fertility if the person subsequently is treated with sex hormones, and unknown effects on brain development. Few data are available on the effect of GnRH analogs on BMD in adolescents with GD/gender incongruence. Initial data in GD/gender-incongruent subjects demonstrated no change of absolute areal BMD during 2 years of GnRH analog therapy but a decrease in BMD z scores (85). A recent study also suggested suboptimal bone mineral accrual during GnRH analog treatment. The study reported a decrease in areal BMD z scores and of bone mineral apparent density z scores (which takes the size of the bone into account) in 19 transgender males treated with GnRH analogs from a mean age of 15.0 years (standard deviation = 2.0 years) for a median duration of 1.5 years (0.3 to 5.2 years) and in 15 transgender females treated from 14.9 (± 1.9) years for 1.3 years (0.5 to 3.8 years), although not all changes were statistically significant (94). There was incomplete catch-up at age 22 years after sex hormone treatment from age 16.6 (± 1.4)

years for a median duration of 5.8 years (3.0 to 8.0 years) in transgender females and from age 16.4 (± 2.3) years for 5.4 years (2.8 to 7.8 years) in transgender males. Little is known about more prolonged use of GnRH analogs. Researchers reported normal BMD z scores at age 35 years in one individual who used GnRH analogs from age 13.7 years until age 18.6 years before initiating sex hormone treatment (65).

Additional data are available from individuals with late puberty or GnRH analog treatment of other indications. Some studies reported that men with constitutionally delayed puberty have decreased BMD in adulthood (95). However, other studies reported that these men have normal BMD (96, 97). Treating adults with GnRH analogs results in a decrease of BMD (98). In children with central precocious puberty, treatment with GnRH analogs has been found to result in a decrease of BMD during treatment by some (99) but not others (100). Studies have reported normal BMD after discontinuing therapy (69, 72, 73, 101, 102). In adolescents treated with growth hormone who are small for gestational age and have normal pubertal timing, 2-year GnRH analog treatments did not adversely affect BMD (103). Calcium supplementation may be beneficial in optimizing bone health in GnRH analog-treated individuals (104). There are no studies of vitamin D supplementation in this context, but clinicians should offer supplements to vitamin D-deficient adolescents. Physical activity, especially during growth, is important for bone mass in healthy individuals (103) and is therefore likely to be beneficial for bone health in GnRH analog-treated subjects.

GnRH analogs did not induce a change in body mass index standard deviation score in GD/gender-incongruent adolescents (94) but caused an increase in fat mass and decrease in lean body mass percentage (92). Studies in girls treated for precocious puberty also reported a stable body mass index standard deviation score during treatment (72) and body mass index and body composition comparable to controls after treatment (73).

Arterial hypertension has been reported as an adverse effect in a few girls treated with GnRH analogs for precocious/early puberty (105, 106). Blood pressure monitoring before and during treatment is recommended.

Individuals may also experience hot flashes, fatigue, and mood alterations as a consequence of pubertal suppression. There is no consensus on treatment of these side effects in this context.

It is recommended that any use of pubertal blockers (and subsequent use of sex hormones, as detailed below) include a discussion about implications for fertility (see recommendation 1.3). Transgender adolescents may

want to preserve fertility, which may be otherwise compromised if puberty is suppressed at an early stage and the individual completes phenotypic transition with the use of sex hormones.

Limited data are available regarding the effects of GnRH analogs on brain development. A single cross-sectional study demonstrated no compromise of executive function (107), but animal data suggest there may be an effect of GnRH analogs on cognitive function (108).

Values and preferences

Our recommendation of GnRH analogs places a higher value on the superior efficacy, safety, and reversibility of the pubertal hormone suppression achieved (as compared with the alternatives) and a relatively lower value on limiting the cost of therapy. Of the available alternatives, depot and oral progestin preparations are effective. Experience with this treatment dates back prior to the emergence of GnRH analogs for treating precocious puberty in papers from the 1960s and early 1970s (109–112). These compounds are usually safe, but some side effects have been reported (113–115). Only two recent studies involved transgender youth (116, 117). One of these studies described the use of oral lynestrenol monotherapy followed by the addition of testosterone treatment in transgender boys who were at Tanner stage B4 or further at the start of treatment (117). They found lynestrenol safe, but gonadotropins were not fully suppressed. The study reported metrorrhagia in approximately half of the individuals, mainly in the first 6 months. Acne, headache, hot flashes, and fatigue were other frequent side effects. Another progestin that has been studied in the United States is medroxyprogesterone. This agent is not as effective as GnRH analogs in lowering endogenous sex hormones either and may be associated with other side effects (116). Progestin preparations may be an acceptable treatment for persons without access to GnRH analogs or with a needle phobia. If GnRH analog treatment is not available (insurance denial, prohibitive cost, or other reasons), postpubertal, transgender female adolescents may be treated with an antiandrogen that directly suppresses androgen synthesis or action (see adult section).

Remarks

Measurements of gonadotropin and sex steroid levels give precise information about gonadal axis suppression, although there is insufficient evidence for any specific short-term monitoring scheme in children treated with GnRH analogs (88). If the gonadal axis is not completely suppressed—as evidenced by (for example) menses, erections, or progressive hair growth—the interval of GnRH analog treatment can be shortened or the dose increased. During treatment, adolescents should be monitored for negative effects of delaying puberty, including a halted growth spurt and impaired bone mineral accretion. Table 7 illustrates a suggested clinical protocol.

Anthropometric measurements and X-rays of the left hand to monitor bone age are informative for evaluating growth. To assess BMD, clinicians can perform dual-energy X-ray absorptiometry scans.

- 2.4. In adolescents who request sex hormone treatment (given this is a partly irreversible treatment), we recommend initiating treatment using a gradually increasing dose schedule (see Table 8) after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years (Table 5). (1 |⊕⊕○○)
- 2.5. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5 to 14 years. As with the care of adolescents ≥16 years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment. (1 |⊕○○○)
- 2.6. We suggest monitoring clinical pubertal development every 3 to 6 months and laboratory parameters every 6 to 12 months during sex hormone treatment (Table 9). (2 |⊕⊕○○)

Table 7. Baseline and Follow-Up Protocol During Suppression of Puberty

Every 3–6 mo
Anthropometry: height, weight, sitting height, blood pressure, Tanner stages
Every 6–12 mo
Laboratory: LH, FSH, E2/T, 25OH vitamin D
Every 1–2 y
Bone density using DXA
Bone age on X-ray of the left hand (if clinically indicated)

Adapted from Hembree *et al.* (118).
Abbreviations: DXA, dual-energy X-ray absorptiometry; E2, estradiol; FSH, follicle stimulating hormone; LH, luteinizing hormone; T, testosterone;

Table 8. Protocol Induction of Puberty

Induction of female puberty with oral 17β -estradiol, increasing the dose every 6 mo:

5 $\mu\text{g/kg/d}$

10 $\mu\text{g/kg/d}$

15 $\mu\text{g/kg/d}$

20 $\mu\text{g/kg/d}$

Adult dose = 2–6 mg/d

In postpubertal transgender female adolescents, the dose of 17β -estradiol can be increased more rapidly:

1 mg/d for 6 mo

2 mg/d

Induction of female puberty with transdermal 17β -estradiol, increasing the dose every 6 mo (new patch is placed every 3.5 d):

6.25–12.5 $\mu\text{g/24 h}$ (cut 25- μg patch into quarters, then halves)

25 $\mu\text{g/24 h}$

37.5 $\mu\text{g/24 h}$

Adult dose = 50–200 $\mu\text{g/24 h}$

For alternatives once at adult dose, see Table 11.

Adjust maintenance dose to mimic physiological estradiol levels (see Table 15).

Induction of male puberty with testosterone esters increasing the dose every 6 mo (IM or SC):

25 $\text{mg/m}^2/2 \text{ wk}$ (or alternatively, half this dose weekly, or double the dose every 4 wk)

50 $\text{mg/m}^2/2 \text{ wk}$

75 $\text{mg/m}^2/2 \text{ wk}$

100 $\text{mg/m}^2/2 \text{ wk}$

Adult dose = 100–200 mg every 2 wk

In postpubertal transgender male adolescents the dose of testosterone esters can be increased more rapidly:

75 mg/2 wk for 6 mo

125 mg/2 wk

For alternatives once at adult dose, see Table 11.

Adjust maintenance dose to mimic physiological testosterone levels (see Table 14).

Adapted from Hembree et al. (118).

Abbreviations: IM, intramuscularly; SC, subcutaneously.

Evidence

Adolescents develop competence in decision making at their own pace. Ideally, the supervising medical professionals should individually assess this competence, although no objective tools to make such an assessment are currently available.

Many adolescents have achieved a reasonable level of competence by age 15 to 16 years (119), and in many countries 16-year-olds are legally competent with regard to medical decision making (120). However, others believe that although some capacities are generally achieved before age 16 years, other abilities (such as good risk

assessment) do not develop until well after 18 years (121). They suggest that health care procedures should be divided along a matrix of relative risk, so that younger adolescents can be allowed to decide about low-risk procedures, such as most diagnostic tests and common therapies, but not about high-risk procedures, such as most surgical procedures (121).

Currently available data from transgender adolescents support treatment with sex hormones starting at age 16 years (63, 122). However, some patients may incur potential risks by waiting until age 16 years. These include the potential risk to bone health if puberty is suppressed

Table 9. Baseline and Follow-up Protocol During Induction of Puberty

Every 3–6 mo

•Anthropometry: height, weight, sitting height, blood pressure, Tanner stages

Every 6–12 mo

•In transgender males: hemoglobin/hematocrit, lipids, testosterone, 25OH vitamin D

•In transgender females: prolactin, estradiol, 25OH vitamin D

Every 1–2 y

•BMD using DXA

•Bone age on X-ray of the left hand (if clinically indicated)

BMD should be monitored into adulthood (until the age of 25–30 y or until peak bone mass has been reached).

For recommendations on monitoring once pubertal induction has been completed, see Tables 14 and 15.

Adapted from Hembree et al. (118).

Abbreviation: DXA, dual-energy X-ray absorptiometry.

for 6 to 7 years before initiating sex hormones (*e.g.*, if someone reached Tanner stage 2 at age 9–10 years old). Additionally, there may be concerns about inappropriate height and potential harm to mental health (emotional and social isolation) if initiation of secondary sex characteristics must wait until the person has reached 16 years of age. However, only minimal data supporting earlier use of gender-affirming hormones in transgender adolescents currently exist (63). Clearly, long-term studies are needed to determine the optimal age of sex hormone treatment in GD/gender-incongruent adolescents.

The MHP who has followed the adolescent during GnRH analog treatment plays an essential role in assessing whether the adolescent is eligible to start sex hormone therapy and capable of consenting to this treatment (Table 5). Support of the family/environment is essential. Prior to the start of sex hormones, clinicians should discuss the implications for fertility (see recommendation 1.5). Throughout pubertal induction, an MHP and a pediatric endocrinologist (or other clinician competent in the evaluation and induction of pubertal development) should monitor the adolescent. In addition to monitoring therapy, it is also important to pay attention to general adolescent health issues, including healthy life style choices, such as not smoking, contraception, and appropriate vaccinations (*e.g.*, human papillomavirus).

For the induction of puberty, clinicians can use a similar dose scheme for hypogonadal adolescents with GD/gender incongruence as they use in other individuals with hypogonadism, carefully monitoring for desired and undesired effects (Table 8). In transgender female adolescents, transdermal 17β -estradiol may be an alternative for oral 17β -estradiol. It is increasingly used for pubertal induction in hypogonadal females. However, the absence of low-dose estrogen patches may be a problem. As a result, individuals may need to cut patches to size themselves to achieve appropriate dosing (123). In transgender male adolescents, clinicians can give testosterone injections intramuscularly or subcutaneously (124, 125).

When puberty is initiated with a gradually increasing schedule of sex steroid doses, the initial levels will not be high enough to suppress endogenous sex steroid secretion. Gonadotropin secretion and endogenous production of testosterone may resume and interfere with the effectiveness of estrogen treatment, in transgender female adolescents (126, 127). Therefore, continuation of GnRH analog treatment is advised until gonadectomy. Given that GD/gender-incongruent adolescents may opt not to have gonadectomy, long-term studies are necessary to examine the potential risks of prolonged GnRH analog treatment. Alternatively, in transgender male adolescents, GnRH analog treatment can be discontinued once an

adult dose of testosterone has been reached and the individual is well virilized. If uterine bleeding occurs, a progestin can be added. However, the combined use of a GnRH analog (for ovarian suppression) and testosterone may enable phenotypic transition with a lower dose of testosterone in comparison with testosterone alone. If there is a wish or need to discontinue GnRH analog treatment in transgender female adolescents, they may be treated with an antiandrogen that directly suppresses androgen synthesis or action (see section 3.0 “Hormonal Therapy for Transgender Adults”).

Values and preferences

The recommendation to initiate pubertal induction only when the individual has sufficient mental capacity (roughly age 16 years) to give informed consent for this partly irreversible treatment places a higher value on the ability of the adolescent to fully understand and oversee the partially irreversible consequences of sex hormone treatment and to give informed consent. It places a lower value on the possible negative effects of delayed puberty. We may not currently have the means to weigh adequately the potential benefits of waiting until around age 16 years to initiate sex hormones vs the potential risks/harm to BMD and the sense of social isolation from having the timing of puberty be so out of sync with peers (128).

Remarks

Before starting sex hormone treatment, effects on fertility and options for fertility preservation should be discussed. Adult height may be a concern in transgender adolescents. In a transgender female adolescent, clinicians may consider higher doses of estrogen or a more rapid tempo of dose escalation during pubertal induction. There are no established treatments yet to augment adult height in a transgender male adolescent with open epiphyses during pubertal induction. It is not uncommon for transgender adolescents to present for clinical services after having completed or nearly completed puberty. In such cases, induction of puberty with sex hormones can be done more rapidly (see Table 8). Additionally, an adult dose of testosterone in transgender male adolescents may suffice to suppress the gonadal axis without the need to use a separate agent. At the appropriate time, the multidisciplinary team should adequately prepare the adolescent for transition to adult care.

3.0 Hormonal Therapy for Transgender Adults

The two major goals of hormonal therapy are (1) to reduce endogenous sex hormone levels, and thus reduce

the secondary sex characteristics of the individual's designated gender, and (2) to replace endogenous sex hormone levels consistent with the individual's gender identity by using the principles of hormone replacement treatment of hypogonadal patients. The timing of these two goals and the age at which to begin treatment with the sex hormones of the chosen gender is codetermined in collaboration with both the person pursuing transition and the health care providers. The treatment team should include a medical provider knowledgeable in transgender hormone therapy, an MHP knowledgeable in GD/gender incongruence and the mental health concerns of transition, and a primary care provider able to provide care appropriate for transgender individuals. The physical changes induced by this sex hormone transition are usually accompanied by an improvement in mental well-being (129, 130).

- 3.1. We recommend that clinicians confirm the diagnostic criteria of GD/gender incongruence and the criteria for the endocrine phase of gender transition before beginning treatment. (1 ⊕⊕⊕⊕)
- 3.2. We recommend that clinicians evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment (Table 10). (1 ⊕⊕⊕⊕)
- 3.3. We suggest that clinicians measure hormone levels during treatment to ensure that endogenous sex steroids are suppressed and administered sex steroids are maintained in the normal physiologic range for the affirmed gender. (2 ⊕⊕⊕⊕)

Evidence

It is the responsibility of the treating clinician to confirm that the person fulfills criteria for treatment. The treating clinician should become familiar with the terms and criteria presented in Tables 1–5 and take a thorough history from the patient in collaboration with the other members of the treatment team. The treating clinician must ensure that the desire for transition is appropriate; the consequences, risks, and benefits of treatment are well understood; and the desire for transition persists. They also need to discuss fertility preservation options (see recommendation 1.3) (67, 68).

Transgender males

Clinical studies have demonstrated the efficacy of several different androgen preparations to induce masculinization in transgender males (Appendix A) (113, 114, 131–134). Regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism (135). Clinicians can use either parenteral or transdermal preparations to achieve testosterone values in the normal male range (this is dependent on the specific assay, but is typically 320 to 1000 ng/dL) (Table 11) (136). Sustained supraphysiologic levels of testosterone increase the risk of adverse reactions (see section 4.0 “Adverse Outcome Prevention and Long-Term Care”) and should be avoided.

Similar to androgen therapy in hypogonadal men, testosterone treatment in transgender males results in increased muscle mass and decreased fat mass, increased facial hair and acne, male pattern baldness in those genetically predisposed, and increased sexual desire (137).

Table 10. Medical Risks Associated With Sex Hormone Therapy

Transgender female: estrogen

Very high risk of adverse outcomes:

- Thromboembolic disease

Moderate risk of adverse outcomes:

- Macroprolactinoma
- Breast cancer
- Coronary artery disease
- Cerebrovascular disease
- Cholelithiasis
- Hypertriglyceridemia

Transgender male: testosterone

Very high risk of adverse outcomes:

- Erythrocytosis (hematocrit > 50%)

Moderate risk of adverse outcomes:

- Severe liver dysfunction (transaminases > threefold upper limit of normal)
- Coronary artery disease
- Cerebrovascular disease
- Hypertension
- Breast or uterine cancer

Table 11. Hormone Regimens in Transgender Persons

Transgender females ^a	
Estrogen	
Oral	
Estradiol	2.0–6.0 mg/d
Transdermal	
Estradiol transdermal patch	0.025–0.2 mg/d
(New patch placed every 3–5 d)	
Parenteral	
Estradiol valerate or cypionate	5–30 mg IM every 2 wk 2–10 mg IM every week
Anti-androgens	
Spironolactone	100–300 mg/d
Cyproterone acetate ^b	25–50 mg/d
GnRH agonist	3.75 mg SQ (SC) monthly 11.25 mg SQ (SC) 3-monthly
Transgender males	
Testosterone	
Parenteral testosterone	
Testosterone enanthate or cypionate	100–200 mg SQ (IM) every 2 wk or SQ (SC) 50% per week
Testosterone undecanoate ^c	1000 mg every 12 wk
Transdermal testosterone	
Testosterone gel 1.6% ^d	50–100 mg/d
Testosterone transdermal patch	2.5–7.5 mg/d

Abbreviations: IM, intramuscularly; SQ, sequentially; SC, subcutaneously.

^aEstrogens used with or without antiandrogens or GnRH agonist.

^bNot available in the United States.

^cOne thousand milligrams initially followed by an injection at 6 wk then at 12-wk intervals.

^dAvoid cutaneous transfer to other individuals.

In transgender males, testosterone will result in clitoromegaly, temporary or permanent decreased fertility, deepening of the voice, cessation of menses (usually), and a significant increase in body hair, particularly on the face, chest, and abdomen. Cessation of menses may occur within a few months with testosterone treatment alone, although high doses of testosterone may be required. If uterine bleeding continues, clinicians may consider the addition of a progestational agent or endometrial ablation (138). Clinicians may also administer GnRH analogs or depot medroxyprogesterone to stop menses prior to testosterone treatment.

Transgender females

The hormone regimen for transgender females is more complex than the transgender male regimen (Appendix B). Treatment with physiologic doses of estrogen alone is insufficient to suppress testosterone levels into the normal range for females (139). Most published clinical studies report the need for adjunctive therapy to achieve testosterone levels in the female range (21, 113, 114, 132–134, 139, 140).

Multiple adjunctive medications are available, such as progestins with antiandrogen activity and GnRH agonists (141). Spironolactone works by directly blocking androgens during their interaction with the androgen

receptor (114, 133, 142). It may also have estrogenic activity (143). Cyproterone acetate, a progestational compound with antiandrogenic properties (113, 132, 144), is widely used in Europe. 5 α -Reductase inhibitors do not reduce testosterone levels and have adverse effects (145).

Dittrich *et al.* (141) reported that monthly doses of the GnRH agonist goserelin acetate in combination with estrogen were effective in reducing testosterone levels with a low incidence of adverse reactions in 60 transgender females. Leuprolide and transdermal estrogen were as effective as cyproterone and transdermal estrogen in a comparative retrospective study (146).

Patients can take estrogen as oral conjugated estrogens, oral 17 β -estradiol, or transdermal 17 β -estradiol. Among estrogen options, the increased risk of thromboembolic events associated with estrogens in general seems most concerning with ethinyl estradiol specifically (134, 140, 141), which is why we specifically suggest that it not be used in any transgender treatment plan. Data distinguishing among other estrogen options are less well established although there is some thought that oral routes of administration are more thrombogenic due to the “first pass effect” than are transdermal and parenteral routes, and that the risk of thromboembolic events is dose-dependent. Injectable estrogen and sublingual

estrogen may benefit from avoiding the first pass effect, but they can result in more rapid peaks with greater overall periodicity and thus are more difficult to monitor (147, 148). However, there are no data demonstrating that increased periodicity is harmful otherwise.

Clinicians can use serum estradiol levels to monitor oral, transdermal, and intramuscular estradiol. Blood tests cannot monitor conjugated estrogens or synthetic estrogen use. Clinicians should measure serum estradiol and serum testosterone and maintain them at the level for premenopausal females (100 to 200 pg/mL and <50 ng/dL, respectively). The transdermal preparations and injectable estradiol cypionate or valerate preparations may confer an advantage in older transgender females who may be at higher risk for thromboembolic disease (149).

Values

Our recommendation to maintain levels of gender-affirming hormones in the normal adult range places a high value on the avoidance of the long-term complications of pharmacologic doses. Those patients receiving endocrine treatment who have relative contraindications to hormones should have an in-depth discussion with their physician to balance the risks and benefits of therapy.

Remarks

Clinicians should inform all endocrine-treated individuals of all risks and benefits of gender-affirming hormones prior to initiating therapy. Clinicians should strongly encourage tobacco use cessation in transgender females to avoid increased risk of VTE and cardiovascular complications. We strongly discourage the unsupervised use of hormone therapy (150).

Not all individuals with GD/gender incongruence seek treatment as described (e.g., male-to-eunuchs and individuals seeking partial transition). Tailoring current protocols to the individual may be done within the context of accepted safety guidelines using a multidisciplinary approach including mental health. No evidence-based protocols are available for these groups (151). We need prospective studies to better understand treatment options for these persons.

- 3.4. We suggest that endocrinologists provide education to transgender individuals undergoing treatment about the onset and time course of physical changes induced by sex hormone treatment. (2 ⊕○○○)

Evidence

Transgender males

Physical changes that are expected to occur during the first 1 to 6 months of testosterone therapy include

cessation of menses, increased sexual desire, increased facial and body hair, increased oiliness of skin, increased muscle, and redistribution of fat mass. Changes that occur within the first year of testosterone therapy include deepening of the voice (152, 153), clitoromegaly, and male pattern hair loss (in some cases) (114, 144, 154, 155) (Table 12).

Transgender females

Physical changes that may occur in transgender females in the first 3 to 12 months of estrogen and anti-androgen therapy include decreased sexual desire, decreased spontaneous erections, decreased facial and body hair (usually mild), decreased oiliness of skin, increased breast tissue growth, and redistribution of fat mass (114, 139, 149, 154, 155, 161) (Table 13). Breast development is generally maximal at 2 years after initiating hormones (114, 139, 149, 155). Over a long period of time, the prostate gland and testicles will undergo atrophy.

Although the time course of breast development in transgender females has been studied (150), precise information about other changes induced by sex hormones is lacking (141). There is a great deal of variability among individuals, as evidenced during pubertal development. We all know that a major concern for transgender females is breast development. If we work with estrogens, the result will be often not what the transgender female expects.

Alternatively, there are transgender females who report an anecdotal improved breast development, mood, or sexual desire with the use of progestogens. However, there have been no well-designed studies of the role of progestogens in feminizing hormone regimens, so the question is still open.

Our knowledge concerning the natural history and effects of different cross-sex hormone therapies on breast

Table 12. Masculinizing Effects in Transgender Males

Effect	Onset	Maximum
Skin oiliness/acne	1–6 mo	1–2 y
Facial/body hair growth	6–12 mo	4–5 y
Scalp hair loss	6–12 mo	— ^a
Increased muscle mass/strength	6–12 mo	2–5 y
Fat redistribution	1–6 mo	2–5 y
Cessation of menses	1–6 mo	— ^b
Clitoral enlargement	1–6 mo	1–2 y
Vaginal atrophy	1–6 mo	1–2 y
Deepening of voice	6–12 mo	1–2 y

Estimates represent clinical observations: Toorians *et al.* (149), Assche-man *et al.* (156), Gooren *et al.* (157), Wierckx *et al.* (158).

^aPrevention and treatment as recommended for biological men.

^bMenorrhagia requires diagnosis and treatment by a gynecologist.

Table 13. Feminizing Effects in Transgender Females

Effect	Onset	Maximum
Redistribution of body fat	3–6 mo	2–3 y
Decrease in muscle mass and strength	3–6 mo	1–2 y
Softening of skin/decreased oiliness	3–6 mo	Unknown
Decreased sexual desire	1–3 mo	3–6 mo
Decreased spontaneous erections	1–3 mo	3–6 mo
Male sexual dysfunction	Variable	Variable
Breast growth	3–6 mo	2–3 y
Decreased testicular volume	3–6 mo	2–3 y
Decreased sperm production	Unknown	>3 y
Decreased terminal hair growth	6–12 mo	>3 y ^a
Scalp hair	Variable	— ^b
Voice changes	None	— ^c

Estimates represent clinical observations: Toorians *et al.* (149), Asscheman *et al.* (156), Gooren *et al.* (157).

^aComplete removal of male sexual hair requires electrolysis or laser treatment or both.

^bFamilial scalp hair loss may occur if estrogens are stopped.

^cTreatment by speech pathologists for voice training is most effective.

development in transgender females is extremely sparse and based on the low quality of evidence. Current evidence does not indicate that progestogens enhance breast development in transgender females, nor does evidence prove the absence of such an effect. This prevents us from drawing any firm conclusion at this moment and demonstrates the need for further research to clarify these important clinical questions (162).

Values and preferences

Transgender persons have very high expectations regarding the physical changes of hormone treatment and are aware that body changes can be enhanced by surgical procedures (*e.g.*, breast, face, and body habitus). Clear expectations for the extent and timing of sex hormone-induced changes may prevent the potential harm and expense of unnecessary procedures.

4.0 Adverse Outcome Prevention and Long-Term Care

Hormone therapy for transgender males and females confers many of the same risks associated with sex hormone replacement therapy in nontransgender persons. The risks arise from and are worsened by inadvertent or intentional use of supraphysiologic doses of sex hormones, as well as use of inadequate doses of sex hormones to maintain normal physiology (131, 139).

- 4.1. We suggest regular clinical evaluation for physical changes and potential adverse changes in response to sex steroid hormones and laboratory monitoring of sex steroid hormone levels every

3 months during the first year of hormone therapy for transgender males and females and then once or twice yearly. (2 ⊕⊕○○)

Evidence

Pretreatment screening and appropriate regular medical monitoring are recommended for both transgender males and females during the endocrine transition and periodically thereafter (26, 155). Clinicians should monitor weight and blood pressure, conduct physical exams, and assess routine health questions, such as tobacco use, symptoms of depression, and risk of adverse events such as deep vein thrombosis/pulmonary embolism and other adverse effects of sex steroids.

Transgender males

Table 14 contains a standard monitoring plan for transgender males on testosterone therapy (154, 159). Key issues include maintaining testosterone levels in the physiologic normal male range and avoiding adverse events resulting from excess testosterone therapy, particularly erythrocytosis, sleep apnea, hypertension, excessive weight gain, salt retention, lipid changes, and excessive or cystic acne (135).

Because oral 17-alkylated testosterone is not recommended, serious hepatic toxicity is not anticipated with parenteral or transdermal testosterone use (163, 164). Past concerns regarding liver toxicity with testosterone have been alleviated with subsequent reports that indicate the risk of serious liver disease is minimal (144, 165, 166).

Transgender females

Table 15 contains a standard monitoring plan for transgender females on estrogens, gonadotropin suppression, or antiandrogens (160). Key issues include avoiding supraphysiologic doses or blood levels of estrogen that may lead to increased risk for thromboembolic disease, liver dysfunction, and hypertension. Clinicians should monitor serum estradiol levels using laboratories participating in external quality control, as measurements of estradiol in blood can be very challenging (167).

VTE may be a serious complication. A study reported a 20-fold increase in venous thromboembolic disease in a large cohort of Dutch transgender subjects (161). This increase may have been associated with the use of the synthetic estrogen, ethinyl estradiol (149). The incidence decreased when clinicians stopped administering ethinyl estradiol (161). Thus, the use of synthetic estrogens and conjugated estrogens is undesirable because of the inability to regulate doses by measuring serum levels and the risk of thromboembolic disease. In a German gender clinic, deep vein thrombosis occurred in 1 of 60 of transgender females treated with a GnRH analog and oral

Table 14. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Male

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of virilization and for development of adverse reactions.
2. Measure serum testosterone every 3 mo until levels are in the normal physiologic male range:^a
 - a. For testosterone enanthate/cypionate injections, the testosterone level should be measured midway between injections. The target level is 400–700 ng/dL to 400 ng/dL. Alternatively, measure peak and trough levels to ensure levels remain in the normal male range.
 - b. For parenteral testosterone undecanoate, testosterone should be measured just before the following injection. If the level is <400 ng/dL, adjust dosing interval.
 - c. For transdermal testosterone, the testosterone level can be measured no sooner than after 1 wk of daily application (at least 2 h after application).
3. Measure hematocrit or hemoglobin at baseline and every 3 mo for the first year and then one to two times a year. Monitor weight, blood pressure, and lipids at regular intervals.
4. Screening for osteoporosis should be conducted in those who stop testosterone treatment, are not compliant with hormone therapy, or who develop risks for bone loss.
5. If cervical tissue is present, monitoring as recommended by the American College of Obstetricians and Gynecologists.
6. Ovariectomy can be considered after completion of hormone transition.
7. Conduct sub- and periareolar annual breast examinations if mastectomy performed. If mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society.

^aAdapted from Lapauw *et al.* (154) and Ott *et al.* (159).

estradiol (141). The patient who developed a deep vein thrombosis was found to have a homozygous C677 T mutation in the methylenetetrahydrofolate reductase gene. In an Austrian gender clinic, administering gender-affirming hormones to 162 transgender females and 89 transgender males was not associated with VTE, despite an 8.0% and 5.6% incidence of thrombophilia (159). A more recent multinational study reported only 10 cases of VTE from a cohort of 1073 subjects (168). Thrombophilia screening of transgender persons initiating hormone treatment should be restricted to those with a personal or family history of VTE (159). Monitoring D-dimer levels during treatment is not recommended (169).

- 4.2. We suggest periodically monitoring prolactin levels in transgender females treated with estrogens. (2 ⊕⊕○○)

Evidence

Estrogen therapy can increase the growth of pituitary lactotroph cells. There have been several reports of prolactinomas occurring after long-term, high-dose

estrogen therapy (170–173). Up to 20% of transgender females treated with estrogens may have elevations in prolactin levels associated with enlargement of the pituitary gland (156). In most cases, the serum prolactin levels will return to the normal range with a reduction or discontinuation of the estrogen therapy or discontinuation of cyproterone acetate (157, 174, 175).

The onset and time course of hyperprolactinemia during estrogen treatment are not known. Clinicians should measure prolactin levels at baseline and then at least annually during the transition period and every 2 years thereafter. Given that only a few case studies reported prolactinomas, and prolactinomas were not reported in large cohorts of estrogen-treated persons, the risk is likely to be very low. Because the major presenting findings of microprolactinomas (hypogonadism and sometimes gynecomastia) are not apparent in transgender females, clinicians may perform radiologic examinations of the pituitary in those patients whose prolactin levels persistently increase despite stable or reduced estrogen levels. Some transgender individuals receive psychotropic medications that can increase prolactin levels (174).

Table 15. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Female

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of feminization and for development of adverse reactions.
2. Measure serum testosterone and estradiol every 3 mo.
 - a. Serum testosterone levels should be <50 ng/dL.
 - b. Serum estradiol should not exceed the peak physiologic range: 100–200 pg/mL.
3. For individuals on spironolactone, serum electrolytes, particularly potassium, should be monitored every 3 mo in the first year and annually thereafter.
4. Routine cancer screening is recommended, as in nontransgender individuals (all tissues present).
5. Consider BMD testing at baseline (160). In individuals at low risk, screening for osteoporosis should be conducted at age 60 years or in those who are not compliant with hormone therapy.

This table presents strong recommendations and does not include lower level recommendations.

- 4.3. We suggest that clinicians evaluate transgender persons treated with hormones for cardiovascular risk factors using fasting lipid profiles, diabetes screening, and/or other diagnostic tools. (2 ⊕⊕○○)

Evidence

Transgender males

Administering testosterone to transgender males results in a more atherogenic lipid profile with lowered high-density lipoprotein cholesterol and higher triglyceride and low-density lipoprotein cholesterol values (176–179). Studies of the effect of testosterone on insulin sensitivity have mixed results (178, 180). A randomized, open-label uncontrolled safety study of transgender males treated with testosterone undecanoate demonstrated no insulin resistance after 1 year (181, 182). Numerous studies have demonstrated the effects of sex hormone treatment on the cardiovascular system (160, 179, 183, 184). Long-term studies from The Netherlands found no increased risk for cardiovascular mortality (161). Likewise, a meta-analysis of 19 randomized trials in nontransgender males on testosterone replacement showed no increased incidence of cardiovascular events (185). A systematic review of the literature found that data were insufficient (due to very low-quality evidence) to allow a meaningful assessment of patient-important outcomes, such as death, stroke, myocardial infarction, or VTE in transgender males (176). Future research is needed to ascertain the potential harm of hormonal therapies (176). Clinicians should manage cardiovascular risk factors as they emerge according to established guidelines (186).

Transgender females

A prospective study of transgender females found favorable changes in lipid parameters with increased high-density lipoprotein and decreased low-density lipoprotein concentrations (178). However, increased weight, blood pressure, and markers of insulin resistance attenuated these favorable lipid changes. In a meta-analysis, only serum triglycerides were higher at ≥24 months without changes in other parameters (187). The largest cohort of transgender females (mean age 41 years, followed for a mean of 10 years) showed no increase in cardiovascular mortality despite a 32% rate of tobacco use (161).

Thus, there is limited evidence to determine whether estrogen is protective or detrimental on lipid and glucose metabolism in transgender females (176). With aging, there is usually an increase of body weight. Therefore, as with nontransgender individuals, clinicians should

monitor and manage glucose and lipid metabolism and blood pressure regularly according to established guidelines (186).

- 4.4. We recommend that clinicians obtain BMD measurements when risk factors for osteoporosis exist, specifically in those who stop sex hormone therapy after gonadectomy. (1 ⊕⊕○○)

Evidence

Transgender males

Baseline bone mineral measurements in transgender males are generally in the expected range for their pre-treatment gender (188). However, adequate dosing of testosterone is important to maintain bone mass in transgender males (189, 190). In one study (190), serum LH levels were inversely related to BMD, suggesting that low levels of sex hormones were associated with bone loss. Thus, LH levels in the normal range may serve as an indicator of the adequacy of sex steroid administration to preserve bone mass. The protective effect of testosterone may be mediated by peripheral conversion to estradiol, both systemically and locally in the bone.

Transgender females

A baseline study of BMD reported T scores less than −2.5 in 16% of transgender females (191). In aging males, studies suggest that serum estradiol more positively correlates with BMD than does testosterone (192, 193) and is more important for peak bone mass (194). Estrogen preserves BMD in transgender females who continue on estrogen and antiandrogen therapies (188, 190, 191, 195, 196).

Fracture data in transgender males and females are not available. Transgender persons who have undergone gonadectomy may choose not to continue consistent sex steroid treatment after hormonal and surgical sex reassignment, thereby becoming at risk for bone loss. There have been no studies to determine whether clinicians should use the sex assigned at birth or affirmed gender for assessing osteoporosis (e.g., when using the FRAX tool). Although some researchers use the sex assigned at birth (with the assumption that bone mass has usually peaked for transgender people who initiate hormones in early adulthood), this should be assessed on a case-by-case basis until there are more data available. This assumption will be further complicated by the increasing prevalence of transgender people who undergo hormonal transition at a pubertal age or soon after puberty. Sex for comparison within risk assessment tools may be based on the age at which hormones were initiated and the length of exposure to hormones. In some cases, it may be

reasonable to assess risk using both the male and female calculators and using an intermediate value. Because all subjects underwent normal pubertal development, with known effects on bone size, reference values for birth sex were used for all participants (154).

- 4.5. We suggest that transgender females with no known increased risk of breast cancer follow breast-screening guidelines recommended for those designated female at birth. (2 ⊕⊕○○)
- 4.6. We suggest that transgender females treated with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 ⊕○○○)

Evidence

Studies have reported a few cases of breast cancer in transgender females (197–200). A Dutch study of 1800 transgender females followed for a mean of 15 years (range of 1–30 years) found one case of breast cancer. The Women's Health Initiative study reported that females taking conjugated equine estrogen without progesterone for 7 years did not have an increased risk of breast cancer as compared with females taking placebo (137).

In transgender males, a large retrospective study conducted at the U.S. Veterans Affairs medical health system identified seven breast cancers (194). The authors reported that this was not above the expected rate of breast cancers in cisgender females in this cohort. Furthermore, they did report one breast cancer that developed in a transgender male patient after mastectomy, supporting the fact that breast cancer can occur even after mastectomy. Indeed, there have been case reports of breast cancer developing in subareolar tissue in transgender males, which occurred after mastectomy (201, 202).

Women with primary hypogonadism (Turner syndrome) treated with estrogen replacement exhibited a significantly decreased incidence of breast cancer as compared with national standardized incidence ratios (203, 204). These studies suggest that estrogen therapy does not increase the risk of breast cancer in the short term (<20 to 30 years). We need long-term studies to determine the actual risk, as well as the role of screening mammograms. Regular examinations and gynecologic advice should determine monitoring for breast cancer.

Prostate cancer is very rare before the age of 40, especially with androgen deprivation therapy (205). Childhood or pubertal castration results in regression of the prostate and adult castration reverses benign prostate hypertrophy (206). Although van Kesteren *et al.* (207) reported that estrogen therapy does not induce hypertrophy or premalignant changes in the prostates of

transgender females, studies have reported cases of benign prostatic hyperplasia in transgender females treated with estrogens for 20 to 25 years (208, 209). Studies have also reported a few cases of prostate carcinoma in transgender females (210–214).

Transgender females may feel uncomfortable scheduling regular prostate examinations. Gynecologists are not trained to screen for prostate cancer or to monitor prostate growth. Thus, it may be reasonable for transgender females who transitioned after age 20 years to have annual screening digital rectal examinations after age 50 years and prostate-specific antigen tests consistent with U.S. Preventive Services Task Force Guidelines (215).

- 4.7. We advise that clinicians determine the medical necessity of including a total hysterectomy and oophorectomy as part of gender-affirming surgery. (Ungraded Good Practice Statement)

Evidence

Although aromatization of testosterone to estradiol in transgender males has been suggested as a risk factor for endometrial cancer (216), no cases have been reported. When transgender males undergo hysterectomy, the uterus is small and there is endometrial atrophy (217, 218). Studies have reported cases of ovarian cancer (219, 220). Although there is limited evidence for increased risk of reproductive tract cancers in transgender males, health care providers should determine the medical necessity of a laparoscopic total hysterectomy as part of a gender-affirming surgery to prevent reproductive tract cancer (221).

Values

Given the discomfort that transgender males experience accessing gynecologic care, our recommendation for the medical necessity of total hysterectomy and oophorectomy places a high value on eliminating the risks of female reproductive tract disease and cancer and a lower value on avoiding the risks of these surgical procedures (related to the surgery and to the potential undesirable health consequences of oophorectomy) and their associated costs.

Remarks

The sexual orientation and type of sexual practices will determine the need and types of gynecologic care required following transition. Additionally, in certain countries, the approval required to change the sex in a birth certificate for transgender males may be dependent on having a complete hysterectomy. Clinicians should help patients research nonmedical administrative criteria and

provide counseling. If individuals decide not to undergo hysterectomy, screening for cervical cancer is the same as all other females.

5.0 Surgery for Sex Reassignment and Gender Confirmation

For many transgender adults, genital gender-affirming surgery may be the necessary step toward achieving their ultimate goal of living successfully in their desired gender role. The type of surgery falls into two main categories: (1) those that directly affect fertility and (2) those that do not. Those that change fertility (previously called sex reassignment surgery) include genital surgery to remove the penis and gonads in the male and removal of the uterus and gonads in the female. The surgeries that effect fertility are often governed by the legal system of the state or country in which they are performed. Other gender-conforming surgeries that do not directly affect fertility are not so tightly governed.

Gender-affirming surgical techniques have improved markedly during the past 10 years. Reconstructive genital surgery that preserves neurologic sensation is now the standard. The satisfaction rate with surgical reassignment of sex is now very high (187). Additionally, the mental health of the individual seems to be improved by participating in a treatment program that defines a pathway of gender-affirming treatment that includes hormones and surgery (130, 144) (Table 16).

Surgery that affects fertility is irreversible. The World Professional Association for Transgender Health Standards of Care (222) emphasizes that the “threshold of 18 should not be seen as an indication in itself for active intervention.” If the social transition has not been satisfactory, if the person is not satisfied with or is ambivalent about the effects of sex hormone treatment, or if the person is ambivalent about surgery then the individual should not be referred for surgery (223, 224).

Gender-affirming genital surgeries for transgender females that affect fertility include gonadectomy, penectomy, and creation of a neovagina (225, 226). Surgeons often invert the skin of the penis to form the wall of the vagina, and several literatures reviews have

reported on outcomes (227). Sometimes there is inadequate tissue to form a full neovagina, so clinicians have revisited using intestine and found it to be successful (87, 228, 229). Some newer vaginoplasty techniques may involve autologous oral epithelial cells (230, 231).

The scrotum becomes the labia majora. Surgeons use reconstructive surgery to fashion the clitoris and its hood, preserving the neurovascular bundle at the tip of the penis as the neurosensory supply to the clitoris. Some surgeons are also creating a sensate pedicled-spot adding a G spot to the neovagina to increase sensation (232). Most recently, plastic surgeons have developed techniques to fashion labia minora. To further complete the feminization, uterine transplants have been proposed and even attempted (233).

Neovaginal prolapse, rectovaginal fistula, delayed healing, vaginal stenosis, and other complications do sometimes occur (234, 235). Clinicians should strongly remind the transgender person to use their dilators to maintain the depth and width of the vagina throughout the postoperative period. Genital sexual responsivity and other aspects of sexual function are usually preserved following genital gender-affirming surgery (236, 237).

Ancillary surgeries for more feminine or masculine appearance are not within the scope of this guideline. Voice therapy by a speech language pathologist is available to transform speech patterns to the affirmed gender (148). Spontaneous voice deepening occurs during testosterone treatment of transgender males (152, 238). No studies have compared the effectiveness of speech therapy, laryngeal surgery, or combined treatment.

Breast surgery is a good example of gender-confirming surgery that does not affect fertility. In all females, breast size exhibits a very broad spectrum. For transgender females to make the best informed decision, clinicians should delay breast augmentation surgery until the patient has completed at least 2 years of estrogen therapy, because the breasts continue to grow during that time (141, 155).

Another major procedure is the removal of facial and masculine-appearing body hair using either electrolysis or

Table 16. Criteria for Gender-Affirming Surgery, Which Affects Fertility

1. Persistent, well-documented gender dysphoria
2. Legal age of majority in the given country
3. Having continuously and responsibly used gender-affirming hormones for 12 mo (if there is no medical contraindication to receiving such therapy)
4. Successful continuous full-time living in the new gender role for 12 mo
5. If significant medical or mental health concerns are present, they must be well controlled
6. Demonstrable knowledge of all practical aspects of surgery (e.g., cost, required lengths of hospitalizations, likely complications, postsurgical rehabilitation)

laser treatments. Other feminizing surgeries, such as that to feminize the face, are now becoming more popular (239–241).

In transgender males, clinicians usually delay gender-affirming genital surgeries until after a few years of androgen therapy. Those surgeries that affect fertility in this group include oophorectomy, vaginectomy, and complete hysterectomy. Surgeons can safely perform them vaginally with laparoscopy. These are sometimes done in conjunction with the creation of a neopenis. The cosmetic appearance of a neopenis is now very good, but the surgery is multistage and very expensive (242, 243). Radial forearm flap seems to be the most satisfactory procedure (228, 244). Other flaps also exist (245). Surgeons can make neopenile erections possible by reinnervation of the flap and subsequent contraction of the muscle, leading to stiffening of the neopenis (246, 247), but results are inconsistent (248). Surgeons can also stiffen the penis by imbedding some mechanical device (*e.g.*, a rod or some inflatable apparatus) (249, 250). Because of these limitations, the creation of a neopenis has often been less than satisfactory. Recently, penis transplants are being proposed (233).

In fact, most transgender males do not have any external genital surgery because of the lack of access, high cost, and significant potential complications. Some choose a metaoidioplasty that brings forward the clitoris, thereby allowing them to void in a standing position without wetting themselves (251, 252). Surgeons can create the scrotum from the labia majora with good cosmetic effect and can implant testicular prostheses (253).

The most important masculinizing surgery for the transgender male is mastectomy, and it does not affect fertility. Breast size only partially regresses with androgen therapy (155). In adults, discussions about mastectomy usually take place after androgen therapy has started. Because some transgender male adolescents present after significant breast development has occurred, they may also consider mastectomy 2 years after they begin androgen therapy and before age 18 years. Clinicians should individualize treatment based on the physical and mental health status of the individual. There are now newer approaches to mastectomy with better outcomes (254, 255). These often involve chest contouring (256). Mastectomy is often necessary for living comfortably in the new gender (256).

- 5.1. We recommend that a patient pursue genital gender-affirming surgery only after the MHP and the clinician responsible for endocrine transition therapy both agree that surgery is medically

necessary and would benefit the patient's overall health and/or well-being. (1 ⊕⊕○○)

- 5.2. We advise that clinicians approve genital gender-affirming surgery only after completion of at least 1 year of consistent and compliant hormone treatment, unless hormone therapy is not desired or medically contraindicated. (Ungraded Good Practice Statement)
- 5.3. We advise that the clinician responsible for endocrine treatment and the primary care provider ensure appropriate medical clearance of transgender individuals for genital gender-affirming surgery and collaborate with the surgeon regarding hormone use during and after surgery. (Ungraded Good Practice Statement)
- 5.4. We recommend that clinicians refer hormone-treated transgender individuals for genital surgery when: (1) the individual has had a satisfactory social role change, (2) the individual is satisfied about the hormonal effects, and (3) the individual desires definitive surgical changes. (1 ⊕○○○)
- 5.5. We suggest that clinicians delay gender-affirming genital surgery involving gonadectomy and/or hysterectomy until the patient is at least 18 years old or legal age of majority in his or her country. (2 ⊕⊕○○)
- 5.6. We suggest that clinicians determine the timing of breast surgery for transgender males based upon the physical and mental health status of the individual. There is insufficient evidence to recommend a specific age requirement. (2 ⊕○○○)

Evidence

Owing to the lack of controlled studies, incomplete follow-up, and lack of valid assessment measures, evaluating various surgical approaches and techniques is difficult. However, one systematic review including a large numbers of studies reported satisfactory cosmetic and functional results for vaginoplasty/neovagina construction (257). For transgender males, the outcomes are less certain. However, the problems are now better understood (258). Several postoperative studies report significant long-term psychological and psychiatric pathology (259–261). One study showed satisfaction with breasts, genitals, and femininity increased significantly and showed the importance of surgical treatment as a key therapeutic option for transgender females (262). Another analysis demonstrated that, despite the young average age at death following surgery and the relatively larger number of individuals with somatic morbidity, the study does not allow for determination of

causal relationships between, for example, specific types of hormonal or surgical treatment received and somatic morbidity and mortality (263). Reversal surgery in regretful male-to-female transsexuals after sexual reassignment surgery represents a complex, multistage procedure with satisfactory outcomes. Further insight into the characteristics of persons who regret their decision postoperatively would facilitate better future selection of applicants eligible for sexual reassignment surgery. We need more studies with appropriate controls that examine long-term quality of life, psychosocial outcomes, and psychiatric outcomes to determine the long-term benefits of surgical treatment.

When a transgender individual decides to have gender-affirming surgery, both the hormone prescribing clinician and the MHP must certify that the patient satisfies criteria for gender-affirming surgery (Table 16).

There is some concern that estrogen therapy may cause an increased risk for venous thrombosis during or following surgery (176). For this reason, the surgeon and the hormone-prescribing clinician should collaborate in making a decision about the use of hormones before and following surgery. One study suggests that preoperative factors (such as compliance) are less important for patient satisfaction than are the physical postoperative results (56). However, other studies and clinical experience dictate that individuals who do not follow medical instructions and do not work with their physicians toward a common goal do not achieve treatment goals (264) and experience higher rates of postoperative infections and other complications (265, 266). It is also important that the person requesting surgery feels comfortable with the anatomical changes that have occurred during hormone therapy. Dissatisfaction with social and physical outcomes during the hormone transition may be a contraindication to surgery (223).

An endocrinologist or experienced medical provider should monitor transgender individuals after surgery. Those who undergo gonadectomy will require hormone replacement therapy, surveillance, or both to prevent adverse effects of chronic hormone deficiency.

Financial Disclosures of the Task Force*

Wylie C. Hembree (chair)—financial or business/organizational interests: none declared, significant financial interest or leadership position: none declared. **Peggy T. Cohen-Kettenis**—financial or business/organizational interests: none declared, significant financial interest or leadership position: none declared. **Louis Gooren**—financial or business/organizational interests: none declared, significant financial

interest or leadership position: none declared. **Sabine E. Hannema**—financial or business/organizational interests: none declared, significant financial interest or leadership position: Ferring Pharmaceuticals Inc. (lecture/conference), Pfizer (lecture). **Walter J. Meyer**—financial or business/organizational interests: none declared, significant financial interest or leadership position: none declared. **M. Hassan Murad****—financial or business/organizational interests: Mayo Clinic, Evidence-based Practice Center, significant financial interest or leadership position: none declared. **Stephen M. Rosenthal**—financial or business/organizational interests: AbbVie (consultant), National Institutes of Health (grantee), significant financial interest or leadership position: Pediatric Endocrine Society (immediate past president). **Joshua D. Safer, FACP**—financial or business/organizational interests: none declared, significant financial interest or leadership position: none declared. **Vin Tangpricha**—financial or business/organizational interests: Cystic Fibrosis Foundation (grantee), National Institutes of Health (grantee), significant financial interest or leadership position, Elsevier *Journal of Clinical and Translational Endocrinology* (editor). **Guy G. T'Sjoen**—financial or business/organizational interests: none declared, significant financial interest or leadership position: none declared.* Financial, business, and organizational disclosures of the task force cover the year prior to publication. Disclosures prior to this time period are archived.**Evidence-based reviews for this guideline were prepared under contract with the Endocrine Society.

Acknowledgments

Correspondence and Reprint Requests: The Endocrine Society, 2055 L Street NW, Suite 600, Washington, DC 20036. E-mail: publications@endocrine.org; Phone: 202971-3636.

Disclosure Summary: See Financial Disclosures.

Disclaimer: The Endocrine Society's clinical practice guidelines are developed to be of assistance to endocrinologists by providing guidance and recommendations for particular areas of practice. The guidelines should not be considered inclusive of all proper approaches or methods, or exclusive of others. The guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgement of healthcare providers and each patient's individual circumstances.

The Endocrine Society makes no warranty, express or implied, regarding the guidelines and specifically excludes any warranties of merchantability and fitness for a particular use or purpose. The Society shall not be liable for direct, indirect,

special, incidental, or consequential damages related to the use of the information contained herein.

References

- Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, Hill S, Jaeschke R, Leng G, Liberati A, Magrini N, Mason J, Middleton P, Mrukowicz J, O'Connell D, Oxman AD, Phillips B, Schünemann HJ, Edejer T, Varonen H, Vist GE, Williams JW, Jr, Zaza S; GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ*. 2004;328(7454):1490.
- Swiglo BA, Murad MH, Schünemann HJ, Kunz R, Vigersky RA, Guyatt GH, Montori VM. A case for clarity, consistency, and helpfulness: state-of-the-art clinical practice guidelines in endocrinology using the grading of recommendations, assessment, development, and evaluation system. *J Clin Endocrinol Metab*. 2008;93(3):666–673.
- Bullough VL. Transsexualism in history. *Arch Sex Behav*. 1975;4(5):561–571.
- Benjamin H. The transsexual phenomenon. *Trans N Y Acad Sci*. 1967;29(4):428–430.
- Meyerowitz J. *How Sex Changed: A History of Transsexuality in the United States*. Cambridge, MA: Harvard University Press; 2002.
- Hirschfeld M. *Was muss das Volk vom Dritten Geschlecht wissen*. Verlag Max Spohr, Leipzig; 1901.
- Fisk NM. Editorial: Gender dysphoria syndrome—the conceptualization that liberalizes indications for total gender re-orientation and implies a broadly based multi-dimensional rehabilitative regimen. *West J Med*. 1974;120(5):386–391.
- Diamond L. Transgender experience and identity. In: Schwartz SJ, Luyckx K, Vignoles VL, eds. *Handbook of Identity Theory and Research*. New York, NY: Springer; 2011:629–647.
- Queen C, Schimmel L, eds. *PoMoSexuals: Challenging Assumptions About Gender and Sexuality*. San Francisco, CA: Cleis Press; 1997.
- Case LK, Ramachandran VS. Alternating gender incongruity: a new neuropsychiatric syndrome providing insight into the dynamic plasticity of brain-sex. *Med Hypotheses*. 2012;78(5):626–631.
- Johnson TW, Wassersug RJ. Gender identity disorder outside the binary: when gender identity disorder-not otherwise specified is not good enough. *Arch Sex Behav*. 2010;39(3):597–598.
- Wibowo E, Wassersug R, Warkentin K, Walker L, Robinson J, Brotto L, Johnson T. Impact of androgen deprivation therapy on sexual function: a response. *Asian J Androl*. 2012;14(5):793–794.
- Pasquosoone V. 7 countries giving transgender people fundamental rights the U.S. still won't. 2014. Available at: <https://mic.com/articles/87149/7-countries-giving-transgender-people-fundamental-rights-the-u-s-still-won-t>. Accessed 26 August 2016.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association Publishing.
- Drescher J, Cohen-Kettenis P, Winter S. Minding the body: situating gender identity diagnoses in the ICD-11. *Int Rev Psychiatry*. 2012;24(6):568–577.
- World Professional Association for Transgender Health. Standards of care for the health of transsexual, transgender, and gender nonconforming people. Available at: http://www.wpath.org/site_page.cfm?pk_association_webpage_menu=1351&pk_association_webpage=3926. Accessed 1 September 2017.
- Kreukels BP, Haraldsen IR, De Cuypere G, Richter-Appelt H, Gijs L, Cohen-Kettenis PT. A European network for the investigation of gender incongruence: the ENIGI initiative. *Eur Psychiatry*. 2012;27(6):445–450.
- Dekker MJ, Wierckx K, Van Caenegem E, Klaver M, Kreukels BP, Elaut E, Fisher AD, van Trotsenburg MA, Schreiner T, den Heijer M, T'Sjoen G. A European network for the investigation of gender incongruence: endocrine part. *J Sex Med*. 2016;13(6):994–999.
- Ruble DN, Martin CL, Berenbaum SA. Gender development. In: Damon WL, Lerner RM, Eisenberg N, eds. *Handbook of Child Psychology: Social, Emotional, and Personality Development*. Vol. 3. 6th ed. New York, NY: Wiley; 2006:858–931.
- Steensma TD, Kreukels BP, de Vries AL, Cohen-Kettenis PT. Gender identity development in adolescence. *Horm Behav*. 2013;64(2):288–297.
- Rosenthal SM. Approach to the patient: transgender youth: endocrine considerations. *J Clin Endocrinol Metab*. 2014;99(12):4379–4389.
- Saraswat A, Weinand JD, Safer JD. Evidence supporting the biologic nature of gender identity. *Endocr Pract*. 2015;21(2):199–204.
- Gooren L. The biology of human psychosexual differentiation. *Horm Behav*. 2006;50(4):589–601.
- Berenbaum SA, Meyer-Bahlburg HF. Gender development and sexuality in disorders of sex development. *Horm Metab Res*. 2015;47(5):361–366.
- Dessens AB, Slijper FME, Drop SLS. Gender dysphoria and gender change in chromosomal females with congenital adrenal hyperplasia. *Arch Sex Behav*. 2005;34(4):389–397.
- Meyer-Bahlburg HFL, Dolezal C, Baker SW, Ehrhardt AA, New MI. Gender development in women with congenital adrenal hyperplasia as a function of disorder severity. *Arch Sex Behav*. 2006;35(6):667–684.
- Frisén L, Nordenström A, Falhammar H, Filipsson H, Holmdahl G, Janson PO, Thorén M, Hagenfeldt K, Möller A, Nordenskjöld A. Gender role behavior, sexuality, and psychosocial adaptation in women with congenital adrenal hyperplasia due to CYP21A2 deficiency. *J Clin Endocrinol Metab*. 2009;94(9):3432–3439.
- Meyer-Bahlburg HFL, Dolezal C, Baker SW, Carlson AD, Obeid JS, New MI. Prenatal androgenization affects gender-related behavior but not gender identity in 5–12-year-old girls with congenital adrenal hyperplasia. *Arch Sex Behav*. 2004;33(2):97–104.
- Cohen-Kettenis PT. Gender change in 46,XY persons with 5 α -reductase-2 deficiency and 17 β -hydroxysteroid dehydrogenase-3 deficiency. *Arch Sex Behav*. 2005;34(4):399–410.
- Reiner WG, Gearhart JP. Discordant sexual identity in some genetic males with cloacal exstrophy assigned to female sex at birth. *N Engl J Med*. 2004;350(4):333–341.
- Meyer-Bahlburg HFL. Gender identity outcome in female-raised 46,XY persons with penile agenesis, cloacal exstrophy of the bladder, or penile ablation. *Arch Sex Behav*. 2005;34(4):423–438.
- Cooldidge FL, Thede LL, Young SE. The heritability of gender identity disorder in a child and adolescent twin sample. *Behav Genet*. 2002;32(4):251–257.
- Heylens G, De Cuypere G, Zucker KJ, Schelfaut C, Elaut E, Vanden Bossche H, De Baere E, T'Sjoen G. Gender identity disorder in twins: a review of the case report literature. *J Sex Med*. 2012;9(3):751–757.
- Fernández R, Esteva I, Gómez-Gil E, Rumbo T, Almaraz MC, Roda E, Haro-Mora J-J, Guillamón A, Pávaro E. Association study of ER β , AR, and CYP19A1 genes and MtF transsexualism. *J Sex Med*. 2014;11(12):2986–2994.
- Henningsson S, Westberg L, Nilsson S, Lundström B, Ekselius L, Bodlund O, Lindström E, Hellstrand M, Rosmond R, Eriksson E, Landén M. Sex steroid-related genes and male-to-female transsexualism. *Psychoneuroendocrinology*. 2005;30(7):657–664.
- Hare L, Bernard P, Sánchez FJ, Baird PN, Vilain E, Kennedy T, Harley VR. Androgen receptor repeat length polymorphism associated with male-to-female transsexualism. *Biol Psychiatry*. 2009;65(1):93–96.
- Lombardo F, Toselli L, Grassetti D, Paoli D, Masciandaro P, Valentini F, Lenzi A, Gandini L. Hormone and genetic study in

- male to female transsexual patients. *J Endocrinol Invest.* 2013;36(8):550–557.
38. Ujike H, Otani K, Nakatsuka M, Ishii K, Sasaki A, Oishi T, Sato T, Okahisa Y, Matsumoto Y, Namba Y, Kimata Y, Kuroda S. Association study of gender identity disorder and sex hormone-related genes. *Prog Neuropsychopharmacol Biol Psychiatry.* 2009;33(7):1241–1244.
 39. Kreukels BP, Guillamon A. Neuroimaging studies in people with gender incongruence. *Int Rev Psychiatry.* 2016;28(1):120–128.
 40. Steensma TD, Biemond R, de Boer F, Cohen-Kettenis PT. Desisting and persisting gender dysphoria after childhood: a qualitative follow-up study. *Clin Child Psychol Psychiatry.* 2011;16(4):499–516.
 41. Wallien MSC, Cohen-Kettenis PT. Psychosexual outcome of gender-dysphoric children. *J Am Acad Child Adolesc Psychiatry.* 2008;47(12):1413–1423.
 42. Steensma TD, McGuire JK, Kreukels BPC, Beekman AJ, Cohen-Kettenis PT. Factors associated with desistence and persistence of childhood gender dysphoria: a quantitative follow-up study. *J Am Acad Child Adolesc Psychiatry.* 2013;52(6):582–590.
 43. Cohen-Kettenis PT, Owen A, Kaijser VG, Bradley SJ, Zucker KJ. Demographic characteristics, social competence, and behavior problems in children with gender identity disorder: a cross-national, cross-clinic comparative analysis. *J Abnorm Child Psychol.* 2003;31(1):41–53.
 44. Dhejne C, Van Vlerken R, Heylens G, Arcelus J. Mental health and gender dysphoria: a review of the literature. *Int Rev Psychiatry.* 2016;28(1):44–57.
 45. Pasterski V, Gilligan L, Curtis R. Traits of autism spectrum disorders in adults with gender dysphoria. *Arch Sex Behav.* 2014;43(2):387–393.
 46. Spack NP, Edwards-Leeper L, Feldman HA, Leibowitz S, Mandel F, Diamond DA, Vance SR. Children and adolescents with gender identity disorder referred to a pediatric medical center. *Pediatrics.* 2012;129(3):418–425.
 47. Terada S, Matsumoto Y, Sato T, Okabe N, Kishimoto Y, Uchitomi Y. Factors predicting psychiatric co-morbidity in gender-dysphoric adults. *Psychiatry Res.* 2012;200(2-3):469–474.
 48. VanderLaan DP, Leef JH, Wood H, Hughes SK, Zucker KJ. Autism spectrum disorder risk factors and autistic traits in gender dysphoric children. *J Autism Dev Disord.* 2015;45(6):1742–1750.
 49. de Vries ALC, Doreleijers TAH, Steensma TD, Cohen-Kettenis PT. Psychiatric comorbidity in gender dysphoric adolescents. *J Child Psychol Psychiatry.* 2011;52(11):1195–1202.
 50. de Vries ALC, Noens ILJ, Cohen-Kettenis PT, van Berckelaer-Onnes IA, Doreleijers TA. Autism spectrum disorders in gender dysphoric children and adolescents. *J Autism Dev Disord.* 2010;40(8):930–936.
 51. Wallien MSC, Swaab H, Cohen-Kettenis PT. Psychiatric comorbidity among children with gender identity disorder. *J Am Acad Child Adolesc Psychiatry.* 2007;46(10):1307–1314.
 52. Kuiper AJ, Cohen-Kettenis PT. Gender role reversal among postoperative transsexuals. Available at: <https://www.atrria.nl/eazines/web/IJT/97-03/numbers/symposium/ijtc0502.htm>. Accessed 26 August 2016.
 53. Landén M, Wålinder J, Lambert G, Lundström B. Factors predictive of regret in sex reassignment. *Acta Psychiatr Scand.* 1998;97(4):284–289.
 54. Olsson S-E, Möller A. Regret after sex reassignment surgery in a male-to-female transsexual: a long-term follow-up. *Arch Sex Behav.* 2006;35(4):501–506.
 55. Pfäfflin F, Junge A, eds. *Geschlechtsumwandlung: Abhandlungen zur Transsexualität.* Stuttgart, Germany: Schattauer; 1992.
 56. Lawrence AA. Factors associated with satisfaction or regret following male-to-female sex reassignment surgery. *Arch Sex Behav.* 2003;32(4):299–315.
 57. Cohen-Kettenis PT, Pfäfflin F. *Transgenderism and Intersexuality in Childhood and Adolescence: Making Choices.* Thousand Oaks, CA: SAGE Publications; 2003.
 58. Di Ceglie D, Freedman D, McPherson S, Richardson P. Children and adolescents referred to a specialist gender identity development service: clinical features and demographic characteristics. Available at: https://www.researchgate.net/publication/276061306_Children_and_Adolescents_Referred_to_a_Specialist_Gender_Identity_Development_Service_Clinical_Features_and_Demographic_Characteristics. Accessed 20 July 2017.
 59. Gijs L, Brewaeys A. Surgical treatment of gender dysphoria in adults and adolescents: recent developments, effectiveness, and challenges. *Annu Rev Sex Res.* 2007;18:178–224.
 60. Cohen-Kettenis PT, van Goozen SHM. Sex reassignment of adolescent transsexuals: a follow-up study. *J Am Acad Child Adolesc Psychiatry.* 1997;36(2):263–271.
 61. Smith YLS, van Goozen SHM, Cohen-Kettenis PT. Adolescents with gender identity disorder who were accepted or rejected for sex reassignment surgery: a prospective follow-up study. *J Am Acad Child Adolesc Psychiatry.* 2001;40(4):472–481.
 62. Smith YLS, Van Goozen SHM, Kuiper AJ, Cohen-Kettenis PT. Sex reassignment: outcomes and predictors of treatment for adolescent and adult transsexuals. *Psychol Med.* 2005;35(1):89–99.
 63. de Vries ALC, McGuire JK, Steensma TD, Wagenaar ECF, Doreleijers TAH, Cohen-Kettenis PT. Young adult psychological outcome after puberty suppression and gender reassignment. *Pediatrics.* 2014;134(4):696–704.
 64. Cole CM, O'Boyle M, Emory LE, Meyer WJ III. Comorbidity of gender dysphoria and other major psychiatric diagnoses. *Arch Sex Behav.* 1997;26(1):13–26.
 65. Cohen-Kettenis PT, Schagen SEE, Steensma TD, de Vries ALC, Delemarre-van de Waal HA. Puberty suppression in a gender-dysphoric adolescent: a 22-year follow-up. *Arch Sex Behav.* 2011;40(4):843–847.
 66. First MB. Desire for amputation of a limb: paraphilia, psychosis, or a new type of identity disorder. *Psychol Med.* 2005;35(6):919–928.
 67. Wierckx K, Van Caenegem E, Pennings G, Elaut E, Dedeker D, Van de Peer F, Weyers S, De Sutter P, T'Sjoen G. Reproductive wish in transsexual men. *Hum Reprod.* 2012;27(2):483–487.
 68. Wierckx K, Stuyver I, Weyers S, Hamada A, Agarwal A, De Sutter P, T'Sjoen G. Sperm freezing in transsexual women. *Arch Sex Behav.* 2012;41(5):1069–1071.
 69. Bertelloni S, Baroncelli GI, Ferdeghini M, Menchini-Fabris F, Saggese G. Final height, gonadal function and bone mineral density of adolescent males with central precocious puberty after therapy with gonadotropin-releasing hormone analogues. *Eur J Pediatr.* 2000;159(5):369–374.
 70. Büchter D, Behre HM, Kliesch S, Nieschlag E. Pulsatile GnRH or human chorionic gonadotropin/human menopausal gonadotropin as effective treatment for men with hypogonadotropic hypogonadism: a review of 42 cases. *Eur J Endocrinol.* 1998;139(3):298–303.
 71. Liu PY, Turner L, Rushford D, McDonald J, Baker HW, Conway AJ, Handelsman DJ. Efficacy and safety of recombinant human follicle stimulating hormone (Gonal-F) with urinary human chorionic gonadotrophin for induction of spermatogenesis and fertility in gonadotrophin-deficient men. *Hum Reprod.* 1999;14(6):1540–1545.
 72. Pasquino AM, Pucarelli I, Accardo F, Demiraj V, Segni M, Di Nardo R. Long-term observation of 87 girls with idiopathic central precocious puberty treated with gonadotropin-releasing hormone analogs: impact on adult height, body mass index, bone mineral content, and reproductive function. *J Clin Endocrinol Metab.* 2008;93(1):190–195.
 73. Magiakou MA, Manousaki D, Papadaki M, Hadjidakis D, Levidou G, Vakaki M, Papaefstathiou A, Lalioti N, Kanakantzenbein C, Piaditis G, Chrousos GP, Dacou-Voutetakis C. The

- efficacy and safety of gonadotropin-releasing hormone analog treatment in childhood and adolescence: a single center, long-term follow-up study. *J Clin Endocrinol Metab.* 2010;**95**(1):109–117.
74. Baba T, Endo T, Honnma H, Kitajima Y, Hayashi T, Ikeda H, Masumori N, Kamiya H, Moriwaka O, Saito T. Association between polycystic ovary syndrome and female-to-male transsexuals. *Hum Reprod.* 2007;**22**(4):1011–1016.
 75. Spinder T, Spijkstra JJ, van den Tweel JG, Burger CW, van Kessel H, Hompes PGA, Gooren LJG. The effects of long term testosterone administration on pulsatile luteinizing hormone secretion and on ovarian histology in eugonadal female to male transsexual subjects. *J Clin Endocrinol Metab.* 1989;**69**(1):151–157.
 76. Baba T, Endo T, Ikeda K, Shimizu A, Honnma H, Ikeda H, Masumori N, Ohmura T, Kiya T, Fujimoto T, Koizumi M, Saito T. Distinctive features of female-to-male transsexualism and prevalence of gender identity disorder in Japan. *J Sex Med.* 2011;**8**(6):1686–1693.
 77. Vujovic S, Popovic S, Sbutega-Milosevic G, Djordjevic M, Gooren L. Transsexualism in Serbia: a twenty-year follow-up study. *J Sex Med.* 2009;**6**(4):1018–1023.
 78. Ikeda K, Baba T, Noguchi H, Nagasawa K, Endo T, Kiya T, Saito T. Excessive androgen exposure in female-to-male transsexual persons of reproductive age induces hyperplasia of the ovarian cortex and stroma but not polycystic ovary morphology. *Hum Reprod.* 2013;**28**(2):453–461.
 79. Trebay G. He's pregnant. You're speechless. *New York Times.* 22 June 2008.
 80. Light AD, Obedin-Maliver J, Sevelius JM, Kerns JL. Transgender men who experienced pregnancy after female-to-male gender transitioning. *Obstet Gynecol.* 2014;**124**(6):1120–1127.
 81. De Sutter P. Donor inseminations in partners of female-to-male transsexuals: should the question be asked? *Reprod Biomed Online.* 2003;**6**(3):382, author reply 282–283.
 82. De Roo C, Tilleman K, T'Sjoen G, De Sutter P. Fertility options in transgender people. *Int Rev Psychiatry.* 2016;**28**(1):112–119.
 83. Wennink JMB, Delemarre-van de Waal HA, Schoemaker R, Schoemaker H, Schoemaker J. Luteinizing hormone and follicle stimulating hormone secretion patterns in boys throughout puberty measured using highly sensitive immunoradiometric assays. *Clin Endocrinol (Oxf).* 1989;**31**(5):551–564.
 84. Cohen-Kettenis PT, Delemarre-van de Waal HA, Gooren LJG. The treatment of adolescent transsexuals: changing insights. *J Sex Med.* 2008;**5**(8):1892–1897.
 85. Delemarre-van de Waal HA, Cohen-Kettenis PT. Clinical management of gender identity disorder in adolescents: a protocol on psychological and paediatric endocrinology aspects. *Eur J Endocrinol.* 2006;**155**:S131–S137.
 86. de Vries ALC, Steensma TD, Doreleijers TAH, Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. *J Sex Med.* 2011;**8**(8):2276–2283.
 87. Bouman MB, van Zeijl MCT, Buncamper ME, Meijerink WJHJ, van Bodegraven AA, Mullender MG. Intestinal vaginoplasty revisited: a review of surgical techniques, complications, and sexual function. *J Sex Med.* 2014;**11**(7):1835–1847.
 88. Carel JC, Eugster EA, Rogol A, Ghizzoni L, Palmert MR, Antoniazzi F, Berenbaum S, Bourguignon JP, Chrousos GP, Coste J, Deal S, de Vries L, Foster C, Heger S, Holland J, Jahnukainen K, Juul A, Kaplowitz P, Lahlou N, Lee MM, Lee P, Merke DP, Neely EK, Oostdijk W, Phillip M, Rosenfield RL, Shulman D, Styne D, Tauber M, Wit JM; ESPE-LWPES GnRH Analogs Consensus Conference Group. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. *Pediatrics.* 2009;**123**(4):e752–e762.
 89. Roth CL, Brendel L, Rückert C, Hartmann K. Antagonistic and agonistic GnRH analogue treatment of precocious puberty: tracking gonadotropin concentrations in urine. *Horm Res.* 2005;**63**(5):257–262.
 90. Roth C. Therapeutic potential of GnRH antagonists in the treatment of precocious puberty. *Expert Opin Investig Drugs.* 2002;**11**(9):1253–1259.
 91. Tuvemo T. Treatment of central precocious puberty. *Expert Opin Investig Drugs.* 2006;**15**(5):495–505.
 92. Schagen SE, Cohen-Kettenis PT, Delemarre-van de Waal HA, Hannema SE. Efficacy and safety of gonadotropin-releasing hormone agonist treatment to suppress puberty in gender dysphoric adolescents. *J Sex Med.* 2016;**13**(7):1125–1132.
 93. Manasco PK, Pescovitz OH, Feuillan PP, Hench KD, Barnes KM, Jones J, Hill SC, Loriaux DL, Cutler GB, Jr. Resumption of puberty after long term luteinizing hormone-releasing hormone agonist treatment of central precocious puberty. *J Clin Endocrinol Metab.* 1988;**67**(2):368–372.
 94. Klink D, Caris M, Heijboer A, van Trotsenburg M, Rotteveel J. Bone mass in young adulthood following gonadotropin-releasing hormone analog treatment and cross-sex hormone treatment in adolescents with gender dysphoria. *J Clin Endocrinol Metab.* 2015;**100**(2):E270–E275.
 95. Finkelstein JS, Klibanski A, Neer RM. A longitudinal evaluation of bone mineral density in adult men with histories of delayed puberty. *J Clin Endocrinol Metab.* 1996;**81**(3):1152–1155.
 96. Bertelloni S, Baroncelli GI, Ferdeghini M, Perri G, Saggese G. Normal volumetric bone mineral density and bone turnover in young men with histories of constitutional delay of puberty. *J Clin Endocrinol Metab.* 1998;**83**(12):4280–4283.
 97. Darelid A, Ohlsson C, Nilsson M, Kindblom JM, Mellström D, Lorentzon M. Catch up in bone acquisition in young adult men with late normal puberty. *J Bone Miner Res.* 2012;**27**(10):2198–2207.
 98. Mittan D, Lee S, Miller E, Perez RC, Basler JW, Bruder JM. Bone loss following hypogonadism in men with prostate cancer treated with GnRH analogs. *J Clin Endocrinol Metab.* 2002;**87**(8):3656–3661.
 99. Saggese G, Bertelloni S, Baroncelli GI, Battini R, Franchi G. Reduction of bone density: an effect of gonadotropin releasing hormone analogue treatment in central precocious puberty. *Eur J Pediatr.* 1993;**152**(9):717–720.
 100. Neely EK, Bachrach LK, Hintz RL, Habiby RL, Slemenda CW, Feeze L, Pescovitz OH. Bone mineral density during treatment of central precocious puberty. *J Pediatr.* 1995;**127**(5):819–822.
 101. Bertelloni S, Baroncelli GI, Sorrentino MC, Perri G, Saggese G. Effect of central precocious puberty and gonadotropin-releasing hormone analogue treatment on peak bone mass and final height in females. *Eur J Pediatr.* 1998;**157**(5):363–367.
 102. Thornton P, Silverman LA, Geffner ME, Neely EK, Gould E, Danoff TM. Review of outcomes after cessation of gonadotropin-releasing hormone agonist treatment of girls with precocious puberty. *Pediatr Endocrinol Rev.* 2014;**11**(3):306–317.
 103. Lem AJ, van der Kaay DC, Hokken-Koelega AC. Bone mineral density and body composition in short children born SGA during growth hormone and gonadotropin releasing hormone analog treatment. *J Clin Endocrinol Metab.* 2013;**98**(1):77–86.
 104. Antoniazzi F, Zamboni G, Bertoldo F, Lauriola S, Mengarda F, Pietrobelli A, Tatò L. Bone mass at final height in precocious puberty after gonadotropin-releasing hormone agonist with and without calcium supplementation. *J Clin Endocrinol Metab.* 2003;**88**(3):1096–1101.
 105. Calcaterra V, Mannarino S, Corana G, Codazzi AC, Mazzola A, Brambilla P, Larizza D. Hypertension during therapy with triptorelin in a girl with precocious puberty. *Indian J Pediatr.* 2013;**80**(10):884–885.
 106. Siomou E, Kosmeri C, Pavlou M, Vlahos AP, Argyropoulou MI, Siamopoulou A. Arterial hypertension during treatment with triptorelin in a child with Williams-Beuren syndrome. *Pediatr Nephrol.* 2014;**29**(9):1633–1636.
 107. Staphorsius AS, Kreukels BPC, Cohen-Kettenis PT, Veltman DJ, Burke SM, Schagen SEE, Wouters FM, Delemarre-van de Waal

- HA, Bakker J. Puberty suppression and executive functioning: an fMRI-study in adolescents with gender dysphoria. *Psychoneuroendocrinology*. 2015;56:190–199.
108. Hough D, Bellingham M, Haraldsen IR, McLaughlin M, Rennie M, Robinson JE, Solbakk AK, Evans NP. Spatial memory is impaired by peripubertal GnRH agonist treatment and testosterone replacement in sheep. *Psychoneuroendocrinology*. 2017; 75:173–182.
109. Collipp PJ, Kaplan SA, Boyle DC, Plachte F, Kogut MD. Constitutional Isosexual Precocious Puberty. *Am J Dis Child*. 1964; 108:399–405.
110. Hahn HB, Jr, Hayles AB, Albert A. Medroxyprogesterone and constitutional precocious puberty. *Mayo Clin Proc*. 1964;39: 182–190.
111. Kaplan SA, Ling SM, Irani NG. Idiopathic isosexual precocity. *Am J Dis Child*. 1968;116(6):591–598.
112. Schoen EJ. Treatment of idiopathic precocious puberty in boys. *J Clin Endocrinol Metab*. 1966;26(4):363–370.
113. Gooren L. Hormone treatment of the adult transsexual patient. *Horm Res*. 2005;64(Suppl 2):31–36.
114. Moore E, Wisniewski A, Dobs A. Endocrine treatment of transsexual people: a review of treatment regimens, outcomes, and adverse effects. *J Clin Endocrinol Metab*. 2003;88(8):3467–3473.
115. Krueger RB, Hembree W, Hill M. Prescription of medroxyprogesterone acetate to a patient with pedophilia, resulting in Cushing's syndrome and adrenal insufficiency. *Sex Abuse*. 2006; 18(2):227–228.
116. Lynch MM, Khandheria MM, Meyer WJ. Retrospective study of the management of childhood and adolescent gender identity disorder using medroxyprogesterone acetate. *Int J Transgenderism*. 2015;16:201–208.
117. Tack LJW, Craen M, Dhondt K, Vanden Bossche H, Laridaen J, Cools M. Consecutive lynestrenol and cross-sex hormone treatment in biological female adolescents with gender dysphoria: a retrospective analysis. *Biol Sex Differ*. 2016;7:14.
118. Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, Gooren LJ, Meyer WJ 3rd, Spack NP, Tangpricha V, Montori VM; Endocrine Society. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2009;94(9):3132–3154.
119. Mann L, Harmoni R, Power C. Adolescent decision-making: the development of competence. *J Adolesc*. 1989;12(3):265–278.
120. Stultiens L, Goffin T, Borry P, Dierickx K, Nys H. Minors and informed consent: a comparative approach. *Eur J Health Law*. 2007;14(1):21–46.
121. Arshagouni P. “But I’m an adult now ... sort of”. Adolescent consent in health care decision-making and the adolescent brain. Available at: <http://digitalcommons.law.umaryland.edu/cgi/viewcontent.cgi?article=1124&context=jhclp>. Accessed 25 June 2017.
122. NHS. Prescribing of cross-sex hormones as part of the gender identity development service for children and adolescents. Available at: <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/08/clinical-com-pol-16046p.pdf>. Accessed 14 June 2017.
123. Ankarberg-Lindgren C, Kriström B, Norjavaara E. Physiological estrogen replacement therapy for puberty induction in girls: a clinical observational study. *Horm Res Paediatr*. 2014;81(4): 239–244.
124. Olson J, Schrager SM, Clark LF, Dunlap SL, Belzer M. Subcutaneous testosterone: an effective delivery mechanism for masculinizing young transgender men. *LGBT Health*. 2014;1(3): 165–167.
125. Spratt DL, Stewart I, Savage C, Craig W, Spack NP, Chandler DW, Spratt LV, Eimicke T, Olshan JS. Subcutaneous injection of testosterone is an effective and preferred alternative to intramuscular injection: demonstration in female-to-male transgender patients. *J Clin Endocrinol Metab*. 2017. doi:10.1210/jc.2017-00359
126. Eisenegger C, von Eckardstein A, Fehr E, von Eckardstein S. Pharmacokinetics of testosterone and estradiol gel preparations in healthy young men. *Psychoneuroendocrinology*. 2013;38(2): 171–178.
127. de Ronde W, ten Kulve J, Woerdeman J, Kaufman J-M, de Jong FH. Effects of oestradiol on gonadotrophin levels in normal and castrated men. *Clin Endocrinol (Oxf)*. 2009;71(6):874–879.
128. Money J, Ehrhardt A. Man & woman, boy & girl: differentiation and dimorphism of gender identity from conception to maturity. Baltimore, MD: Johns Hopkins University Press; 1972:202–206.
129. Heylens G, Verroken C, De Cock S, T'Sjoen G, De Cuypere G. Effects of different steps in gender reassignment therapy on psychopathology: a prospective study of persons with a gender identity disorder. *J Sex Med*. 2014;11(1):119–126.
130. Costa R, Colizzi M. The effect of cross-sex hormonal treatment on gender dysphoria individuals' mental health: a systematic review. *Neuropsychiatr Dis Treat*. 2016;12:1953–1966.
131. Gooren LJG, Giltay EJ. Review of studies of androgen treatment of female-to-male transsexuals: effects and risks of administration of androgens to females. *J Sex Med*. 2008;5(4):765–776.
132. Levy A, Crown A, Reid R. Endocrine intervention for transsexuals. *Clin Endocrinol (Oxf)*. 2003;59(4):409–418.
133. Tangpricha V, Ducharme SH, Barber TW, Chipkin SR. Endocrinologic treatment of gender identity disorders. *Endocr Pract*. 2003;9(1):12–21.
134. Meriggiola MC, Gava G. Endocrine care of transpeople part I. A review of cross-sex hormonal treatments, outcomes and adverse effects in transmen. *Clin Endocrinol (Oxf)*. 2015;83(5):597–606.
135. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM. Testosterone therapy in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2006;91(6): 1995–2010.
136. Pelusi C, Costantino A, Martelli V, Lambertini M, Bazzocchi A, Ponti F, Battista G, Venturoli S, Meriggiola MC. Effects of three different testosterone formulations in female-to-male transsexual persons. *J Sex Med*. 2014;11(12):3002–3011.
137. Anderson GL, Limacher M, Assaf AR, Bassford T, Beresford SA, Black H, Bonds D, Brunner R, Brzyski R, Caan B, Chlebowski R, Curb D, Gass M, Hays J, Heiss J, Hendrix S, Howard BV, Hsia J, Hubbell A, Jackson R, Johnson KC, Judd H, Kotchen JM, Kuller L, LaCroix AZ, Lane D, Langer RD, Lasser N, Lewis CE, Manson J, Margolis K, Ockene J, O'Sullivan MJ, Phillips L, Prentice RL, Ritenbaugh C, Robbins J, Rossouw JE, Sarto G, Stefanick ML, Van Horn L, Wactawski-Wende J, Wallace R, Wassertheil-Smoller S; Women's Health Initiative Steering Committee. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA*. 2004;291(14):1701–1712.
138. Dickersin K, Munro MG, Clark M, Langenberg P, Scherer R, Frick K, Zhu Q, Hallock L, Nichols J, Yalcinkaya TM; Surgical Treatments Outcomes Project for Dysfunctional Uterine Bleeding (STOP-DUB) Research Group. Hysterectomy compared with endometrial ablation for dysfunctional uterine bleeding: a randomized controlled trial. *Obstet Gynecol*. 2007;110(6): 1279–1289.
139. Gooren LJ, Giltay EJ, Bunck MC. Long-term treatment of transsexuals with cross-sex hormones: extensive personal experience. *J Clin Endocrinol Metab*. 2008;93(1):19–25.
140. Prior JC, Vigna YM, Watson D. Spironolactone with physiological female steroids for presurgical therapy of male-to-female transsexualism. *Arch Sex Behav*. 1989;18(1):49–57.
141. Dittrich R, Binder H, Cupisti S, Hoffmann I, Beckmann MW, Mueller A. Endocrine treatment of male-to-female transsexuals using gonadotropin-releasing hormone agonist. *Exp Clin Endocrinol Diabetes*. 2005;113(10):586–592.

142. Stripp B, Taylor AA, Bartter FC, Gillette JR, Loriaux DL, Easley R, Menard RH. Effect of spironolactone on sex hormones in man. *J Clin Endocrinol Metab.* 1975;41(4):777–781.
143. Levy J, Burshell A, Marbach M, Aflalo L, Glick SM. Interaction of spironolactone with oestradiol receptors in cytosol. *J Endocrinol.* 1980;84(3):371–379.
144. Wierckx K, Elaut E, Van Hoorde B, Heylens G, De Cuypere G, Monstrey S, Weyers S, Hoebeke P, T'Sjoen G. Sexual desire in trans persons: associations with sex reassignment treatment. *J Sex Med.* 2014;11(1):107–118.
145. Chiriaco G, Cauci S, Mazzon G, Trombetta C. An observational retrospective evaluation of 79 young men with long-term adverse effects after use of finasteride against androgenetic alopecia. *Andrology.* 2016;4(2):245–250.
146. Gava G, Cerpolini S, Martelli V, Battista G, Seracchioli R, Meriggiola MC. Cyproterone acetate vs leuprolide acetate in combination with transdermal oestradiol in transwomen: a comparison of safety and effectiveness. *Clin Endocrinol (Oxf).* 2016;85(2):239–246.
147. Casper RF, Yen SS. Rapid absorption of micronized estradiol-17 beta following sublingual administration. *Obstet Gynecol.* 1981;57(1):62–64.
148. Price TM, Blauer KL, Hansen M, Stanczyk F, Lobo R, Bates GW. Single-dose pharmacokinetics of sublingual versus oral administration of micronized 17 β -estradiol. *Obstet Gynecol.* 1997;89(3):340–345.
149. Toorians AWFT, Thomassen MCLGD, Zweegman S, Magdeleyns EJP, Tans G, Gooren LJG, Rosing J. Venous thrombosis and changes of hemostatic variables during cross-sex hormone treatment in transsexual people. *J Clin Endocrinol Metab.* 2003;88(12):5723–5729.
150. Mepham N, Bouman WP, Arcelus J, Hayter M, Wylie KR. People with gender dysphoria who self-prescribe cross-sex hormones: prevalence, sources, and side effects knowledge. *J Sex Med.* 2014;11(12):2995–3001.
151. Richards C, Bouman WP, Seal L, Barker MJ, Nieder TO, T'Sjoen G. Non-binary or genderqueer genders. *Int Rev Psychiatry.* 2016;28(1):95–102.
152. Cosyns M, Van Borsel J, Wierckx K, Dedeker D, Van de Peer F, Daelman T, Laenen S, T'Sjoen G. Voice in female-to-male transsexual persons after long-term androgen therapy. *Laryngoscope.* 2014;124(6):1409–1414.
153. Deuster D, Matulat P, Knief A, Zitzmann M, Rosslau K, Szukaj M, am Zehnhoff-Dinnesen A, Schmidt CM. Voice deepening under testosterone treatment in female-to-male gender dysphoric individuals. *Eur Arch Otorhinolaryngol.* 2016;273(4):959–965.
154. Lapauw B, Taes Y, Simoens S, Van Caenegem E, Weyers S, Goemaere S, Toye K, Kaufman J-M, T'Sjoen GG. Body composition, volumetric and areal bone parameters in male-to-female transsexual persons. *Bone.* 2008;43(6):1016–1021.
155. Meyer III WJ, Webb A, Stuart CA, Finkelstein JW, Lawrence B, Walker PA. Physical and hormonal evaluation of transsexual patients: a longitudinal study. *Arch Sex Behav.* 1986;15(2):121–138.
156. Asscheman H, Gooren LJ, Assies J, Smits JP, de Slegte R. Prolactin levels and pituitary enlargement in hormone-treated male-to-female transsexuals. *Clin Endocrinol (Oxf).* 1988;28(6):583–588.
157. Gooren LJ, Harmsen-Louman W, van Kessel H. Follow-up of prolactin levels in long-term oestrogen-treated male-to-female transsexuals with regard to prolactinoma induction. *Clin Endocrinol (Oxf).* 1985;22(2):201–207.
158. Wierckx K, Van Caenegem E, Schreiner T, Haraldsen I, Fisher AD, Toye K, Kaufman JM, T'Sjoen G. Cross-sex hormone therapy in trans persons is safe and effective at short-time follow-up: results from the European network for the investigation of gender incongruence. *J Sex Med.* 2014;11(8):1999–2011.
159. Ott J, Kaufmann U, Bentz EK, Huber JC, Tempfer CB. Incidence of thrombophilia and venous thrombosis in transsexuals under cross-sex hormone therapy. *Fertil Steril.* 2010;93(4):1267–1272.
160. Giltay EJ, Hoogeveen EK, Elbers JMH, Gooren LJG, Asscheman H, Stehouwer CDA. Effects of sex steroids on plasma total homocysteine levels: a study in transsexual males and females. *J Clin Endocrinol Metab.* 1998;83(2):550–553.
161. van Kesteren PJM, Asscheman H, Megens JAJ, Gooren LJG. Mortality and morbidity in transsexual subjects treated with cross-sex hormones. *Clin Endocrinol (Oxf).* 1997;47(3):337–343.
162. Wierckx K, Gooren L, T'Sjoen G. Clinical review: breast development in trans women receiving cross-sex hormones. *J Sex Med.* 2014;11(5):1240–1247.
163. Bird D, Vowles K, Anthony PP. Spontaneous rupture of a liver cell adenoma after long term methyltestosterone: report of a case successfully treated by emergency right hepatic lobectomy. *Br J Surg.* 1979;66(3):212–213.
164. Westaby D, Ogle SJ, Paradinas FJ, Randell JB, Murray-Lyon IM. Liver damage from long-term methyltestosterone. *Lancet.* 1977;2(8032):262–263.
165. Weinand JD, Safer JD. Hormone therapy in transgender adults is safe with provider supervision; a review of hormone therapy sequelae for transgender individuals. *J Clin Transl Endocrinol.* 2015;2(2):55–60.
166. Roberts TK, Kraft CS, French D, Ji W, Wu AH, Tangpricha V, Fantz CR. Interpreting laboratory results in transgender patients on hormone therapy. *Am J Med.* 2014;127(2):159–162.
167. Vesper HW, Botelho JC, Wang Y. Challenges and improvements in testosterone and estradiol testing. *Asian J Androl.* 2014;16(2):178–184.
168. Asscheman H, T'Sjoen G, Lemaire A, Mas M, Meriggiola MC, Mueller A, Kuhn A, Dhejne C, Morel-Journel N, Gooren LJ. Venous thrombo-embolism as a complication of cross-sex hormone treatment of male-to-female transsexual subjects: a review. *Andrologia.* 2014;46(7):791–795.
169. Righini M, Perrier A, De Moerloose P, Bounameaux H. D-dimer for venous thromboembolism diagnosis: 20 years later. *J Thromb Haemost.* 2008;6(7):1059–1071.
170. Gooren LJ, Assies J, Asscheman H, de Slegte R, van Kessel H. Estrogen-induced prolactinoma in a man. *J Clin Endocrinol Metab.* 1988;66(2):444–446.
171. Kovacs K, Stefanescu L, Ezzat S, Smyth HS. Prolactin-producing pituitary adenoma in a male-to-female transsexual patient with protracted estrogen administration. A morphologic study. *Arch Pathol Lab Med.* 1994;118(5):562–565.
172. Serri O, Noiseux D, Robert F, Hardy J. Lactotroph hyperplasia in an estrogen treated male-to-female transsexual patient. *J Clin Endocrinol Metab.* 1996;81(9):3177–3179.
173. Cunha FS, Domenice S, Câmara VL, Sircili MH, Gooren LJ, Mendonça BB, Costa EM. Diagnosis of prolactinoma in two male-to-female transsexual subjects following high-dose cross-sex hormone therapy. *Andrologia.* 2015;47(6):680–684.
174. Nota NM, Dekker MJHJ, Klaver M, Wiepjes CM, van Trotsenburg MA, Heijboer AC, den Heijer M. Prolactin levels during short- and long-term cross-sex hormone treatment: an observational study in transgender persons. *Andrologia.* 2017;49(6).
175. Bunck MC, Debono M, Giltay EJ, Verheijen AT, Diamant M, Gooren LJ. Autonomous prolactin secretion in two male-to-female transgender patients using conventional oestrogen dosages. *BMJ Case Rep.* 2009;2009:bcr0220091589.
176. Elamin MB, Garcia MZ, Murad MH, Erwin PJ, Montori VM. Effect of sex steroid use on cardiovascular risk in transsexual individuals: a systematic review and meta-analyses. *Clin Endocrinol (Oxf).* 2010;72(1):1–10.
177. Berra M, Armillotta F, D'Emidio L, Costantino A, Martorana G, Pelusi G, Meriggiola MC. Testosterone decreases adiponectin

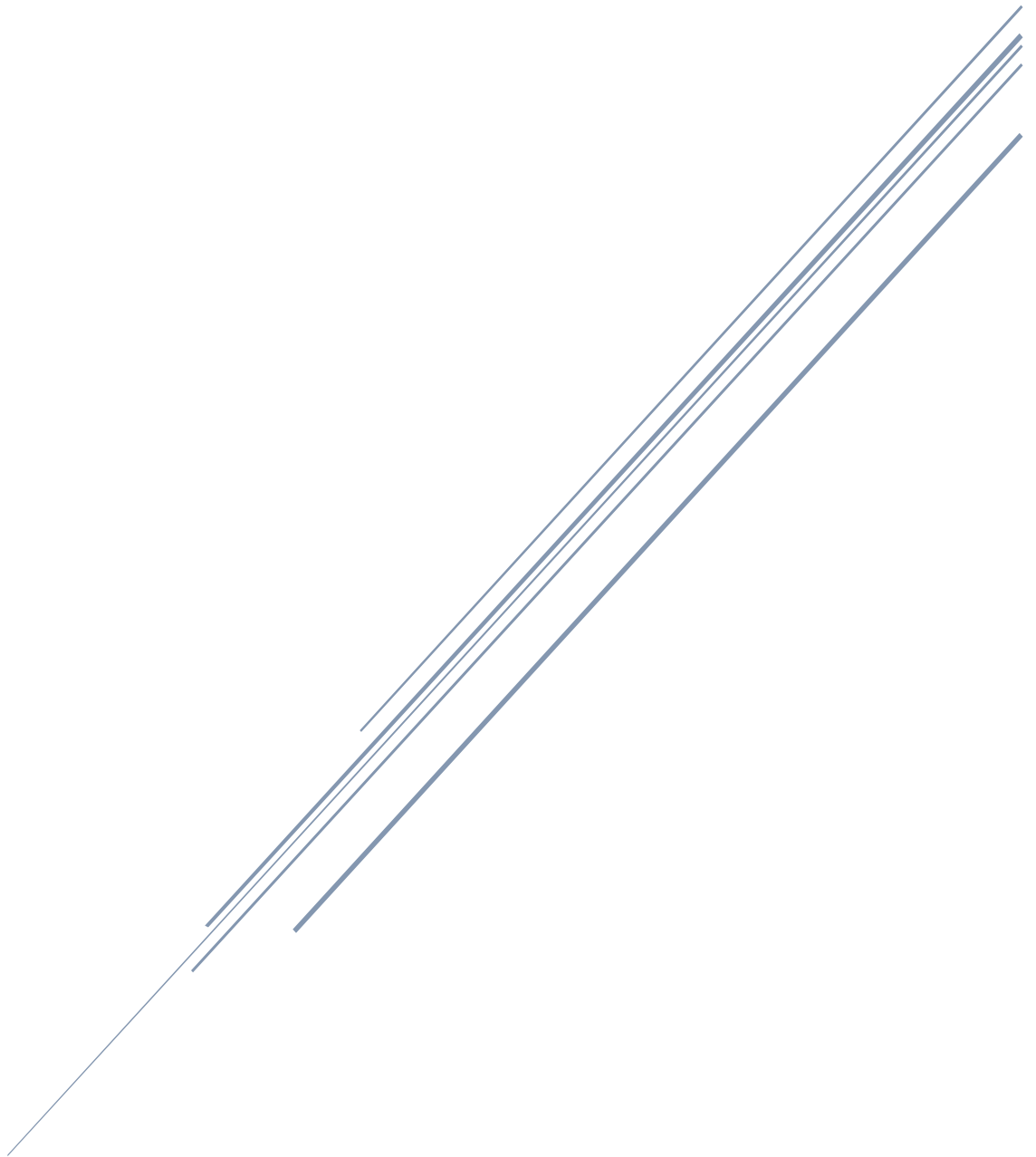
- levels in female to male transsexuals. *Asian J Androl.* 2006;8(6):725–729.
178. Elbers JMH, Giltay EJ, Teerlink T, Scheffer PG, Asscheman H, Seidell JC, Gooren LJG. Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. *Clin Endocrinol (Oxf).* 2003;58(5):562–571.
 179. Giltay EJ, Lambert J, Gooren LJG, Elbers JMH, Steyn M, Stehouwer CDA. Sex steroids, insulin, and arterial stiffness in women and men. *Hypertension.* 1999;34(4 Pt 1):590–597.
 180. Polderman KH, Gooren LJ, Asscheman H, Bakker A, Heine RJ. Induction of insulin resistance by androgens and estrogens. *J Clin Endocrinol Metab.* 1994;79(1):265–271.
 181. Maraka S. Effect of sex steroids on lipids, venous thromboembolism, cardiovascular disease and mortality in transgender individuals: a systematic review and meta-analysis. Available at: <http://press.endocrine.org/doi/abs/10.1210/endo-meetings.2016.RE.15.FRI-136>. Accessed 3 July 2017.
 182. Meriggiola MC, Armillotta F, Costantino A, Altieri P, Saad F, Kalhorn T, Perrone AM, Ghi T, Pelusi C, Pelusi G. Effects of testosterone undecanoate administered alone or in combination with letrozole or dutasteride in female to male transsexuals. *J Sex Med.* 2008;5(10):2442–2453.
 183. Giltay EJ, Toorians AW, Sarabdjitsingh AR, de Vries NA, Gooren LJ. Established risk factors for coronary heart disease are unrelated to androgen-induced baldness in female-to-male transsexuals. *J Endocrinol.* 2004;180(1):107–112.
 184. Giltay EJ, Verhoeve P, Gooren LJG, Geleijnse JM, Schouten EG, Stehouwer CDA. Oral and transdermal estrogens both lower plasma total homocysteine in male-to-female transsexuals. *Atherosclerosis.* 2003;168(1):139–146.
 185. Calof OM, Singh AB, Lee ML, Kenny AM, Urban RJ, Tenover JL, Bhasin S. Adverse events associated with testosterone replacement in middle-aged and older men: a meta-analysis of randomized, placebo-controlled trials. *J Gerontol A Biol Sci Med Sci.* 2005;60(11):1451–1457.
 186. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA.* 2001;285(19):2486–2497.
 187. Murad MH, Elamin MB, Garcia MZ, Mullan RJ, Murad A, Erwin PJ, Montori VM. Hormonal therapy and sex reassignment: a systematic review and meta-analysis of quality of life and psychosocial outcomes. *Clin Endocrinol (Oxf).* 2010;72(2):214–231.
 188. Van Caenegem E, Wierckx K, Taes Y, Schreiner T, Vandewalle S, Toye K, Lapauw B, Kaufman JM, T'Sjoen G. Body composition, bone turnover, and bone mass in trans men during testosterone treatment: 1-year follow-up data from a prospective case-controlled study (ENIGI). *Eur J Endocrinol.* 2015;172(2):163–171.
 189. Turner A, Chen TC, Barber TW, Malabanan AO, Holick MF, Tangpricha V. Testosterone increases bone mineral density in female-to-male transsexuals: a case series of 15 subjects. *Clin Endocrinol (Oxf).* 2004;61(5):560–566.
 190. van Kesteren P, Lips P, Gooren LJG, Asscheman H, Megens J. Long-term follow-up of bone mineral density and bone metabolism in transsexuals treated with cross-sex hormones. *Clin Endocrinol (Oxf).* 1998;48(3):347–354.
 191. Van Caenegem E, Taes Y, Wierckx K, Vandewalle S, Toye K, Kaufman JM, Schreiner T, Haraldsen I, T'Sjoen G. Low bone mass is prevalent in male-to-female transsexual persons before the start of cross-sex hormonal therapy and gonadectomy. *Bone.* 2013;54(1):92–97.
 192. Amin S, Zhang Y, Sawin CT, Evans SR, Hannan MT, Kiel DP, Wilson PW, Felson DT. Association of hypogonadism and estradiol levels with bone mineral density in elderly men from the Framingham study. *Ann Intern Med.* 2000;133(12):951–963.
 193. Gennari L, Khosla S, Bilezikian JP. Estrogen and fracture risk in men. *J Bone Miner Res.* 2008;23(10):1548–1551.
 194. Khosla S, Melton LJ III, Atkinson EJ, O'Fallon WM, Klee GG, Riggs BL. Relationship of serum sex steroid levels and bone turnover markers with bone mineral density in men and women: a key role for bioavailable estrogen. *J Clin Endocrinol Metab.* 1998;83(7):2266–2274.
 195. Mueller A, Dittrich R, Binder H, Kuehnel W, Maltaris T, Hoffmann I, Beckmann MW. High dose estrogen treatment increases bone mineral density in male-to-female transsexuals receiving gonadotropin-releasing hormone agonist in the absence of testosterone. *Eur J Endocrinol.* 2005;153(1):107–113.
 196. Ruetsche AG, Kneubuehl R, Birkhaeuser MH, Lippuner K. Cortical and trabecular bone mineral density in transsexuals after long-term cross-sex hormonal treatment: a cross-sectional study. *Osteoporos Int.* 2005;16(7):791–798.
 197. Ganly I, Taylor EW. Breast cancer in a trans-sexual man receiving hormone replacement therapy. *Br J Surg.* 1995;82(3):341.
 198. Pritchard TJ, Pankowsky DA, Crowe JP, Abdul-Karim FW. Breast cancer in a male-to-female transsexual. A case report. *JAMA.* 1988;259(15):2278–2280.
 199. Symmers WS. Carcinoma of breast in trans-sexual individuals after surgical and hormonal interference with the primary and secondary sex characteristics. *BMJ.* 1968;2(5597):83–85.
 200. Brown GR. Breast cancer in transgender veterans: a ten-case series. *LGBT Health.* 2015;2(1):77–80.
 201. Shao T, Grossbard ML, Klein P. Breast cancer in female-to-male transsexuals: two cases with a review of physiology and management. *Clin Breast Cancer.* 2011;11(6):417–419.
 202. Nikolic DV, Djordjevic ML, Granic M, Nikolic AT, Stanimirovic VV, Zdravkovic D, Jelic S. Importance of revealing a rare case of breast cancer in a female to male transsexual after bilateral mastectomy. *World J Surg Oncol.* 2012;10:280.
 203. Bösze P, Tóth A, Török M. Hormone replacement and the risk of breast cancer in Turner's syndrome. *N Engl J Med.* 2006;355(24):2599–2600.
 204. Schoemaker MJ, Swerdlow AJ, Higgins CD, Wright AF, Jacobs PA; UK Clinical Cytogenetics Group. Cancer incidence in women with Turner syndrome in Great Britain: a national cohort study. *Lancet Oncol.* 2008;9(3):239–246.
 205. Smith RA, Cokkinides V, Eyre HJ. American Cancer Society guidelines for the early detection of cancer, 2006. *CA Cancer J Clin.* 2006;56(1):11–25, quiz 49–50.
 206. Wilson JD, Roehrborn C. Long-term consequences of castration in men: lessons from the Skoptzy and the eunuchs of the Chinese and Ottoman courts. *J Clin Endocrinol Metab.* 1999;84(12):4324–4331.
 207. van Kesteren P, Meinhardt W, van der Valk P, Geldof A, Megens J, Gooren L. Effects of estrogens only on the prostates of aging men. *J Urol.* 1996;156(4):1349–1353.
 208. Brown JA, Wilson TM. Benign prostatic hyperplasia requiring transurethral resection of the prostate in a 60-year-old male-to-female transsexual. *Br J Urol.* 1997;80(6):956–957.
 209. Casella R, Bubendorf L, Schaefer DJ, Bachmann A, Gasser TC, Sulser T. Does the prostate really need androgens to grow? Transurethral resection of the prostate in a male-to-female transsexual 25 years after sex-changing operation. *Urol Int.* 2005;75(3):288–290.
 210. Dorff TB, Shazer RL, Nepomuceno EM, Tucker SJ. Successful treatment of metastatic androgen-independent prostate carcinoma in a transsexual patient. *Clin Genitourin Cancer.* 2007;5(5):344–346.
 211. Thurston AV. Carcinoma of the prostate in a transsexual. *Br J Urol.* 1994;73(2):217.

212. van Harst EP, Newling DW, Gooren LJ, Asscheman H, Prenger DM. Metastatic prostatic carcinoma in a male-to-female transsexual. *BJU Int*. 1998;81:776.
213. Turo R, Jallad S, Prescott S, Cross WR. Metastatic prostate cancer in transsexual diagnosed after three decades of estrogen therapy. *Can Urol Assoc J*. 2013;7(7–8):E544–E546.
214. Miksad RA, Bubley G, Church P, Sanda M, Rofsky N, Kaplan I, Cooper A. Prostate cancer in a transgender woman 41 years after initiation of feminization. *JAMA*. 2006;296(19):2316–2317.
215. Moyer VA; U.S. Preventive Services Task Force. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2012;157(2):120–134.
216. Futterweit W. Endocrine therapy of transsexualism and potential complications of long-term treatment. *Arch Sex Behav*. 1998;27(2):209–226.
217. Miller N, Bédard YC, Cooter NB, Shaul DL. Histological changes in the genital tract in transsexual women following androgen therapy. *Histopathology*. 1986;10(7):661–669.
218. O'Hanlan KA, Dibble SL, Young-Spint M. Total laparoscopic hysterectomy for female-to-male transsexuals. *Obstet Gynecol*. 2007;110(5):1096–1101.
219. Dizon DS, Tejada-Berges T, Koelliker S, Steinhoff M, Granai CO. Ovarian cancer associated with testosterone supplementation in a female-to-male transsexual patient. *Gynecol Obstet Invest*. 2006;62(4):226–228.
220. Hage JJ, Dekker JJML, Karim RB, Verheijen RHM, Bloemena E. Ovarian cancer in female-to-male transsexuals: report of two cases. *Gynecol Oncol*. 2000;76(3):413–415.
221. Mueller A, Gooren L. Hormone-related tumors in transsexuals receiving treatment with cross-sex hormones. *Eur J Endocrinol*. 2008;159(3):197–202.
222. Coleman E, Bockting W, Botzer M, Cohen-Kettenis P, DeCuypere G, Feldman J, Fraser L, Green J, Knudson G, Meyer WJ, Monstrey S, Adler RK, Brown GR, Devor AH, Ehrbar R, Ettner R, Eyley E, Garofalo R, Karasic DH, Lev AI, Mayer G, Meyer-Bahlburg H, Hall BP, Pfaefflin F, Rachlin K, Robinson B, Schechter LS, Tangpricha V, van Trotsenburg M, Vitale A, Winter S, Whittle S, Wylie KR, Zucker K. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, version 7. *Int J Transgenderism*. 2012;13:165–232.
223. Colebunders B, D'Arpa S, Weijers S, Lumen N, Hoebeke P, Monstrey S. Female-to-male gender reassignment surgery. In: Ettner R, Monstrey S, Coleman E, eds. *Principles of Transgender Medicine and Surgery*. 2nd ed. New York, NY: Routledge Taylor & Francis Group; 2016:279–317.
224. Monstrey S, Hoebeke P, Dhont M, De Cuypere G, Rubens R, Moerman M, Hamdi M, Van Landuyt K, Blondeel P. Surgical therapy in transsexual patients: a multi-disciplinary approach. *Acta Chir Belg*. 2001;101(5):200–209.
225. Selvaggi G, Ceulemans P, De Cuypere G, VanLanduyt K, Blondeel P, Hamdi M, Bowman C, Monstrey S. Gender identity disorder: general overview and surgical treatment for vaginoplasty in male-to-female transsexuals. *Plast Reconstr Surg*. 2005;116(6):135e–145e.
226. Tugnet N, Goddard JC, Vickery RM, Khoosal D, Terry TR. Current management of male-to-female gender identity disorder in the UK. *Postgrad Med J*. 2007;83(984):638–642.
227. Horbach SER, Bouman M-B, Smit JM, Özer M, Buncamper ME, Mullender MG. Outcome of vaginoplasty in male-to-female transsexuals: a systematic review of surgical techniques. *J Sex Med*. 2015;12(6):1499–1512.
228. Wroblewski P, Gustafsson J, Selvaggi G. Sex reassignment surgery for transsexuals. *Curr Opin Endocrinol Diabetes Obes*. 2013;20(6):570–574.
229. Morrison SD, Satterwhite T, Grant DW, Kirby J, Laub DR, Sr, VanMaasdam J. Long-term outcomes of rectosigmoid neocolporrhaphy in male-to-female gender reassignment surgery. *Plast Reconstr Surg*. 2015;136(2):386–394.
230. Dessy LA, Mazzocchi M, Corrias F, Ceccarelli S, Marchese C, Scuderi N. The use of cultured autologous oral epithelial cells for vaginoplasty in male-to-female transsexuals: a feasibility, safety, and advantageousness clinical pilot study. *Plast Reconstr Surg*. 2014;133(1):158–161.
231. Li FY, Xu YS, Zhou CD, Zhou Y, Li SK, Li Q. Long-term outcomes of vaginoplasty with autologous buccal micromucosa. *Obstet Gynecol*. 2014;123(5):951–956.
232. Kanhai RC. Sensate vagina pedicled-spot for male-to-female transsexuals: the experience in the first 50 patients. *Aesthetic Plast Surg*. 2016;40(2):284–287.
233. Straayer C. Transplants for transsexuals? Ambitions, concerns, ideology. Paper presented at: Trans*Studies: An International Transdisciplinary Conference on Gender, Embodiment, and Sexuality; 7–10 September 2016; University of Arizona, Tucson, AZ.
234. Bucci S, Mazzon G, Liguori G, Napoli R, Pavan N, Bormioli S, Olandini G, De Concilio B, Trombetta C. Neovaginal prolapse in male-to-female transsexuals: an 18-year-long experience. *Biomed Res Int*. 2014;2014:240761.
235. Raigosa M, Avvedimento S, Yoon TS, Cruz-Gimeno J, Rodriguez G, Fontdevila J. Male-to-female genital reassignment surgery: a retrospective review of surgical technique and complications in 60 patients. *J Sex Med*. 2015;12(8):1837–1845.
236. Green R. Sexual functioning in post-operative transsexuals: male-to-female and female-to-male. *Int J Impot Res*. 1998;10(Suppl 1):S22–S24.
237. Hess J, Rossi Neto R, Panic L, Rübhen H, Senf W. Satisfaction with male-to-female gender reassignment surgery. *Dtsch Arztebl Int*. 2014;111(47):795–801.
238. Nygren U, Nordenskjöld A, Arver S, Sodersten M. Effects on voice fundamental frequency and satisfaction with voice in trans men during testosterone treatment—a longitudinal study. *J Voice*. 2016;30(6):766.e23–766.e34.
239. Becking AG, Tuinzing DB, Hage JJ, Gooren LJG. Transgender feminization of the facial skeleton. *Clin Plast Surg*. 2007;34(3):557–564.
240. Giraldo F, Esteva I, Bergero T, Cano G, González C, Salinas P, Rivada E, Lara JS, Soriguer F; Andalusia Gender Team. Corona glans clitoroplasty and urethrepupial vestibuloplasty in male-to-female transsexuals: the vulval aesthetic refinement by the Andalusia Gender Team. *Plast Reconstr Surg*. 2004;114(6):1543–1550.
241. Goddard JC, Vickery RM, Terry TR. Development of feminizing genitoplasty for gender dysphoria. *J Sex Med*. 2007;4(4 Pt 1):981–989.
242. Hage JJ, de Graaf FH, Bouman FG, Bloem JJAM. Sculpturing the glans in phalloplasty. *Plast Reconstr Surg*. 1993;92(1):157–161, discussion 162.
243. Thiagaraj D, Gunasegaram R, Loganath A, Peh KL, Kottegoda SR, Ratnam SS. Histopathology of the testes from male transsexuals on oestrogen therapy. *Ann Acad Med Singapore*. 1987;16(2):347–348.
244. Monstrey SJ, Ceulemans P, Hoebeke P. Sex reassignment surgery in the female-to-male transsexual. *Semin Plast Surg*. 2011;25(3):229–244.
245. Perovic SV, Djinnovic R, Bumbasirevic M, Djordjevic M, Vukovic P. Total phalloplasty using a musculocutaneous latissimus dorsi flap. *BJU Int*. 2007;100(4):899–905, discussion 905.
246. Vesely J, Hyza P, Ranno R, Cigna E, Monni N, Stupka I, Justan I, Dvorak Z, Novak P, Ranno S. New technique of total phalloplasty with reinnervated latissimus dorsi myocutaneous free flap in female-to-male transsexuals. *Ann Plast Surg*. 2007;58(5):544–550.
247. Ranno R, Vesely J, Hýza P, Stupka I, Justan I, Dvorák Z, Monni N, Novák P, Ranno S. Neo-phalloplasty with re-innervated latissimus dorsi free flap: a functional study of a novel technique. *Acta Chir Plast*. 2007;49(1):3–7.

248. Garcia MM, Christopher NA, De Luca F, Spilotros M, Ralph DJ. Overall satisfaction, sexual function, and the durability of neophallus dimensions following staged female to male genital gender confirming surgery: the Institute of Urology, London U.K. experience. *Transl Androl Urol.* 2014;3(2):156–162.
249. Chen H-C, Gedebo TM, Yazar S, Tang Y-B. Prefabrication of the free fibula osteocutaneous flap to create a functional human penis using a controlled fistula method. *J Reconstr Microsurg.* 2007;23(3):151–154.
250. Hoebeke PB, Decaestecker K, Beysens M, Opdenakker Y, Lumen N, Monstrey SM. Erectile implants in female-to-male transsexuals: our experience in 129 patients. *Eur Urol.* 2010;57(2):334–341.
251. Hage JJ. Metaidoioplasty: an alternative phalloplasty technique in transsexuals. *Plast Reconstr Surg.* 1996;97(1):161–167.
252. Cohanad S. Extensive metoidioplasty as a technique capable of creating a compatible analogue to a natural penis in female transsexuals. *Aesthetic Plast Surg.* 2016;40(1):130–138.
253. Selvaggi G, Hoebeke P, Ceulemans P, Hamdi M, Van Landuyt K, Blondeel P, De Cuypere G, Monstrey S. Scrotal reconstruction in female-to-male transsexuals: a novel scrotoplasty. *Plast Reconstr Surg.* 2009;123(6):1710–1718.
254. Bjerrome Ahlin H, Kölby L, Elander A, Selvaggi G. Improved results after implementation of the Ghent algorithm for subcutaneous mastectomy in female-to-male transsexuals. *J Plast Surg Hand Surg.* 2014;48(6):362–367.
255. Wolter A, Diedrichson J, Scholz T, Arens-Landwehr A, Liebau J. Sexual reassignment surgery in female-to-male transsexuals: an algorithm for subcutaneous mastectomy. *J Plast Reconstr Aesthet Surg.* 2015;68(2):184–191.
256. Richards C, Barrett J. The case for bilateral mastectomy and male chest contouring for the female-to-male transsexual. *Ann R Coll Surg Engl.* 2013;95(2):93–95.
257. Sutcliffe PA, Dixon S, Akehurst RL, Wilkinson A, Shippam A, White S, Richards R, Caddy CM. Evaluation of surgical procedures for sex reassignment: a systematic review. *J Plast Reconstr Aesthet Surg.* 2009;62(3):294–306, discussion 306–308.
258. Selvaggi G, Elander A. Penile reconstruction/formation. *Curr Opin Urol.* 2008;18(6):589–597.
259. Dhejne C, Lichtenstein P, Boman M, Johansson ALV, Långström N, Landén M. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. *PLoS One.* 2011;6(2):e16885.
260. Kuhn A, Bodmer C, Stadlmayr W, Kuhn P, Mueller MD, Birkhäuser M. Quality of life 15 years after sex reassignment surgery for transsexualism. *Fertil Steril.* 2009;92(5):1685–1689.e3.
261. Papadopoulos NA, Lellé JD, Zavlin D, Herschbach P, Henrich G, Kovacs L, Ehrenberger B, Kluger AK, Machens HG, Schaff J. Quality of life and patient satisfaction following male-to-female sex reassignment surgery. *J Sex Med.* 2017;14(5):721–730.
262. Simonsen RK, Hald GM, Kristensen E, Giraldi A. Long-term follow-up of individuals undergoing sex-reassignment surgery: somatic morbidity and cause of death. *Sex Med.* 2016;4(1):e60–e68.
263. Djordjevic ML, Bizic MR, Duisin D, Bouman MB, Buncamper M. Reversal Surgery in regretful male-to-female transsexuals after sex reassignment surgery. *J Sex Med.* 2016;13(6):1000–1007.
264. Liberopoulos EN, Florentin M, Mikhailidis DP, Elisaf MS. Compliance with lipid-lowering therapy and its impact on cardiovascular morbidity and mortality. *Expert Opin Drug Saf.* 2008;7(6):717–725.
265. Forbes SS, Stephen WJ, Harper WL, Loeb M, Smith R, Christoffersen EP, McLean RF. Implementation of evidence-based practices for surgical site infection prophylaxis: results of a pre- and postintervention study. *J Am Coll Surg.* 2008;207(3):336–341.
266. Davis PJ, Spady D, de Gara C, Forgie SE. Practices and attitudes of surgeons toward the prevention of surgical site infections: a provincial survey in Alberta, Canada. *Infect Control Hosp Epidemiol.* 2008;29(12):1164–1166.

INTERNATIONAL RESEARCH LITERATURE REVIEW

SCEG Project for Review and Redraft of Guidance for
Transgender Inclusion in Domestic Sport 2020



Carbmill Consulting

This document is produced specifically as part of the Review and Redraft of the Guidance for Transgender Inclusion in Sport for the Sports Councils' Equality Group of UK.

The literature review includes published scientific research relating to transgender inclusion in sport, and is based largely on peer-reviewed data, but also some pertinent opinion pieces (outlined in the text). It is written in a general chronological order, with reference to important milestones in international sport to provide context and relevance to historical events and policy decisions. In keeping with the remit from UKSport, the document focusses on scientific and medical literature related to performance, rather than sociological or ethical considerations. For simplicity and clarity, the terminology used here is male/female and transgender man/transgender woman/transgender people.

Contents

Executive summary	1
Introduction	2
Population-based differences between the sexes.....	2
Derivation of performance difference between the sexes in sport	4
History of sex categories and inclusion of transgender athletes.....	4
Debate about the Role of Testosterone	8
Medical and Psychosocial Aspects.....	8
Ethical Considerations.....	10
Conclusion.....	10
REFERENCES	11

Executive summary

The research base for the inclusion of transgender people in sport remains limited but is rapidly evolving.

The evidence outlining the sex dimorphism, or physical variance, between the sexes is robust: There are significant differences between the sexes which render direct competition between males and females unfair in most 'gender-affected sports' due to the physical advantages of males, and often unsafe in sports which allow physical contact and collisions.

Recent international guidelines, and subsequent policies, on the inclusion of transgender people (particularly transgender women) have attempted to negate male physical advantage, thereby allowing fair (and safe) competition. However, there is currently no direct evidence that this can be achieved by suppression of hormone levels. On the contrary, there are apparent life-long physiological advantages in the adult male, only some of which can be reversed, and it is not known whether physical benefit(s) may be retained in someone who does not achieve full maturity.

Transgender people face health concerns related to their transition and are prone to chronic side effects which are likely to be ameliorated by physical activity. On the other hand, female athletes are subject to specific health and injury concerns in direct relation to their reproductive physiology and

cyclic metabolism. It is not known if these differences create a meaningful disparity in performance sport.

Everyone benefits from physical activity for both physical and mental health, and there are reported advantages in relation to the social aspects of team sports in particular. These benefits should be available to everyone in our community, and it is known that transgender people face barriers in access to sport.

This short review presents a chronological precis of current evidence which impacts decision making on how best to include transgender people in sport.

Introduction

Transgender inclusion transects the established categorisation in sport and, by including those who have transitioned from the alternate sex category, has created challenges. The binary of sex categories in sport has existed for more than a century and arguably since the beginning of sport in ancient times when females were largely excluded. Sports have historically been developed for able-bodied males by able-bodied males, and the opportunity for females, children, masters' athletes, and disabled people has been an evolution of increased opportunity and inclusion through categorisation over many decades. It is important to note that all subsequent categories within competitive sport, including weight categories, have always been underpinned by the sex binary, and inclusion of other groups has been largely by the addition of new and separate competition within that binary.

Research literature for the evidential basis of inclusion for transgender people in sport remains limited. The definitive longitudinal studies tracking prospective gender transition in athletes, with appropriate objective measurements, competition results and with a relevant control population, have not yet been reported. Further, the scientific literature on performance differences between males and females across the sports is also limited because, until now, the relevance of this difference was questionable as the sexes have not routinely competed against each other. Hence much of the known information is laboratory based, rather than specific to sporting competition.

Population-based differences between the sexes – the rationale for gender-affected competition

In adulthood, there are clear differences in muscle mass, strength, and physiological capacity even after controlling for differences in height and weight between the sexes. On average, males have 40-50% greater upper limb strength, 20-40% greater lower limb strength, and an average of 12kg more skeletal muscle mass than age-matched females at any given body weight (Janssen et al 2000, Handelsman et al 2018).

Following full growth, males are measured at an average 13-15cm (5-6 inches) taller than females. The National Health Service in 2018 quotes the average young adult male in England at a height of 178.0cm (5ft 10in) with an estimated standard deviation (SD) of 9.19cm. The average young adult female in England is 164.1cm (5ft 4 1/2in), SD 7.51cm. In the USA the statistics are very similar: Males average 175.9cm, SD 7.42cm, and females average 162.1cm, SD 7.11cm.

When plotted across the population it is evident that 50% of males are taller than some 97% of females. So, in any random grouping of males and females, half of the males will be taller than nearly all females.

Handgrip dynamometry is probably the most commonly used method to characterize overall human muscle strength (Bohannon et al 2019). European data of over 2000 young adult males and females demonstrates “mean maximal hand-grip strength showed clear difference between men (541 Newtons) and women (329 Newtons); 90% of females produced less force than 95% of males”. And further.... “highly trained female athletes corresponded to only the 25th percentile of the (untrained) male subjects” (Leyk et al, 2007).

Therefore, this would mean that in a random group of ten males and ten females, only the strongest female is likely to be stronger than the weakest male.

Males have a larger, stronger and denser skeleton, with longer levers (arms and legs), and bigger hands and feet. Males also have larger hearts and greater blood volume with higher haemoglobin concentration, and hence greater oxygen carrying capacity, with bigger lungs and airway capacity compared with females. The differences in physical/physiological capacity are synergistic such that males are larger, stronger and faster, with greater aerobic capacity and for which the summation is likely to be greater than the individual differences.

The muscle strength, physiological and size differences between the sexes correlate with significant sporting achievement from around 10-12% for most linear swimming and running events, 20% difference in jumping events, and a 35% difference in weightlifting ability in weight matched males and females. If an average sized male is compared with an average size female (based on the NHS data, 2018) the weightlifting ability increases to 50% greater for males (World Record Snatch; 85kg Male - 187kg lift; 69kg Female - 123kg lift).

It is often assumed that children have similar physical capacity regardless of their sex, and hence mixed competition is allowed in many sports up until the age of around 11 years (to coincide with puberty). However large-scale data reports on children from the age of six show that young males have significant advantage in cardiovascular endurance, muscular strength, muscular endurance, speed/agility and power tests, but score lower on flexibility tests (Tambalis et al, 2016; Catley & Tomkinson, 2013).

In adults the average advantage of 10-12% in running events can be interpreted for both the ‘average’ competitor, as well as for elite performers where the percentage difference remains the same for similarly trained people. When measured in absolute time, i.e. the difference to reach the finish line, this will vary based on the ability of the athletes; but the distance between the competitors remains the same. In this way a 10-12% better performance by a competitor would see Adam Peaty being beaten by half a length in the short-course 100m breaststroke and Dina Asher Smith by 22m in the 200m track sprint. And Sir Mo Farah would be lapped twice in the 10,000m track race.

While there may be many differences between competitors of the same sex (such as height, skill, and training methods), what is relevant about the advantage between the sexes and the reason for the category division, is the scale of advantage across virtually all sports. World Rugby (2020) has referred to “...the almost perfect sensitivity of biological sex.... since in a ranking list of the top thousand performances in most sport, every year, every single one will be biologically male”. The winning margin (the difference in performance by which a competitor misses a gold medal, any medal, or making the final) in elite athletics or swimming events during the last three Olympics is

less than just 1% for both male and female events, compared with up to a 50% difference between sex-based performances.

Derivation of performance difference between the sexes in sport

The known dichotomy in athletic performance between the sexes has long been acknowledged to largely be in relation to the difference in gonadal androgens, namely testes derived testosterone and its more potent metabolite dihydrotestosterone in males, and ovarian estrogen in females.

Males are prenatally (before birth) and perinatally (soon after birth) exposed to high level androgens, and then experience a further surge in testosterone levels during puberty, which is maintained throughout adult life. On the other hand, females normally never experience testosterone exposure beyond a basal level at any time during life ($<2\text{nmol/L}$). From the onset of male puberty, the testes secrete 20 times more testosterone, resulting in circulating testosterone levels that are 15 times greater in healthy young males than in age-similar healthy females (Handelsman et al 2018).

However, females enter maturational puberty at least a year before males, and this may create a brief equivalence in the height of children around the age of 10, before males enter puberty from around the age of 11.

Anabolic steroids, of which testosterone is the significant 'natural' form, were one of the original groups of banned drugs when anti-doping practices developed in the 1970s. Both endogenous (made within the body) and exogenous testosterone (delivered into the body from an external source) are identical chemical substances and have equivalent effects in the body. Testosterone concentration positively correlates with leg press strength, thigh muscle volume and haemoglobin levels, and the anabolic response to testosterone can largely be predicted by the dose administered (Bhasin et al 2001). Testosterone is largely responsible for the increased muscle mass through increases in muscle fibre numbers and size, muscle satellite cell numbers, numbers of myonuclei (muscle cells nucleus), and size of motor neurones (nerve cells) as well as advantageous biochemical changes in muscle function in males. Importantly stimulation of myonuclei is life-long (Handelsman et al 2018). This is so-called 'muscle memory' and is one of the reasons why doping sanctions were increased to four years to try to account for this long-term effect on performance.

For ethical and doping control reasons it has not been possible to evaluate the effect of testosterone in healthy young athletes beyond cross sectional studies, but observational reports have lent credence to this understanding. During the era of the former German Democratic Republic, systematic doping of athletes was developed and later confirmed on release of the so-called 'Stasi Files'. Regime scientists stated after the 1972 Munich Olympics: "the effects of the treatment with androgenic hormones were so spectacular, particularly in female athletes in strength dependent events, that few competitors not using the drugs had a chance of winning". Further, the long-term effect of androgenic/anabolic steroids was attested by the acknowledgement that "after a critical period of increase in muscle strength, a higher performance level is reached that does not return to pre-treatment values after the drug is withdrawn" (Franke & Berendonk 1997).

History of sex categories and inclusion of transgender athletes

Previous practices of 'gender (sex) verification' for female athletes were developed "in order to exclude those in which a genetic alteration gives the competitor registered as a female anatomical advantages of masculinization" (Hay 1985). There was no perception that females would pose a

competitive threat to male athletes. Genetic testing, which received “great support” from athletes, was contentious within the scientific community and was subsequently abandoned in 2000 for the Sydney Olympics (Ljungqvist 2000). This was largely due to some infamous cases in which inadequate processes resulted in inappropriate disqualification of athletes.

The Stockholm Consensus of the IOC in 2003 established the first international policy for transgender inclusion in international sport. This was not a referenced document; “at the time, there was no published scientific literature that would justify the inclusion of transgender women” (Harper 2015). Transgender people were at this time required to have full surgical transition in order to compete in their acquired gender.

Dr Arne Ljungqvist, the then IOC Medical Commission Chair, is reported (Harper 2015) to have relied heavily on the opinion of Dr Louis Gooren who went on to publish in 2004 the first comparative study of the physical/physiological attributes of transsexual men and women. In this study the metabolic and morphological changes of 17 transgender men and 19 transgender women were studied before and after their gender-affirming medication. The pre-treatment data serves as control groups for the respective treatment groups for statistical analysis. Muscle mass (measured by MRI) and serum haemoglobin were compared across one and then three years of treatment.

Following one year of androgen(testosterone) deprivation, muscle mass decreased significantly in the transgender women, but remained significantly higher than the pre-treatment transgender men (female) group. On the other hand, the transgender men on testosterone supplementation increased muscle mass such that there was no statistical difference between these subjects and the pre-treatment transgender women (male) group. There was no difference between the treatment groups (transgender men and transgender women) after one year of treatment. There was a further non-significant loss of muscle mass following a further two years of treatment of transgender women. Haemoglobin levels converted into the respective ranges of the acquired gender in each group within the first year. This would have a corresponding effect on blood oxygen carrying capacity, and hence aerobic ability. It was noted that height was a strong independent predictor of muscle mass in both males and females, and both pre- and post- gender transition (Gooren and Bunck 2004).

Following cessation of gender/sex (chromosomal) testing in 2000, athletes with Disorders (Differences) of Sexual Development (DSD) were successful in major athletic competitions; notably at the Athletics World Championships in 2009. There followed a decade during which several athletes with the genetic disorder ‘46XY 5ARD’ (46 XY chromosome women in which an enzyme abnormality causes testosterone to rise to high levels) were in dispute with the IAAF/World Athletics through lengthy court proceedings in relation to their hyperandrogenic status. While these cases do not have direct relevance to transgender inclusion in sport what is important is that as a result of the requirement for evidence and information for court documentation, there was a significant increase in both the research and academic literature on the effect of testosterone in sports performance over this period.

During the Daegu World Athletics Championships in 2011, research on behalf of the IAAF and WADA on the normative values of serum androgen levels of elite track and field athletes was conducted in order to inform the blood steroidal module of the Athlete Biological Passport for doping control (Bermon et al 2014). This research was able to define the median value of serum testosterone in elite female athletes at 0.69 nmol/L with a 25-75% range of 0.50 to 0.91nmol/L, and a 99th percentile calculated at 3.08nmol/L. The testosterone levels in the DSD group were as high as 29.30nmol/L, while the standard male range of testosterone is 7.7 to 29.4nmol/L (Handelsman 2018). It was

calculated that, within the elite athlete population, hyperandrogenism in relation to XY DSD was 140 times more common than in the general population.

Researcher Joanna Harper published comparative data in 2015, around the time that the second IOC Consensus Statement on Sex Reassignment was published. In this study, the race times of eight transgender/transsexual women were recorded both pre- and post- transition. All subjects were recreational distance runners who self-reported race times (which were verified where possible) in equivalent events over a period stretching from one year up to twenty-seven years apart. No testosterone levels were reported for the athletes, either before or after the transition. Calculations were made to compare their race times with those of age-graded performances in the respective gender. The findings indicated that the comparative race times were equivalent pre- and post-transition, and this implies that transition did not give these transgender women a competitive advantage (Harper 2015). This was the first study to attempt to measure physical performance following transition, compared with pre-transition ability and, while there were several acknowledged limitations to the study, this information appears to have been crucial in the subsequent deliberations of the second IOC Consensus Meeting.

The second Consensus Paper of the IOC was published in November 2015. Surgery is no longer required to be eligible to compete, and transgender women are required to suppress testosterone levels to below 10nmol/L for 12 months before competition. This testosterone level is 5-10 times the testosterone level of females of any age and remains within the accepted range for males, and it has not been defined as to how this level was determined by the IOC. Transgender men can enter male competition without requirement.

Over the past two decades there have been a dozen published research papers (five of which were published in 2018-20) for a total of some 800 participants which investigated the effect of testosterone suppression on muscle mass, and in some instances muscle strength, in transgender women.

Post-suppression testosterone levels measured in these studies were all less than 10nmol/L, most being below 5nmol/L, and seven studies where testosterone level was less than 1nmol/L (ie at the level of females). Most studies included estrogen therapy for participants. On review by Hilton and Lundberg, the findings from the composite of existing research was that loss of muscle mass and/or strength following 12 months of testosterone suppression is relatively modest compared with the initial advantage. The average loss of muscle mass across all studies was around 5%, which is less than the 9% loss measured in the seminal work of Gooren and Bunck. In those studies which recorded the retained muscle mass/strength, there was an average of 25% residual advantage for transgender women at 12 months treatment compared with reference a group of females (Hilton and Lundberg 2020).

In the most recent study, by Wiik and colleagues from the Karolinska Institute in Sweden, there was minimal loss of muscle mass or strength in transgender women following 12 months of testosterone suppression, and some subjects gained strength. After treatment transgender women remained 48% stronger, with 35% larger quadriceps mass compared with the control population of females (Wiik et al 2020).

Harper and colleagues also reviewed the available scientific literature and published in the British Journal of Sports Medicine in March 2021. They concluded that “haemoglobin levels rapidly reduce in transwomen” while “strength may be well preserved during the first 3 years of hormone therapy” (Harper et al 2021).

Recent research citing retrospective data from military personnel in the US has shown that transgender women retain an advantage in running speed after more than two years of follow-up on testosterone suppression, at a residual of some 12% faster than the known normative values for females. In the same study, values for numbers of 'push-ups' and 'sit-ups' had reverted to female levels, but data on training levels and performance targets was lacking. Results for the transgender men studied exceeded those of the average performance for age-matched males after one year of testosterone supplementation (Roberts et al, 2020).

From the synthesis of current research, the understanding is that testosterone suppression for the mandated one year before competition will result in little or no change to the anatomical differences between the sexes, and a more complete reversal of some acute phase metabolic pathways such as haemoglobin levels although the impact on running performance appears limited, and a modest change in muscle mass and strength: The average of around 5% loss of muscle mass and strength will not reverse the average 40-50% difference in strength that typically exists between the two sexes. These findings are at odds with the accepted intention of current policy in sport, in which twelve months of testosterone suppression is expected to create equivalence between transgender women and females.

It is recognised that research to date has not been carried out in an elite athletic population (although military data includes well-trained individuals), and it is not known if the relative muscle loss will be more or less in those who are undergoing training, relative to the published results in non-athletic populations. It is known however, that males who undergo androgen suppression as part of treatment for prostate cancer can improve muscle strength and mass when also undertaking a training program, whereas the absence of training results in 4% reductions in muscle mass, similar to those observed in trans women whose testosterone is suppressed without training (Galvao et al 2006). The implication is that training during a period of testosterone suppression may attenuate the reductions observed in the longitudinal studies, which would increase the retained advantage when comparisons are made with a reference group of females.

The notion of safety in sport is related to size and maturity of competitors and is one of the reasons that junior athletes are not routinely eligible to play against adults in contact and collision sports. Because the two sexes have not historically competed against each other as adults in these sports, there is not yet experience of the injury risk to which females may be exposed in such competition, nor with the inclusion of transgender people beyond anecdotal reports. Injury risk can be appreciated through analysis of the combination of mass and speed of competitors and hence the force that can be generated, in which the larger and faster opponent will pose a risk to those that are smaller and slower when tackled. At a conference convened by World Rugby in London in February 2020, information was presented (and subsequently published as part of World Rugby Transgender Guideline) of a theoretical framework for injury risk based on validated mechanical modelling, relevant to the size differential of male players compared with female players. While not including the speed of a bigger opponent, nor the neck strength of the smaller, the increased mass alone accounted for an estimated increase in the risk factors for head and neck injury of 20-30%. Given the modest reduction of body mass by testosterone reduction in transgender women this was estimated to pose an unacceptable risk to female players and, in part, resulted in the decision to render transgender women ineligible to compete in international contact rugby union (World Rugby 2020).

Debate about the role of testosterone

Writing an 'Observation' in the Scientific American journal in June 2019, Rebecca Jordan-Young and Katrina Karkazis, authors of "Testosterone; an Unauthorised Biography", question the validity of ascribing the differences between male and female athletes solely to endogenous levels of testosterone. They draw attention to the inconsistency between measured testosterone levels and performance. The research published on behalf of the IAAF (Bermón & Garnier 2017) received criticism from the scientific community and required formal correction. Jordan-Young and Karkazis stress that in three of the eleven running events cited, it was the group with the lowest testosterone levels who performed best, and there was a strong negative association between testosterone levels and 100m race time.

The authors quote published work from Pielke, Tucker and Boye (2019), which questions the validity of IAAF(WA) research which was requisite by the Court of Arbitration in Sport (CAS) to demonstrate that "high androgen levels confer a significant performance advantage over other female competitors, comparable to the performance advantage that male athletes enjoy over female athletes".

In the event, the full evidence base presented by IAAF/World Athletics was ultimately successful at CAS, and this was defended again on appeal. However, the contention remains in the scientific community that the case has not been made that circulating testosterone can fully explain all the observed difference in male/female performance variables (Jordan-Young & Karkazis 2019).

Importantly, the corollary of circulating testosterone levels not being fully accountable for this difference is that there must be another, as yet undefined factor(s), which must account for the remaining differences following testosterone suppression. The retained advantage may mean that previous testosterone exposure is responsible for long-term effects, or there is another explanation, perhaps referable to genetic differences, which has not yet been identified.

Following the legal cases, World Athletics also created policy for the inclusion of transgender women based on suppression of testosterone levels to 5nmol/L. Between 2018 to 2019, several major sporting international governing bodies developed policies at the 5nmol/L level for transgender women, in comparison with the 10nmol/L defined by the IOC.

Medical and Psychosocial Aspects

A review published in 2017 by Bethany Jones and colleagues from Nottingham/Loughborough Universities looked at research that explored the experience of transgender people in sport, as well as the policies which were in place at the time which influenced such experience. While only eight research papers met the criteria for the study, in those which looked at the experience of transgender inclusion, it was acknowledged that the experience of transgender people in sport was largely negative. The authors' assessment of the available literature on physical parameters was to highlight the lack of direct comparative data in athletes on which to base exclusionary policies. They indicate that 'There are several areas of future research required to significantly improve our knowledge of transgender people's experience in sport, inform the development of more inclusive sport policies, and most importantly, enhance the lives of transgender people, both physically and psychosocially' (Jones et al, 2017).

Differences in physiology and health parameters between males and females have long been acknowledged and recent research has shed light on how this affects performance, as well as health,

illness and injury. The menstrual cycle creates challenges for many female athletes and the variable nature of ovarian hormones can limit training and performance, and also alter perceptions of wellbeing. Furthermore, amenorrhoea (loss of menstrual cycling) is common in sport due to high training loads and inadequate energy intake. This has secondary consequence of not just altered fertility but increased rates of injury and illness. The naturally lower bone density of females is further reduced with the hormonal deprivation of amenorrhoea and this group is particularly prone to stress fractures, a significant problem in running sports. Female athletes are not immune to gynaecological illnesses, and endometriosis which has an incidence of up to 20% in the general population, has plagued the career of several high-profile athletes who have chosen to go public with their inability to compete as a result of pain and illness.

Recent research has highlighted the relationship of the menstrual cycle and the observed increased injury incidence and slower recovery in women compared with men, in particular for concussion (McGroarty et al 2020), and major ligament injury such as anterior cruciate ligament tears (Wojtys et al 2002). The physical problems related to the menstrual cycle are now so well appreciated that ongoing research in health and hormonal monitoring is taking place in the UK (Football Association) and abroad. This research is designed to define parameters whereby limitations to training and performance can be minimised.

By way of comparison, it is known that transgender people suffer increased risk of ill-health as a result of medication and cross-sex hormone therapy. Transgender women face heightened risk of thrombo-embolic disease, arterial disease, liver dysfunction and breast cancer (although at levels lower than females). Transgender men risk high red cell levels (polycythaemia), hypertension and arterial disease, as well as reproductive cancer. These are chronic conditions for which exercise is both preventive and therapeutic and are unlikely to present any direct negative effects in relation to sporting performance. Certainly, evidence indicates that bone health and density is maintained in transgender women despite testosterone suppression (Van Caenegem et al 2015).

Over time it may become apparent that medically transitioning will lead to health and injury issues specific to transgender athletes, but this will not have the cyclical nature of gynaecological function and any sport specific concerns are likely to be different to those experienced by females and males. It will be important to track and define the health consequence of the required medical treatments required by sports agencies to compete in one's affirmed gender.

We are not aware of research which will allow any conclusions to be drawn on the current medical practice of transition in younger people, and what effect this may have on physical and sporting capacity. In the UK, so-called 'puberty blockers' are generally not used until Tanner maturation stage 2-3 (i.e. after puberty has progressed into early sexual maturation), and medical practice is currently under review. As described above it is evident that current knowledge cannot explain the exact derivation of all the performance differences between the sexes, and correspondingly what, if anything, can be done to reverse these differences in adults.

While exercise and activity are known to positively impact mental health, elite level training and competition are known to increase stress. Both competitive athletes and transgender people have separately reported high levels of mental ill-health, notably anxiety states, depression, and poor coping mechanisms with stress: These include self-harm and eating disorders. It is not known how the stresses of competition may affect transgender athletes.

Reports of suicidality in transgender people are contentious. A recent large-scale meta-analysis of five peer-reviewed papers of over 1000 study subjects found a prevalence of suicide attempts of 14.8% (Surace et al, 2020). This is at odds with other commissioned reports of smaller sample sizes which give much higher estimates.

There is no contention however as to the value of physical activity and community membership on mental health outcomes. These benefits should be available to all.

Ethical Considerations

The notion of ethics within sport is largely based on established theories of fairness and fair play, advantage, inclusion, safety and values. The competing 'rights' of individuals can be explored through both legal and philosophical discourse. These writings are beyond the scope of this document; however, it is relevant to consider the implication of sporting rules (such as testosterone suppression or use of puberty blockers) which may or may not have a desired outcome, and which have can have unintended poor health outcomes for the individual. Further, the development of protocols within sport which create an environment whereby 'case-by-case' analysis judgements of an individual may restrict their rights, as well as those of others, can be fraught.

Conclusion

Sexual dimorphism in relation to sport is significant and the most important determinant of sporting capacity. The challenge to sporting bodies is most evident in the inclusion of transgender people in female sport.

Current international rules require testosterone suppression to achieve equity in female sporting competition. In the light of existing evidence, the following is likely to be true:

Testosterone supplementation in transgender men results in strength and stamina (haemoglobin) parity with males within twelve months. Skeletal differences (smaller physique) will remain in keeping with female dimensions.

Testosterone suppression has differing effects for different body systems, and this can be correlated with the factors of 'gender-affected sport'; Strength, Stamina and Physique;

- Strength; Modest change within 12 months: Muscle mass (and perhaps cardiac size) and hence strength - appears retained at significantly higher levels than females.
- Stamina; Restoration of haemoglobin levels to female typical levels within 12 months: with relevant effect on oxygen carrying capacity as yet undefined.
- Physique; Minimal change: Structural features including the skeleton, bone density, height, lung and airway size, and tendon/ligament strength will remain, with modest loss of muscle mass.

This evidence suggests that parity in physical performance in relation to gender-affected sport cannot be achieved for transgender people in female sport through testosterone suppression. Theoretical estimation in contact and collision sport indicate injury risk is likely to be increased for female competitors.

There are significant ethical and legal considerations associated with the requirement for treatment which may not result in the desired outcome. Ongoing research may allow better understanding of comparative data to inform decision making.

The health and social imperative to include transgender people in physical activity and sport is paramount. The task for the National Governing Bodies of sport is to achieve safe, fair and inclusive sport, and/or inclusive, fair and safe sport. How this can be achieved will be explored within this review process.

REFERENCES

- Bermon S, Garnier PY, Hirschberg AL, et al (2014). Serum Androgen Levels in Elite Female Athletes; *The Journal of Clinical Endocrinology & Metabolism*; Vol 99: Issue 11, 4328-4335
- Bermon S, Garnier PY (2017). Serum androgen levels and their relation to performance in track and field: mass spectrometry results from 2127 observations in male and female elite athletes. *British Journal Sports Medicine*; Vol 51: Issue 17
- Bhasin S, Woodhouse L, Casaburi R, Singh AB et al (2001). Testosterone dose-response relationships in healthy young men. *American Journal of Physiology, Endocrinology and Metabolism*; Vol 281: E1, 172-181.
- Bohannon RW, Wang YC, Yen SC, Grogan KA (2019). Handgrip strength: A Comparison of Values Obtained from the NHANES and NIH Toolbox studies. *American Journal of Occupational Therapy*; March/April, Vol 73: No 2, 1-9
- Catley MJ & Tomkinson GR (2013). Normative health-related fitness values for children: analysis of 85347 test results on 9-17-year-old Australians since 1985. *British Journal of Sports Medicine*; Vol 47: 98-109.
- Equality Act (2010) UK <https://www.legislation.gov.uk/ukpga/2010/15/contents>
- Franke WW, Berendonk B (1997). Hormonal doping and androgenization of athletes: a secret program of the German Democratic Republic Government. *Clinical Chemistry*; Vol 43(7):1262-1279
- Galvao DA, Nosaka K, Taaffe DR et al (2006). Resistance training and reduction of treatment side effects in prostate cancer patients. *Med Sci Sports Exercise*; 38:2045-52.
- Gooren LJG and Bunck MCM (2004). Transsexuals and competitive sports. *European Journal of Endocrinology*; 151: 425-429
- Handelsman DJ, Hirschberg AL, Bermon S; (2018). Circulating testosterone as the Hormonal Basis of Sex Differences in Athletic Performance: *Endocrine Reviews*; Vol 39: 803-82
- Harper, J (2015). Race Times for Transgender Athletes: *Journal of Sporting Cultures and Identities*; Vol 6: Issue 1
- Harper J, O'Donnell E, Khorashad BS, McDermott H, Witcomb GL (2021). How does hormone transition in transgender women change body composition, muscle strength and haemoglobin? Systematic review with a focus on the implications for sport participation. *British Journal of Sports Medicine*; 10.1136/bjsports-2020-103106
- Hay E (1985). Femininity Controls in the Olympic Games: Sports Medicine in Track & Field Athletics; *IAAF Medical Congress (Proceedings)*; Canberra, Australia, pages 49-52.

- Hilton EN, Lundberg TR (2020). Transgender Women in the Female Category of Sport: Perspectives on Testosterone Suppression and Performance Advantage. *Sports Medicine*; <https://doi.org/10.1007/s40279-020-01389-3>
- Janssen I, Heymsfield SB, Wang ZM, Ross R (2000). Skeletal muscle mass and distribution in 468 men and women aged 18-88yr. *J Appl Physiol*; Vol 89(1):81-88
- Jones, BA, Arcelus J, Bouman WP, Haycraft E. (2017) Sport and Transgender People: A Systematic Review of the Literature Relating to Sport Participation and Competitive Sport Policies. *Sports Medicine*; 47: 701-716
- Jordan-Young RM, Karkazis K. (2019) 4 Myths about Testosterone. *Scientific American*; 18 June 2019. <https://blogs.scientificamerican.com/observations/4-myths-about-testosterone/>
- Leyk, D, Gorges, W, Ridder, D et al. (2007). Hand-grip strength of young men, women and highly trained female athletes. *European Journal of Applied Physiology*; 99: 415–421. <https://doi.org/10.1007/s00421-006-0351-1>
- Ljungqvist A (2000). Gender Verification: *The Encyclopaedia of Sports Medicine (IOC & ISMF)*; Vol VIII: Chapter 13
- McGroarty NK, Brown SM, Mulcahey MK (2020). Sport-Related Concussion in Female Athletes, A Systemic Review: *Orthopaedic Journal of Sports Medicine*; 8(7) [https://DOI: 10.1177/2325967120932306](https://DOI:10.1177/2325967120932306)
- National Health Service: Health Survey for England (2018) <http://digital.nhs.uk/pubs/hse2018>
- Pielke, R, Tucker, R & Boye, E (2019). Scientific integrity and the IAAF testosterone regulations. *International Sports Law Journal*; 19: 18–26. <https://doi.org/10.1007/s40318-019-00143-w>
- Roberts TA, Smalley J, Ahrendt K (2020). Effect of gender affirming hormones on athletics performance in transwomen and transmen: implication for sporting organisations and legislators. *British Journal of Sports Medicine*. Accepted 28 August 2020. <http://dx.doi.org/10.1136/bjsports-2020-102329>
- Surace T, Fuser-Poli L, Voza L, Cavone V, Arcidiacono C et al (2020). Lifetime prevalence of suicidal ideation and suicidal behaviors in gender non-confirming youths: a meta-analysis. *European Journal Child Adolescent Psychiatry* Mar 13, DOI: [10.1007/s00787-020-01508-5](https://doi.org/10.1007/s00787-020-01508-5)
- Tambalis KD, Panagiotakos DB, Psarra G, Daskalakis S, Kavouras SA, Geladas N, Tokmakidis S & Sidossis LS (2016). Physical fitness normative values for 6-18-year-old Greek boys and girls, using the empirical distribution and lambda, mu, and sigma statistical method. *European Journal of Sport Science*; 16:6 736-746
- Van Caenegem E, Wierckx K, Taes Y et al (2015). Preservation of volumetric bone density and geometry in transwomen during cross-sex hormonal therapy: a prospective observational study. *Osteoporosis Int*; 26(1): 35-47
- Wiik A, Lundberg TR, Rullman E et al (2020). Muscle strength, size, and composition following twelve months of gender-affirming treatment in transgender individuals. *Journ Clin Endocrinol Metab*; 105(3):805-813 doi:10.1210/clinem/dgz247

Wojtys EM, Huston LJ, Boynton MD, Spindler KP& Lindendfeld TN (2002). The Effect of the Menstrual Cycle on Anterior Cruciate Ligament Injuries in Women as Determined by Hormone Levels; *American Journal of Sport Medicine*; 30(2): 182-188.

World Rugby: Player Welfare and Guidelines: 2020

<https://playerwelfare.worldrugby.org/?subsection=84>

<https://playerwelfare.worldrugby.org/?subsection=5>

Effect of gender affirming hormones on athletic performance in transwomen and transmen: implications for sporting organisations and legislators

Timothy A Roberts ,¹ Joshua Smalley,² Dale Ahrendt²

¹Pediatrics, Children's Mercy Division of Adolescent Medicine, Kansas City, Missouri, USA
²Pediatrics, San Antonio Military Medical Center, Fort Sam Houston, Texas, USA

Correspondence to

Dr Timothy A Roberts, Pediatrics, Children's Mercy Division of Adolescent Medicine, Kansas City, Missouri, USA; taroberts@cmh.edu

Accepted 28 August 2020
Published Online First
7 December 2020

ABSTRACT:

Objective To examine the effect of gender affirming hormones on athletic performance among transwomen and transmen.

Methods We reviewed fitness test results and medical records of 29 transmen and 46 transwomen who started gender affirming hormones while in the United States Air Force. We compared pre- and post-hormone fitness test results of the transwomen and transmen with the average performance of all women and men under the age of 30 in the Air Force between 2004 and 2014. We also measured the rate of hormone associated changes in body composition and athletic performance.

Results Participants were 26.2 years old (SD 5.5). Prior to gender affirming hormones, transwomen performed 31% more push-ups and 15% more sit-ups in 1 min and ran 1.5 miles 21% faster than their female counterparts. After 2 years of taking feminising hormones, the push-up and sit-up differences disappeared but transwomen were still 12% faster. Prior to gender affirming hormones, transmen performed 43% fewer push-ups and ran 1.5 miles 15% slower than their male counterparts. After 1 year of taking masculinising hormones, there was no longer a difference in push-ups or run times, and the number of sit-ups performed in 1 min by transmen exceeded the average performance of their male counterparts.

Summary The 15–31% athletic advantage that transwomen displayed over their female counterparts prior to starting gender affirming hormones declined with feminising therapy. However, transwomen still had a 9% faster mean run speed after the 1 year period of testosterone suppression that is recommended by World Athletics for inclusion in women's events.

BACKGROUND

Most competitive sports segregate male and female athletes due to biologic differences between the sexes. Because exposure to testosterone in males leads to physiologic advantages in strength and endurance, female sports need to be a protected category to ensure fairness in competition.¹ Questions arise then as to which category a transgender athlete competes in and how society balances benefits to the athlete of sports participation in their experienced gender with perceptions of fairness to other athletes.^{2–5} Supraphysiologic doses of androgens have a positive effect on athletic performance.^{6–7} However, gender affirming hormones have an unknown effect on athletic performance among transgender individuals during gender transition, making it difficult to develop guidelines for

transgender inclusion in sports. Several guidelines for inclusion of transgender athletes in elite international or professional sports exist but they are based on limited research.^{8–9} The World Athletics (IAAF) and the International Olympic Committee (IOC) created guidelines requiring female athletes to demonstrate suppression of testosterone levels to less than 5–10 nmol/L for at least 12 months prior to competing in women's events. However, athletes have challenged the section of these guidelines applying to women with disorders of sexual development and other causes of hyperandrogenism, citing a lack of supporting evidence, which calls these guidelines into question.^{10–11}

Gender affirming administration of testosterone in transmen decreases adiposity, and increases muscle mass, thigh muscle volume, haemoglobin, grip strength and thigh strength.^{9–12–14} Gender affirming blockage of testosterone and administration of oestrogen in transwomen (oestrogen) has the opposite effect, but transwomen retain an advantage in muscle mass, volume, and strength over female controls after 1 year on oestrogen.^{9–14–17} Most changes in body composition occur within the first year on testosterone or oestrogen, with slower changes after that time.^{9–16–18–20}

How do these body composition changes affect athletic performance? A retrospective review of self-reported run times among eight transwomen runners found an overall decline in times collected months to years before and after starting oestrogen but not in the runners' performance relative to runners of the same age and gender. No other studies have examined the effect of testosterone or oestrogen on athletic performance.²¹

We conducted this study to examine the effect of gender affirming hormones on body composition and athletic performance among transgender individuals to help improve future guidelines for transgender inclusion in sporting competition.

METHODS

Study population

This was a retrospective review of medical records and fitness tests results from 222 self-identified military personnel who filed a request to begin gender transition or continue testosterone or oestrogen while serving in the United States Air Force (Air Force).

Patient involvement

The idea for this study arose from our discussions with servicemembers seen in the Air Force



© Author(s) (or their employer(s)) 2021. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Roberts TA, Smalley J, Ahrendt D. *Br J Sports Med* 2021;**55**:577–583.

Transgender Clinic about the effect of testosterone or oestrogen on body composition and athletic performance on the Air Force physical fitness assessment. We did not know how to advise them based on the medical literature. We conducted this study to address this concern.

Demographic variables

We recorded the servicemember's age, service branch, military rank, gender assigned at birth, date testosterone or oestrogen started, type of testosterone or oestrogen used and days between starting testosterone or oestrogen and the first serum hormone level in the adult range recorded in the military electronic medical record. For transwomen, we also recorded the days between starting oestrogen and the first laboratory test indicating suppression of endogenous testosterone. We had incomplete records of testosterone or oestrogen obtained outside the military healthcare system.

Outcome measures

The Air Force requires servicemembers to participate in a physical fitness assessment every 12 months, including measurement of height, weight, waist circumference, number of push-ups and sit-ups performed in 1 min each, and time required to run 1.5 miles. The Air Force uses these tests to assess suitability for promotion, inclusion in specialised programmes and retention in the military service. The Air Force requires servicemembers to participate in all events unless a medical provider grants them a waiver for participation in a specific event secondary to a medical condition. Servicemembers with a waiver for a portion of the assessment must retake the assessment every 6 months. Enlisted servicemembers engage in regular group exercise. However, the type and intensity of training vary by occupation. The Air Force requires servicemembers who fail to meet physical fitness standards to attend additional physical training sessions outside of normal work hours until they can meet the fitness requirements or leave military service.

We assessed pretreatment fitness using the most recent score from each event on the physical fitness assessment prior to starting testosterone or oestrogen. We assessed post-treatment fitness using all fitness test scores occurring in the first 30 months after starting testosterone or oestrogen. We also recorded the time elapsed between starting testosterone or oestrogen and the occurrence of each event. The primary outcome for this study was change in fitness assessment score between the pre-hormone assessment and post-hormone assessment.

We used the results of the Air Force fitness tests performed by men (>2.3 million) and women (>567 000) under the age of 30 between 2004 and 2014 as a proxy for average performance among men (CM) and women (CW) in the Air Force.²² We used the results of all fitness tests performed by men (>3.5 million) and women (>777 000) in the Air Force between 2004 and 2014 as a proxy for height and weight among men (CM) and women (CW) in the Air Force.²²

Statistical analysis

We used generalised linear mixed models with a first order autoregressive repeated covariance type in SPSS V.24 to assess the association of hormonal therapy with changes in physical fitness assessment scores. We selected this analysis method to account for correlation between repeated measures, variable number of follow-up assessments, variable follow-up times and missing data points for each participant. From this analysis we obtained an estimated mean of push-ups performed in 1 min,

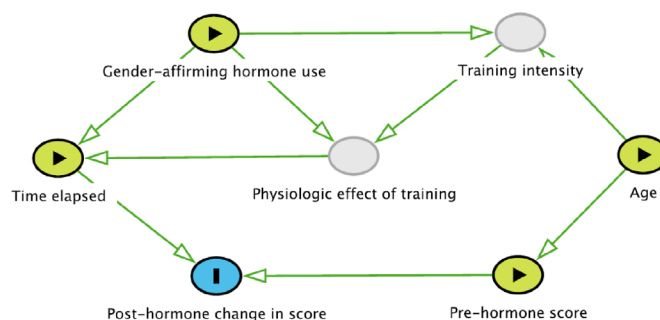


Figure 1 Directed acyclic graph of our multivariable model. Pre-hormone score: the results of the most recent physical fitness assessment prior to starting gender affirming therapy. Age: age in years when starting gender affirming hormone therapy. Training intensity: type and amount of exercise performed by the servicemember. Physiologic effect of training: effect of training performed on the servicemember's strength and endurance. Time elapsed: time interval (months) between starting gender affirming hormone therapy and the assessment of physical performance. Post-hormone change in score: change in push-ups, sit-ups and run times between the pre-hormone assessment and the current assessment (primary study outcome).

sit-ups performed in 1 min and 1.5 mile run times for transmen and transwomen before testosterone or oestrogen, between 0 and 1 years on testosterone or oestrogen, 1–2 years on testosterone or oestrogen and over 2 years on testosterone or oestrogen. We then compared these results with the average performance of CM and CW.

We conducted a multivariable assessment of the association between months on gender affirming hormones and changes from pre-testosterone or oestrogen fitness after adjusting for pre-testosterone or oestrogen performance and age at initiation of testosterone or oestrogen. Figure 1 is a directed acyclic graph representing the conceptual model underlying our multivariable model. Our null hypothesis for this model is that testosterone and oestrogen are not associated with a subsequent change in athletic performance for any length of testosterone or oestrogen use or pre-testosterone or oestrogen athletic performance. We performed analyses separately for transmen and transwomen.

RESULTS

Research participant characteristics

Two hundred and twenty-two servicemembers self-identified as transgender in 2016–2018 and filed a request to begin or continue gender affirming care while serving in the Air Force. We excluded 147 of these participants for the following reasons: 28 had not started testosterone or oestrogen, 3 were on testosterone or oestrogen but did not have a start date available, 99 did not have pre-testosterone or oestrogen physical assessment scores available and 16 did not have any post-testosterone or oestrogen physical assessment scores available. We included the remaining 29 transmen and 46 transwomen in our study. (table 1) The mean age of our sample was 26.2 years (SD 5.5) with a median age of 25 years (range 19–46). The majority (78.3%) of our participants were <age 30 when they began testosterone or oestrogen. Among CM, mean height was 178.2 cm (6.8) and weight was 83.5 kg (12.0). Among CW, mean height was 164.4 cm (6.4) and weight was 65.7 kg (9.8).

The baseline physical fitness assessment occurred an average of 144.4 ± 101.4 days before starting testosterone or oestrogen. We followed participants for an average of 394.0 ± 288.2 days after they started testosterone or oestrogen. Participants

Table 1 Pretreatment demographics and body composition

Pretreatment demographics and body composition	Transwomen (n=46)	Transmen (n=29)
	Mean (SD)	Mean (SD)
Age at initiation of gender affirming hormones (years)	26.6 (4.8)	25.6 (6.6)
Height (cm)	176.3 (7.1)	165.6 (5.3)
Weight (kg)	76.7 (12.6)	69.5 (10.0)
Body mass index (kg/m ²)	24.4 (3.7)	25.3 (3.3)
Waist circumference (cm)	80.8 (8.4)	76.7 (8.9)
Rank (%)		
Enlisted	100	93.10
Officer		6.90
Duty status (%)		
Active duty	95.70	86.20
Reserves	2.20	6.90
Air National Guard	2.20	6.90

had an average of 2.2 ± 0.9 assessments after starting testosterone or oestrogen (median 2, range 1–4). Among transmen, two participants were medically excused from the push-up assessment during the follow-up period, and 11 were excused from the run. Among transwomen, two were excused from the push-up assessment, one from the sit-up assessment, and four from the run. Details of the testosterone or oestrogen prescribed and time to first therapeutic hormone levels are listed in [table 2](#).

Effect of gender affirming hormones on body composition and athletic performance

[Tables 3–5](#) and [figure 2](#) provide a summary of changes in patient outcomes while on testosterone or oestrogen. In multivariable analyses, including baseline performance, age at initiation of testosterone or oestrogen, and months on testosterone or oestrogen, we rejected the null hypothesis. In our analyses, a higher baseline score was associated with a greater decline (or smaller increase) in score at follow-up for all outcomes except for 1.5 mile run time among transwomen, where baseline run time had no effect on the changes observed at follow-up (data not shown). Age at initiation of testosterone or oestrogen had no significant effect on outcomes (data not shown). For transwomen, time on oestrogen was associated with an increase in weight ([table 3](#))

Table 3 Effect of gender affirming hormones on weight and waist circumference

Weight (kg)	Transwomen	Transmen
	Mean (95% CI)	Mean (95% CI)
Time on gender affirming hormones		
Pretreatment	76.7 (73.3 to 80.2)	69.5 (66.0 to 72.9)
0–1 years	75.6 (72.1 to 79.1)	72.1 (68.6 to 75.5)
1–2 years	77.1 (73.4 to 80.9)	71.1 (67.4 to 74.8)
2–2.5 years	76.7 (70.8 to 82.6)	70.0 (65.8 to 74.2)
	β (95% CI)	β (95% CI)
Change in weight per month on hormones*	0.15 (0.04 to 0.25)	–0.07 (–0.21 to 0.06)
Waist circumference (cm)		
	Mean (95% CI)	Mean (95% CI)
Time on gender affirming hormones		
Preretreatment	80.8 (78.7 to 82.8)	76.7 (74.2 to 79.2)
0–1 years	79.0 (77.0 to 81.0)	79.2 (76.5 to 81.8)
1–2 years	78.9 (76.2 to 81.5)	78.5 (75.2 to 81.8)
2–2.5 years	82.0 (76.5 to 87.5)	78.4 (74.4 to 82.3)
	β (95% CI)	β (95% CI)
Change in waist per month on hormones*	0.05 (–0.08 to 0.18)	–0.03 (–0.15 to 0.10)

All analyses adjusted for variation in the number of measurements per research participant.

*Adjusted for pretreatment measurements and age when started gender affirming hormones.

and a decline in athletic performance ([table 4](#) and [figure 2](#)). For transmen, time on testosterone had no effect on body composition ([table 3](#)) but was associated with an improvement in athletic performance ([table 5](#) and [figure 2](#)). Prior to treatment, transwomen were heavier than CW (mean difference 11.0 kg, 95% CI 7.6 to 14.4) and lighter than CM (–6.8 kg, –10.2 to –3.4). Transmen were lighter than CM (–14.0 kg, –17.5 to –10.5) and heavier than CW (3.8 kg, 0.3 to 7.3). Both transwomen and transmen maintained these differences over the first 2.5 years on testosterone or oestrogen (data not shown).

Athletic performance among transgender servicemembers

Prior to oestrogen, transwomen performed fewer push-ups in 1 min than CM and this gap increased with oestrogen. Transwomen performed more push-ups than CW prior to oestrogen but this difference disappeared after 2 years on

Table 2 Gender affirming hormones prescribed

	Transwomen (n=46)	Transmen (n=29)
Gender affirming hormones prescribed	Oral oestradiol: 67.4% Transdermal oestradiol: 15.2% Oestradiol valerate IM: 13.0% Oestradiol cypionate IM: 2.2% Unknown: 2.2%	Testosterone cypionate: 89.7% Testosterone enanthate: 3.4% Transdermal testosterone: 3.4% Testosterone 2% gel: 3.4%
Time to first therapeutic level (39 transwomen, 26 transmen) (days) (median (range))	234.0 (27–1270)	98.5 (23–1116)
Testosterone blockade prescribed (transwomen only)	Spironolactone: 80.4% Spironolactone and finasteride: 13.0% GnRH agonist IM: 2.2% GnRH agonist and spironolactone: 2.2% Unknown: 2.2%	
Time to first documented suppression (n=35) (days) (median (range))	200 (27–979)	
GnRH, gonadotropin releasing hormone.		

Table 4 Effect of gender affirming hormones on athletic performance among transwomen

Push-ups in 1 min	Mean (95% CI)	Mean difference transwomen vs CW (95% CI)	Mean difference transwomen vs CM (95% CI)
Time on hormones			
Pretreatment	47.3 (44.6 to 50.0)	14.8 (12.1 to 17.4)	−6.2 (−8.9 to −3.6)
0–1 years	44.6 (41.8 to 47.4)	12.1 (9.3 to 14.8)	−8.9 (−11.7 to −6.1)
1–2 years	43.2 (39.3 to 47.1)	10.7 (6.8 to 14.5)	−10.3 (−14.2 to −6.5)
2–2.5 years	34.6 (26.1 to 43.1)	2.1 (−6.4 to 10.5)	−18.9 (−27.3 to −10.5)
	β (95% CI)		
Change in push-ups per month on hormones*	−0.38 (−0.63 to −0.13)		
Sit-ups in 1 min			
Time on hormones			
Pretreatment	53.5 (51.3 to 55.7)	7.9 (5.7 to 10.0)	1.1 (−1.7 to 3.2)
0–1 years	54.1 (51.9 to 56.3)	8.5 (6.3 to 10.7)	1.7 (−0.5 to 3.9)
1–2 years	51.8 (48.6 to 55.0)	6.2 (3.0 to 9.3)	−0.6 (−3.8 to 2.5)
2–2.5 years	44.8 (37.1 to 52.4)	−0.9 (−8.4 to 6.7)	−7.7 (−15.2 to −0.1)
	β (95% CI)		
Change in sit-ups per month on hormones*	−0.37 (−0.58 to −0.15)		
1.5 mile run time (s)			
Time on hormones			
Pretreatment	708 (681 to 734)	−147 (−173 to −121)	−12 (−38 to 14)
0–1 years	758 (731 to 786)	−97 (−124 to −70)	39 (12 to 65)
1–2 years	791 (753 to 829)	−64 (−101 to −26)	72 (34 to 109)
2–2.5 years	765 (685 to 846)	−90 (−169 to −10)	45 (−34 to 125)
	β (95% CI)		
Change in run time per month on hormones*	2.9 (0.5 to 5.3)		

All analyses adjusted for variation in the number of measurements per research participant.

CW, average performance on Air Force physical fitness tests by females <30 years old conducted between 2004 and 2014.²²

CM, average performance on Air Force physical fitness tests by males <30 years old conducted between 2004 and 2014.²²

*Adjusted for pretreatment measurements and age when started gender affirming hormones.

oestrogen (table 4 and figure 2). Prior to oestrogen there was no difference in sit-ups performed in 1 min among transwomen compared with CM but there was a difference with CW. After 2 years on oestrogen, transwomen performed fewer sit-ups than CM, but the difference with CW had disappeared (table 4 and figure 2). Run times among transwomen were similar to times among CM and faster than times among CW prior to oestrogen. Run times worsened among transwomen after starting oestrogen and became slower than times in CM but remained faster than CW at all time points (table 4 and figure 2).

Transmen performed more push-ups in 1 min than CW prior to testosterone and this gap increased with testosterone. Transmen performed fewer push-ups than CM prior to testosterone but this gap closed after 1 year on testosterone (table 5, figure 2). Transmen consistently performed more sit-ups than CW before and after testosterone. Transmen and CM completed a similar number of sit-ups in 1 min prior to starting testosterone, and transmen performance exceeded that of CM after 1 year on testosterone. There was no difference in 1.5 mile run times between transmen and CW prior to testosterone, but transmen were faster after 1 year on testosterone. Transmen were slower than CM prior to testosterone but had closed the time gap after 1 year (table 5 and figure 2).

DISCUSSION

In this study, we assessed the effects of gender affirming hormones on transgender individuals over time by means of a standardised test in a non-laboratory setting. Athletic

performance improved among transmen and declined among transwomen. Among transwomen, competitive advantages from the effects of prior testosterone exposure continued beyond the 12 month standard currently proposed for inclusion in women's elite competition.¹⁰ This finding suggests that governing bodies for sporting competition should require more than 1 year of testosterone suppression prior to competition when creating guidelines for inclusion of transwomen in women's elite athletics.

Study findings and prior research

Like previous studies, our study showed an association between testosterone and increased strength among transgender men.^{13 17} We confirmed the decrease in strength associated with oestrogen in transgender women that was found in some studies,^{14–16} but not others.¹⁷ Unlike several of these previous studies, our measures of muscular strength assessed repeated submaximal efforts (push-ups and sit-ups) over a 1 min period as opposed to a single maximal effort. Our results capture differences in both endurance and strength rather than just strength and probably have more relevance to sports that require sustained effort over time rather than single explosive efforts like power lifting. Our assessments of muscular strength are also confounded by differences in weight between our transgender participants and reference populations. For example, as a group, transwomen weigh more than CW. Thus transwomen will have a higher power output than CW when performing an equivalent number of push-ups. Therefore, our study may underestimate the

Table 5 Effect of gender affirming hormones on athletic performance among transmen

Push-ups in 1 min	Mean (95% CI)	Mean difference transmen vs CW (95% CI)	Mean difference transmen vs CM (95% CI)
Time on hormones			
Pretreatment	37.4 (33.2 to 41.5)	4.8 (0.7 to 9.0)	-16.1 (-20.3 to -12.0)
0–1 years	44.8 (40.5 to 49.0)	12.2 (8.1 to 16.4)	-8.7 (-12.9 to -4.6)
1–2 years	51.8 (46.2 to 57.5)	19.3 (13.8 to 24.8)	-1.7 (-7.2 to 3.9)
2–2.5 years	56.1 (49.9 to 62.4)	25.6 (19.4 to 31.8)	4.6 (-6.4 to 10.5)
	β (95% CI)		
Change in push-ups per month on hormones*	0.46 (0.22 to 0.70)		
Sit-ups in 1 min			
Time on hormones			
Pretreatment	50.4 (47.4 to 53.4)	4.8 (1.8 to 7.7)	-2.0 (-4.9 to 0.9)
0–1 years	52.8 (49.8 to 55.8)	7.2 (4.2 to 10.2)	0.4 (-2.6 to 3.4)
1–2 years	58.2 (54.0 to 62.3)	12.5 (8.5 to 16.6)	5.7 (1.7 to 9.8)
2–2.5 years	58.3 (53.8 to 62.8)	12.7 (8.2 to 17.1)	5.9 (1.4 to 10.3)
	β (95% CI)		
Change in sit-ups per month on hormones*	0.32 (0.16 to 0.49)		
1.5 mile run time (s)			
Time on hormones			
Pretreatment	850 (802 to 899)	-4 (-52 to 43)	131 (83 to 178)
0–1 years	826 (776 to 876)	-29 (-78 to 20)	106 (57 to 155)
1–2 years	751 (687 to 815)	-104 (-167 to -41)	31 (-32 to 94)
2–2.5 years	711 (640 to 783)	-144 (-214 to -74)	-9 (-79 to 61)
	β (95% CI)		
Change in run time per month on hormones*	-3.2 (-5.3 to -1.2)		

All analyses adjusted for variation in the number of measurements per research participant.

CW, average performance on Air Force physical fitness tests by females aged <30 years conducted between 2004 and 2014.²²

CM, average performance on Air Force physical fitness tests by males aged <30 years conducted between 2004 and 2014.²²

*Adjusted for pretreatment measurements and age when started gender affirming hormones.

advantage in strength that transwomen have over CW. Further studies are needed to determine if the changes we saw in our study also apply to measures of explosive strength. Participants' exercise intentions or training habits were unknown, making it difficult to determine the aetiology of the pretreatment differences in push-up performance between transgender servicemembers and all servicemembers under the age of 30 in the Air Force. It is possible that transmen performed exercises to increase upper body muscle mass in order to give them a more masculine appearance and decrease their gender dysphoria while also improving push-up performance relative to CW. Gender dysphoria could stimulate the opposite behaviour in transwomen, decreasing push-up performance and explaining why transwomen performed fewer push-ups than CM prior to starting oestrogen. Differences in exercise habits could also influence the relationship between athletic performance and testosterone or oestrogen examined in this study. However, without the information on strength training it is impossible to make any definitive determinations.

Transmen also performed more sit-ups in 1 min than CW prior to starting testosterone. This difference in sit-up performance may also reflect a behavioural response to gender dysphoria among transmen. There was no difference between transmen and CM in sit-up performance. Unlike the increased size of upper body musculature associated with push-ups, a flat and toned appearing abdomen is seen as a positive attribute for achieving an ideal masculine or feminine appearance, making it less likely that transwomen would avoid this exercise type at a greater rate than CM.

In addition, we demonstrated a worsening of run times associated with oestrogen among transwomen that was seen in a previous study using a smaller sample and self-reported data.²¹ Testosterone exposure is associated with an increase in muscle volume and blood haemoglobin content, producing most of the ergogenic effects.¹ The improvement in run times seen among transmen with exposure to testosterone and the decline among transwomen undergoing testosterone blockade demonstrates this ergogenic effect of testosterone. However, exposure to testosterone during puberty results in sex differences in height, pelvic architecture and leg bones in the lower limbs that confer an athletic advantage to males after puberty.¹ These anatomical differences do not respond to changes in testosterone exposure among post-pubertal adults. These pretreatment anatomical differences may explain why transwomen retained an advantage in 1.5 mile run times over CW after beginning oestrogen as an adult, while push-up and sit-up performance, which are less influenced by differences in skeletal architecture, declined to the level of CW after 2 years on oestrogen. It is possible that these results could be different among transwomen who begin gender affirming hormone therapy shortly after the onset of puberty and never experienced the ergogenic benefits of testosterone exposure. Further research is required to determine if the effects of testosterone or oestrogen on athletic performance vary by level of pubertal development at the time of initiating testosterone or oestrogen and if guidelines for transgender inclusion in sports need to account for the athlete's pubertal stage when testosterone or oestrogen began.

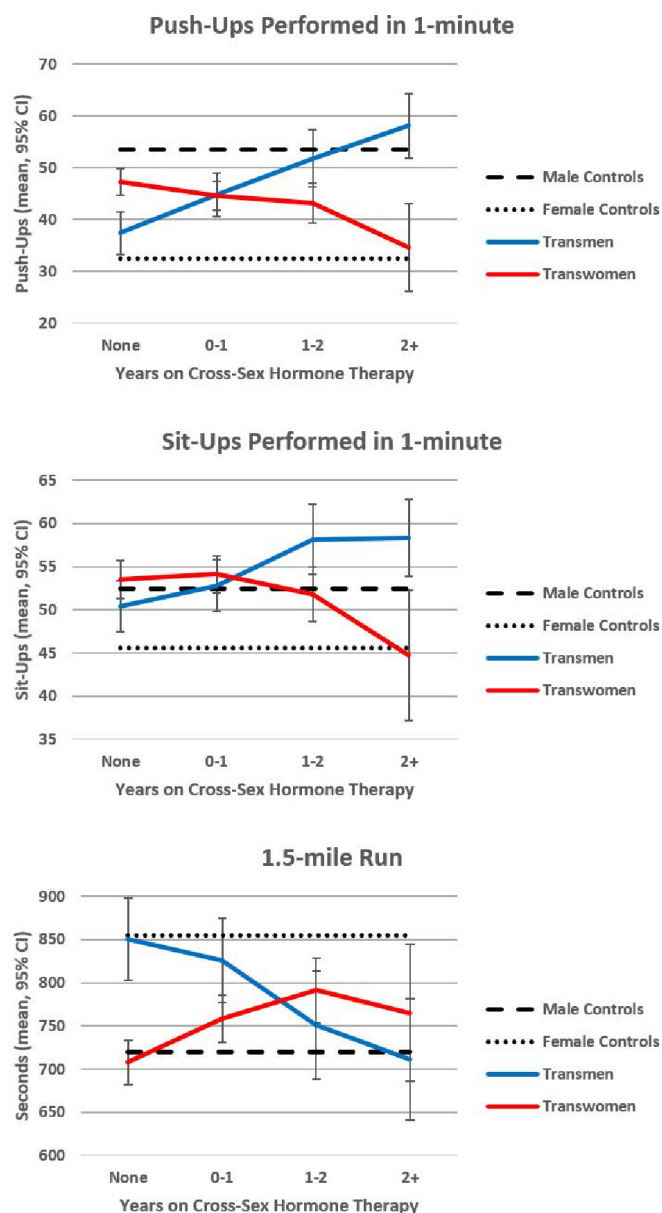


Figure 2 Gender affirming therapy and athletic performance. Male controls line represents the average performance on over 2.3 million Air Force physical fitness tests performed by males under the age of 30 between 2004 and 2014.²² Female controls line represents the average performance on over 567 000 Air Force physical fitness tests performed by females under the age of 30 between 2004 and 2014.²²

What are the new findings?

- ▶ Transwomen retain an advantage in upper body strength (push-ups) over female controls for 1–2 years after starting gender affirming hormones.
- ▶ Transwomen retain an advantage in endurance (1.5 mile run) over female controls for over 2 years after starting gender affirming hormones.
- ▶ Transwomen are currently mandated to have 1 year of testosterone suppression before being permitted to compete at the elite level. This may be too short if the aim is a level playing field.

Study limitations and future directions

The strengths of this study include a larger sample size than previous studies, a longer follow-up period and a focus on performance on a standardised fitness test rather than isolated muscle strength. This study has limitations as well. The lack of a longitudinal control group not on testosterone or oestrogen makes changes in performance due to the passage of time a potential confounding factor. The high variability in time between baseline assessment and starting testosterone or oestrogen could also confound our assessment of the effect of time on testosterone or oestrogen. However, the uniformity of the data showing improvement in performance scores in transmen and the decline in transwomen makes it unlikely that the changes in performance are random or can be attributed to changes over time alone. The conceptual model for our multivariable analysis could be wrong and incorrectly estimate the relationship of testosterone or oestrogen with changes in athletic performance. Finally, testosterone and oestrogen protocols were not standardised for our participants. Variations in hormonal exposure between patients could confound our measurement of the effects of testosterone or oestrogen on athletic performance and body composition. Most participants had documentation of therapeutic hormone levels and suppression of testosterone, suggesting dosing at physiologic levels, although the time between starting testosterone or oestrogen and documentation of physiologic levels varied widely between participants. We do not know to what extent this variability represents differences in medication dosing or inadequate access to medical records from outside the military healthcare system. Future studies should address these limitations. Development of evidence based guidelines for transgender inclusion in elite athletic competition by governing bodies for athletics, such as the IOC and World Athletics, requires further research to define the timing of changes associated with testosterone or oestrogen.

CONCLUSION

In this study, we confirmed that use of gender affirming hormones are associated with changes in athletic performance and demonstrated that the pretreatment differences between transgender and cis gender women persist beyond the 12 month time requirement currently being proposed for athletic competition by the World Athletics and the IOC.¹⁰ This study suggests that more than 12 months of testosterone suppression may be needed to ensure that transgender women do not have an unfair competitive advantage when participating in elite level athletic competition.

Acknowledgements The authors thank the Medical Writing Center at Children's Mercy Kansas City for editing this manuscript for style and clarity.

Contributors All authors listed on this manuscript have contributed to the following tasks: substantial contributions to the conception or design of the work, or the acquisition, analysis or interpretation of data; drafting the work or revising it critically for important intellectual content; final approval of the version published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Disclaimer The views expressed are solely those of the authors and do not reflect the official policy or position of the US Army, US Navy, US Air Force, the Department of Defense or the US Government.

Competing interests TAR receives research funding for an unrelated project as part of the Merck Pharmaceuticals Investigator Directed Research Programme. JS

is on active duty with the United States Air Force. DA is an employee of the United States Department of Defense.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the methods section for further details.

Patient consent for publication Not required.

Ethics approval This study was approved by the 59th Medical Wing institutional review board.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement A de-identified copy of the data is available from the corresponding author upon reasonable request.

ORCID iD

Timothy A Roberts <http://orcid.org/0000-0003-4966-7079>

REFERENCES

- Handelsman DJ, Hirschberg AL, Bermon S. Circulating testosterone as the hormonal basis of sex differences in athletic performance. *Endocr Rev* 2018;39:803–29.
- Singh B, Singh K, Sharma N. Equality, equity and inclusion: transgender athletes' participation in competitive sports - a new era. *Phys Cult Sport Stud Res* 2010;49:85–8.
- Semerjian TZ, Cohen JH. "FTM means female to me": transgender athletes performing gender. *Women Sport Phys Act J* 2016;15:28–43.
- Genel M. Transgender athletes: how can they be accommodated? *Curr Sports Med Rep* 2017;16:12–13.
- Bianchi A. Transgender women in sport. *J Philos Sport* 2017;44:229–42.
- Hartgens F, Kuipers H. Effects of androgenic-anabolic steroids in athletes. *Sports Med* 2004;34:513–54.
- Franke WW, Berendonk B. Hormonal doping and androgenization of athletes: a secret program of the German Democratic Republic government. *Clin Chem* 1997;43:1262–79.
- Ingram BJ, Thomas CL. Transgender policy in sport, a review of current policy and commentary of the challenges of policy creation. *Curr Sports Med Rep* 2019;18:239–47.
- Gooren LJG, Bunck MCM. Transsexuals and competitive sports. *Eur J Endocrinol* 2004;151:425–9.
- International Olympic Committee. IOC consensus meeting on sex reassignment and hyperandrogenism, 2016. Available: http://www.olympic.org/Documents/Commissions_PDFfiles/Medical_commission/2015-11_ioc_consensus_meeting_on_sex_reassignment_and_hyperandrogenism-en.pdf [Accessed 30 Dec 2019].
- Camporesi S. A question of 'fairness': Why ethics should factor in the Court of Arbitration for sport's decision on the IAAF hyperandrogenism regulations. *Br J Sports Med* 2019;53:797–8.
- Van Caenegem E, Wierckx K, Taes Y, et al. Bone mass, bone geometry, and body composition in female-to-male transsexual persons after long-term cross-sex hormonal therapy. *J Clin Endocrinol Metab* 2012;97:2503–11.
- Van Caenegem E, Wierckx K, Taes Y, et al. Body composition, bone turnover, and bone mass in trans men during testosterone treatment: 1-year follow-up data from a prospective case-controlled study (ENIGI). *Eur J Endocrinol* 2015;172:163–71.
- Scharff M, Wiepjes CM, Klaver M, et al. Change in grip strength in trans people and its association with lean body mass and bone density. *Endocr Connect* 2019;8:1020–8.
- Lapauw B, Taes Y, Simoens S, et al. Body composition, volumetric and areal bone parameters in male-to-female transsexual persons. *Bone* 2008;43:1016–21.
- Van Caenegem E, Wierckx K, Taes Y, et al. Preservation of volumetric bone density and geometry in trans women during cross-sex hormonal therapy: a prospective observational study. *Osteoporos Int* 2015;26:35–47.
- Wiik A, Lundberg TR, Rullman E, et al. Muscle strength, size, and composition following 12 months of gender-affirming treatment in transgender individuals. *J Clin Endocrinol Metab* 2020;105:dgz247:e805–13.
- Elbers JM, Asscheman H, Seidell JC, et al. Effects of sex steroid hormones on regional fat depots as assessed by magnetic resonance imaging in transsexuals. *Am J Physiol* 1999;276:E317–25.
- Mueller A, Zollver H, Kronawitter D, et al. Body composition and bone mineral density in male-to-female transsexuals during cross-sex hormone therapy using gonadotrophin-releasing hormone agonist. *Exp Clin Endocrinol Diabetes* 2011;119:95–100.
- Figuera TM, da Silva E, Lindenau JD-R, et al. Impact of cross-sex hormone therapy on bone mineral density and body composition in transwomen. *Clin Endocrinol* 2018;88:856–62.
- Harper J. Race times for transgender athletes. *Journal of Sporting Cultures and Identities* 2015;6:1–9.
- Griffith JR. The air force fitness test: creating new fitness assessment charts using waist to height ratios (2017). Theses and dissertations. 782. Available: <https://scholar.afit.edu/etd/782> [Accessed 29 Apr 2020].



Transgender Women in the Female Category of Sport: Perspectives on Testosterone Suppression and Performance Advantage

Emma N. Hilton¹ · Tommy R. Lundberg^{2,3} 

Published online: 8 December 2020
© The Author(s) 2020

Abstract

Males enjoy physical performance advantages over females within competitive sport. The sex-based segregation into male and female sporting categories does not account for transgender persons who experience incongruence between their biological sex and their experienced gender identity. Accordingly, the International Olympic Committee (IOC) determined criteria by which a transgender woman may be eligible to compete in the female category, requiring total serum testosterone levels to be suppressed below 10 nmol/L for at least 12 months prior to and during competition. Whether this regulation removes the male performance advantage has not been scrutinized. Here, we review how differences in biological characteristics between biological males and females affect sporting performance and assess whether evidence exists to support the assumption that testosterone suppression in transgender women removes the male performance advantage and thus delivers fair and safe competition. We report that the performance gap between males and females becomes significant at puberty and often amounts to 10–50% depending on sport. The performance gap is more pronounced in sporting activities relying on muscle mass and explosive strength, particularly in the upper body. Longitudinal studies examining the effects of testosterone suppression on muscle mass and strength in transgender women consistently show very modest changes, where the loss of lean body mass, muscle area and strength typically amounts to approximately 5% after 12 months of treatment. Thus, the muscular advantage enjoyed by transgender women is only minimally reduced when testosterone is suppressed. Sports organizations should consider this evidence when reassessing current policies regarding participation of transgender women in the female category of sport.

Key Points

Given that biological males experience a substantial performance advantage over females in most sports, there is currently a debate whether inclusion of transgender women in the female category of sports would compromise the objective of fair and safe competition.

Here, we report that current evidence shows the biological advantage, most notably in terms of muscle mass and strength, conferred by male puberty and thus enjoyed by most transgender women is only minimally reduced when testosterone is suppressed as per current sporting guidelines for transgender athletes.

This evidence is relevant for policies regarding participation of transgender women in the female category of sport.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s40279-020-01389-3>.

✉ Tommy R. Lundberg
tommy.lundberg@ki.se

¹ Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

² Department of Laboratory Medicine/ANA Futura, Division of Clinical Physiology, Karolinska Institutet, Alfred Nobels Allé 8B, Huddinge, 141 52 Stockholm, Sweden

³ Unit of Clinical Physiology, Karolinska University Hospital, Stockholm, Sweden

1 Introduction

Sporting performance is strongly influenced by a range of physiological factors, including muscle force and power-producing capacity, anthropometric characteristics, cardiorespiratory capacity and metabolic factors [1, 2]. Many of these physiological factors differ significantly between biological males and females as a result of genetic differences and androgen-directed development of secondary sex characteristics [3, 4]. This confers large sporting performance advantages on biological males over females [5].

When comparing athletes who compete directly against one another, such as elite or comparable levels of school-aged athletes, the physiological advantages conferred by biological sex appear, on assessment of performance data, insurmountable. Further, in sports where contact, collision or combat are important for gameplay, widely different physiological attributes may create safety and athlete welfare concerns, necessitating not only segregation of sport into male and female categories, but also, for example, into weight and age classes. Thus, to ensure that both men and women can enjoy sport in terms of fairness, safety and inclusivity, most sports are divided, in the first instance, into male and female categories.

Segregating sports by biological sex does not account for transgender persons who experience incongruence between their biological sex and their experienced gender identity, and whose legal sex may be different to that recorded at birth [6, 7]. More specifically, transgender women (observed at birth as biologically male but identifying as women) may, before or after cross-hormone treatment, wish to compete in the female category. This has raised concerns about fairness and safety within female competition, and the issue of how to fairly and safely accommodate transgender persons in sport has been subject to much discussion [6–13].

The current International Olympic Committee (IOC) policy [14] on transgender athletes states that “it is necessary to ensure insofar as possible that trans athletes are not excluded from the opportunity to participate in sporting competition”. Yet the policy also states that “the overriding sporting objective is and remains the guarantee of fair competition”. As these goals may be seen as conflicting if male performance advantages are carried through to competition in the female category, the IOC concludes that “restrictions on participation are appropriate to the extent that they are necessary and proportionate to the achievement of that objective”.

Accordingly, the IOC determined criteria by which transgender women may be eligible to compete in the female category. These include a solemn declaration that her gender identity is female and the maintenance of total

serum testosterone levels below 10 nmol/L for at least 12 months prior to competing and during competition [14]. Whilst the scientific basis for this testosterone threshold was not openly communicated by the IOC, it is surmised that the IOC believed this testosterone criterion sufficient to reduce the sporting advantages of biological males over females and deliver fair and safe competition within the female category.

Several studies have examined the effects of testosterone suppression on the changing biology, physiology and performance markers of transgender women. In this review, we aim to assess whether evidence exists to support the assumption that testosterone suppression in transgender women removes these advantages. To achieve this aim, we first review the differences in biological characteristics between biological males and females, and examine how those differences affect sporting performance. We then evaluate the studies that have measured elements of performance and physical capacity following testosterone suppression in untrained transgender women, and discuss the relevance of these findings to the supposition of fairness and safety (i.e. removal of the male performance advantage) as per current sporting guidelines.

2 The Biological Basis for Sporting Performance Advantages in Males

The physical divergence between males and females begins during early embryogenesis, when bipotential gonads are triggered to differentiate into testes or ovaries, the tissues that will produce sperm in males and ova in females, respectively [15]. Gonad differentiation into testes or ovaries determines, via the specific hormone milieu each generates, downstream in utero reproductive anatomy development [16], producing male or female body plans. We note that in rare instances, differences in sex development (DSDs) occur and the typical progression of male or female development is disrupted [17]. The categorisation of such athletes is beyond the scope of this review, and the impact of individual DSDs on sporting performance must be considered on their own merits.

In early childhood, prior to puberty, sporting participation prioritises team play and the development of fundamental motor and social skills, and is sometimes mixed sex. Athletic performance differences between males and females prior to puberty are often considered inconsequential or relatively small [18]. Nonetheless, pre-puberty performance differences are not unequivocally negligible, and could be mediated, to some extent, by genetic factors and/or activation of the hypothalamic–pituitary–gonadal axis during the neonatal period, sometimes referred to as “minipuberty”. For example, some 6500 genes are differentially expressed between males and females [19] with an estimated 3000 sex-specific

differences in skeletal muscle likely to influence composition and function beyond the effects of androgenisation [3], while increased testosterone during minipuberty in males aged 1–6 months may be correlated with higher growth velocity and an “imprinting effect” on BMI and bodyweight [20, 21]. An extensive review of fitness data from over 85,000 Australian children aged 9–17 years old showed that, compared with 9-year-old females, 9-year-old males were faster over short sprints (9.8%) and 1 mile (16.6%), could jump 9.5% further from a standing start (a test of explosive power), could complete 33% more push-ups in 30 s and had 13.8% stronger grip [22]. Male advantage of a similar magnitude was detected in a study of Greek children, where, compared with 6-year-old females, 6-year-old males completed 16.6% more shuttle runs in a given time and could jump 9.7% further from a standing position [23]. In terms of aerobic capacity, 6- to 7-year-old males have been shown to have a higher absolute and relative (to body mass) $\text{VO}_{2\text{max}}$ than 6- to 7-year-old females [24]. Nonetheless, while some biological sex differences, probably genetic in origin, are measurable and affect performance pre-puberty, we consider the effect of androgenizing puberty more influential on performance, and have focused our analysis on musculoskeletal differences hereafter.

Secondary sex characteristics that develop during puberty have evolved under sexual selection pressures to improve reproductive fitness and thus generate anatomical divergence beyond the reproductive system, leading to adult body types that are measurably different between sexes. This phenomenon is known as sex dimorphism. During puberty, testes-derived testosterone levels increase 20-fold in males, but remain low in females, resulting in circulating testosterone concentrations at least 15 times higher in males than in females of any age [4, 25]. Testosterone in males induces changes in muscle mass, strength, anthropometric variables and hemoglobin levels [4], as part of the range of sexually dimorphic characteristics observed in humans.

Broadly, males are bigger and stronger than females. It follows that, within competitive sport, males enjoy significant performance advantages over females, predicated on the superior physical capacity developed during puberty in response to testosterone. Thus, the biological effects of elevated pubertal testosterone are primarily responsible for driving the divergence of athletic performances between males and females [4]. It is acknowledged that this divergence has been compounded historically by a lag in the cultural acceptance of, and financial provision for, females in sport that may have had implications for the rate of improvement in athletic performance in females. Yet, since the 1990s, the difference in performance records between males and females has been relatively stable, suggesting that biological differences created by androgenization explain most of the male advantage, and are insurmountable [5, 26, 27].

Table 1 outlines physical attributes that are major parameters underpinning the male performance advantage [28–38]. Males have: larger and denser muscle mass, and stiffer connective tissue, with associated capacity to exert greater muscular force more rapidly and efficiently; reduced fat mass, and different distribution of body fat and lean muscle mass, which increases power to weight ratios and upper to lower limb strength in sports where this may be a crucial determinant of success; longer and larger skeletal structure, which creates advantages in sports where levers influence force application, where longer limb/digit length is favorable, and where height, mass and proportions are directly responsible for performance capacity; superior cardiovascular and respiratory function, with larger blood and heart volumes, higher hemoglobin concentration, greater cross-sectional area of the trachea and lower oxygen cost of respiration [3, 4, 39, 40]. Of course, different sports select for different physiological characteristics—an advantage in one discipline may be neutral or even a disadvantage in another—but examination of a variety of record and performance metrics in any discipline reveals there are few sporting disciplines where males do not possess performance advantage over females as a result of the physiological characteristics affected by testosterone.

3 Sports Performance Differences Between Males and Females

3.1 An Overview of Elite Adult Athletes

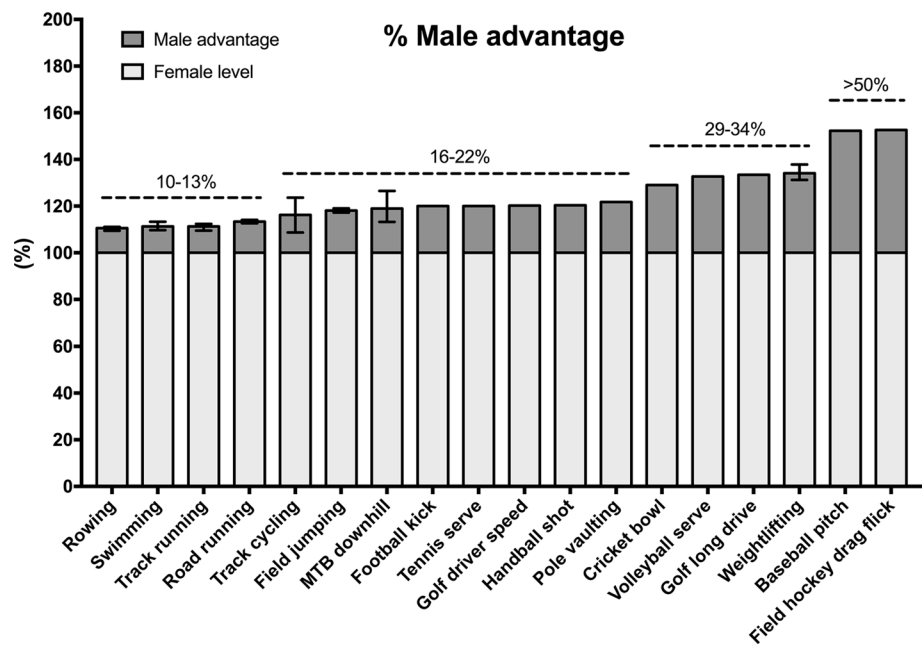
A comparison of adult elite male and female achievements in sporting activities can quantify the extent of the male performance advantage. We searched publicly available sports federation databases and/or tournament/competition records to identify sporting metrics in various events and disciplines, and calculated the performance of males relative to females. Although not an exhaustive list, examples of performance gaps in a range of sports with various durations, physiological performance determinants, skill components and force requirements are shown in Fig. 1.

The smallest performance gaps were seen in rowing, swimming and running (11–13%), with low variation across individual events within each of those categories. The performance gap increases to an average of 16% in track cycling, with higher variation across events (from 9% in the 4000 m team pursuit to 24% in the flying 500 m time trial). The average performance gap is 18% in jumping events (long jump, high jump and triple jump). Performance differences larger than 20% are generally present when considering sports and activities that involve extensive upper body contributions. The gap between fastest recorded tennis serve

Table 1 Selected physical difference between untrained/moderately trained males and females. Female levels are set as the reference value

Variable	Magnitude of sex difference (%)	References
Body composition		
Lean body mass	45	Lee et al. [28]
Fat%	– 30	
Muscle mass		
Lower body	33	Janssen et al. [29]
Upper body	40	
Muscle strength		
Grip strength	57	Bohannon et al. [30]
Knee extension peak torque	54	Neder et al. [31]
Anthropometry and bone geometry		
Femur length	9.4	Jantz et al. [32]
Humerus length	12.0	Brinckmann et al. [33]
Radius length	14.6	
Pelvic width relative to pelvis height	– 6.1	
Tendon properties		
Force	83	Lepley et al. [34]
Stiffness	41	
VO _{2max}		
Absolute values	50	Pate et al. [35]
Relative values	25	
Respiratory function		
Pulmonary ventilation (maximal)	48	Åstrand et al. [36]
Cardiovascular function		
Left ventricular mass	31	Åstrand et al. [36]
Cardiac output (rest)	22	Best et al. [37]
Cardiac output (maximal)	30	Tong et al. [38]
Stroke volume (rest)	43	
Stroke volume (maximal)	34	
Hemoglobin concentration	11	

Fig. 1 The male performance advantage over females across various selected sporting disciplines. The female level is set to 100%. In sport events with multiple disciplines, the male value has been averaged across disciplines, and the error bars represent the range of the advantage. The metrics were compiled from publicly available sports federation databases and/or tournament/competition records. *MTB* mountain bike



is 20%, while the gaps between fastest recorded baseball pitches and field hockey drag flicks exceed 50%.

Sports performance relies to some degree on the magnitude, speed and repeatability of force application, and, with respect to the speed of force production (power), vertical jump performance is on average 33% greater in elite men than women, with differences ranging from 27.8% for endurance sports to in excess of 40% for precision and combat sports [41]. Because implement mass differs, direct comparisons are not possible in throwing events in track and field athletics. However, the performance gap is known to be substantial, and throwing represents the widest sex difference in motor performance from an early age [42]. In Olympic javelin throwers, this is manifested in differences in the peak linear velocities of the shoulder, wrist, elbow and hand, all of which are 13–21% higher for male athletes compared with females [43].

The increasing performance gap between males and females as upper body strength becomes more critical for performance is likely explained to a large extent by the observation that males have disproportionately greater strength in their upper compared to lower body, while females show the inverse [44, 45]. This different distribution of strength compounds the general advantage of increased muscle mass in upper body dominant disciplines. Males also have longer arms than females, which allows greater torque production from the arm lever when, for example, throwing a ball, punching or pushing.

3.2 Olympic Weightlifting

In Olympic weightlifting, where weight categories differ between males and females, the performance gap is between 31 and 37% across the range of competitive body weights between 1998 and 2020 (Fig. 1). It is important to note that at all weight categories below the top/open category, performances are produced within weight categories

with an upper limit, where strength can be correlated with “fighting weight”, and we focused our analysis of performance gaps in these categories.

To explore strength–mass relationships further, we compared Olympic weightlifting data between equivalent weight categories which, to some extent, limit athlete height, to examine the hypothesis that male performance advantage may be largely (or even wholly) mediated by increased height and lever-derived advantages (Table 2). Between 1998 and 2018, a 69 kg category was common to both males and females, with the male record holder (69 kg, 1.68 m) lifting a combined weight 30.1% heavier than the female record holder (69 kg, 1.64 m). Weight category changes in 2019 removed the common 69 kg category and created a common 55 kg category. The current male record holder (55 kg, 1.52 m) lifts 29.5% heavier than the female record holder (55 kg, 1.52 m). These comparisons demonstrate that males are approximately 30% stronger than females of equivalent stature and mass. However, importantly, male vs. female weightlifting performance gaps increase with increasing bodyweight. For example, in the top/open weight category of Olympic weightlifting, in the absence of weight (and associated height) limits, maximum male lifting strength exceeds female lifting strength by nearly 40%. This is further manifested in powerlifting, where the male record (total of squat, bench press and deadlift) is 65% higher than the female record in the open weight category of the World Open Classic Records. Further analysis of Olympic weightlifting data shows that the 55-kg male record holder is 6.5% stronger than the 69-kg female record holder (294 kg vs 276 kg), and that the 69-kg male record is 3.2% higher than the record held in the female open category by a 108-kg female (359 kg vs 348 kg). This Olympic weightlifting analysis reveals key differences between male and female strength capacity. It shows that, even after adjustment for mass, biological males are significantly stronger (30%) than females, and

Table 2 Olympic weightlifting data between equivalent male–female and top/open weight categories

	Sex	Weight (kg)	Height (m)	Combined record (kg)	Strength to weight ratio	Relative performance (%)
2019 record in the 55 kg weight-limited category						
Liao Qiuyun	F	55	1.52	227	4.13	
Om Yun-chol	M	55	1.52	294	5.35	29.5
1998–2018 record in the 69-kg weight-limited category						
Oxsana Slivenko	F	69	1.64	276	4.00	
Liao Hui	M	69	1.68	359	5.20	30.1
Comparative performances for top/open categories (all time heaviest combined lifts)						
Tatiana Kashirina	F	108	1.77	348	3.22	
Lasha Talakhadze	M	168	1.97	484	2.88	39.1

F female, M male

that females who are 60% heavier than males do not overcome these strength deficits.

3.3 Perspectives on Elite Athlete Performance Differences

Figure 1 illustrates the performance gap between adult elite males and adult elite females across various sporting disciplines and activities. The translation of these advantages, assessed as the performance difference between the very best males and very best females, are significant when extended and applied to larger populations. In running events, for example, where the male–female gap is approximately 11%, it follows that many thousands of males are faster than the very best females. For example, approximately 10,000 males have personal best times that are faster than the current Olympic 100 m female champion (World Athletics, personal communication, July 2019). This has also been described elsewhere [46, 47], and illustrates the true effect of an 11% typical difference on population comparisons between males and females. This is further apparent upon examination of selected junior male records, which surpass adult elite female performances by the age of 14–15 years (Table 3), demonstrating superior male athletic performance over elite females within a few years of the onset of puberty.

These data overwhelmingly confirm that testosterone-driven puberty, as the driving force of development of male secondary sex characteristics, underpins sporting advantages that are so large no female could reasonably hope to succeed without sex segregation in most sporting competitions. To ensure, in light of these analyses, that female athletes can be included in sporting competitions in a fair and safe manner, most sports have a female category the purpose of which is the protection of both fairness and, in some sports, safety/welfare of athletes who do not benefit from the physiological changes induced by male levels of testosterone from puberty onwards.

Table 3 Selected junior male records in comparison with adult elite female records

Event	Schoolboy male record	Elite female (adult) record
100 m	10.20 (age 15)	10.49
800 m	1:51.23 (age 14)	1:53.28
1500 m	3:48.37 (age 14)	3:50.07
Long jump	7.85 m (age 15)	7.52 m
Discus throw	77.68 m (age 15)	76.80 m

M meters

Time format: minutes:seconds.hundredths of a second

3.4 Performance Differences in Non-elite Individuals

The male performance advantages described above in athletic cohorts are similar in magnitude in untrained people. Even when expressed relative to fat-free weight, $\text{VO}_{2\text{max}}$ is 12–15% higher in males than in females [48]. Records of lower-limb muscle strength reveal a consistent 50% difference in peak torque between males and females across the lifespan [31]. Hubal et al. [49] tested 342 women and 243 men for isometric (maximal voluntary contraction) and dynamic strength (one-repetition maximum; 1RM) of the elbow flexor muscles and performed magnetic resonance imaging (MRI) of the biceps brachii to determine cross-sectional area. The males had 57% greater muscle size, 109% greater isometric strength, and 89% greater 1RM strength than age-matched females. This reinforces the finding in athletic cohorts that sex differences in muscle size and strength are more pronounced in the upper body.

Recently, sexual dimorphism in arm force and power was investigated in a punch motion in moderately-trained individuals [50]. The power produced during a punch was 162% greater in males than in females, and the least powerful man produced more power than the most powerful woman. This highlights that sex differences in parameters such as mass, strength and speed may combine to produce even larger sex differences in sport-specific actions, which often are a product of how various physical capacities combine. For example, power production is the product of force and velocity, and momentum is defined as mass multiplied by velocity. The momentum and kinetic energy that can be transferred to another object, such as during a tackle or punch in collision and combat sports are, therefore, dictated by: the mass; force to accelerate that mass, and; resultant velocity attained by that mass. As there is a male advantage for each of these factors, the net result is likely synergistic in a sport-specific action, such as a tackle or a throw, that widely surpasses the sum of individual magnitudes of advantage in isolated fitness variables. Indeed, already at 17 years of age, the average male throws a ball further than 99% of 17-year-old females [51], despite no single variable (arm length, muscle mass etc.) reaching this numerical advantage. Similarly, punch power is 162% greater in men than women even though no single parameter that produces punching actions achieves this magnitude of difference [50].

4 Is the Male Performance Advantage Lost when Testosterone is Suppressed in Transgender Women?

The current IOC criteria for inclusion of transgender women in female sports categories require testosterone suppression below 10 nmol/L for 12 months prior to and during competition. Given the IOC's stated position that the "overriding sporting objective is and remains the guarantee of fair competition" [14], it is reasonable to assume that the rationale for this requirement is that it reduces the male performance advantages described previously to an acceptable degree, thus permitting fair and safe competition. To determine whether this medical intervention is sufficient to remove (or reduce) the male performance advantage, which we described above, we performed a systematic search of the scientific literature addressing anthropometric and muscle characteristics of transgender women. Search terms and filtering of peer-reviewed data are given in Supplementary Table S1.

4.1 Anthropometrics

Given its importance for the general health of the transgender population, there are multiple studies of bone health, and reviews of these data. To summarise, transgender women often have low baseline (pre-intervention) bone mineral density (BMD), attributed to low levels of physical activity, especially weight-bearing exercise, and low vitamin D levels [52, 53]. However, transgender women generally maintain bone mass over the course of at least 24 months of testosterone suppression. There may even be small but significant increases in BMD at the lumbar spine [54, 55]. Some retrieved studies present data pertaining to maintained BMD in transgender women after many years of testosterone suppression. One such study concluded that "BMD is preserved over a median of 12.5 years" [56]. In support, no increase in fracture rates was observed over 12 months of testosterone suppression [54]. Current advice, including that from the International Society for Clinical Densitometry, is that transgender women, in the absence of other risk factors, do not require monitoring of BMD [52, 57]. This is explicable under current standard treatment regimes, given the established positive effect of estrogen, rather than testosterone, on bone turnover in males [58].

Given the maintenance of BMD and the lack of a plausible biological mechanism by which testosterone suppression might affect skeletal measurements such as bone length and hip width, we conclude that height and skeletal parameters remain unaltered in transgender women, and

that sporting advantage conferred by skeletal size and bone density would be retained despite testosterone reductions compliant with the IOC's current guidelines. This is of particular relevance to sports where height, limb length and handspan are key (e.g. basketball, volleyball, handball) and where high movement efficiency is advantageous. Male bone geometry and density may also provide protection against some sport-related injuries—for example, males have a lower incidence of knee injuries, often attributed to low quadriceps (*Q*) angle conferred by a narrow pelvic girdle [59, 60].

4.2 Muscle and Strength Metrics

As discussed earlier, muscle mass and strength are key parameters underpinning male performance advantages. Strength differences range between 30 and 100%, depending upon the cohort studied and the task used to assess strength. Thus, given the important contribution made by strength to performance, we sought studies that have assessed strength and muscle/lean body mass changes in transgender women after testosterone reduction. Studies retrieved in our literature search covered both longitudinal and cross-sectional analyses. Given the superior power of the former study type, we will focus on these.

The pioneer work by Gooren and colleagues, published in part in 1999 [61] and in full in 2004 [62], reported the effects of 1 and 3 years of testosterone suppression and estrogen supplementation in 19 transgender women (age 18–37 years). After the first year of therapy, testosterone levels were reduced to 1 nmol/L, well within typical female reference ranges, and remained low throughout the study course. As determined by MRI, thigh muscle area had decreased by –9% from baseline measurement. After 3 years, thigh muscle area had decreased by a further –3% from baseline measurement (total loss of –12% over 3 years of treatment). However, when compared with the baseline measurement of thigh muscle area in transgender men (who are born female and experience female puberty), transgender women retained significantly higher thigh muscle size. The final thigh muscle area, after three years of testosterone suppression, was 13% larger in transwomen than in the transmen at baseline ($p < 0.05$). The authors concluded that testosterone suppression in transgender women does not reverse muscle size to female levels.

Including Gooren and Bunck [62], 12 longitudinal studies [53, 63–73] have examined the effects of testosterone suppression on lean body mass or muscle size in transgender women. The collective evidence from these studies suggests that 12 months, which is the most commonly examined intervention period, of testosterone suppression to female-typical reference levels results in a modest (approximately –5%) loss of lean body mass or muscle size (Table 4). No

Table 4 Longitudinal studies of muscle and strength changes in adult transgender women undergoing cross-sex hormone therapy

Study	Participants (age)	Therapy	Confirmed serum testosterone levels	Muscle/strength data	Comparison with reference females
Polderman et al. [73]	$N=12$ TW 18–36 yr (age range)	T suppression + E supplementation	<2 nmol/L at 4 mo	<i>LBM</i> 4 mo – 2.2%	<i>LBM</i> 4 mo 16%
Gooren and Bunck [62]	$N=19$ TW 26 ± 6 yr	T suppression + E supplementation	≤ 1 nmol/L at 1 and 3 yr	<i>Thigh area</i> 1 yr – 9% / 3 yr – 12%	<i>Thigh area</i> 1 yr 16%/3 yr 13%
Haraldsen et al. [63]	$N=12$ TW 29 ± 8 yr	E supplementation	<10 nmol/L at 3 mo and 1 yr	<i>LBM</i> 3 mo/1 yr—small changes, unclear magnitude	
Mueller et al. [64]	$N=84$ TW 36 ± 11 yr	T suppression + E supplementation	≤ 1 nmol/L at 1 and 2 yr	<i>LBM</i> 1 yr – 4%/2 yr – 7%	
Wierckx et al. [65]	$N=53$ TW 31 ± 14 yr	T suppression + E supplementation	<10 nmol/L at 1 yr	<i>LBM</i> 1 yr – 5%	<i>LBM</i> 1 yr 39%
Van Caenegem et al. [53] (and Van Caenegem et al. [76])	$N=49$ TW 33 ± 14 yr	T suppression + E supplementation	≤ 1 nmol/L at 1 and 2 yr	<i>LBM</i> 1 yr – 4%/2 yr – 0.5% <i>Grip strength</i> 1 yr – 7%/2 yr – 9% <i>Calf area</i> 1 yr – 2%/2 yr – 4% <i>Forearm area</i> 1 yr – 8%/2 yr – 4%	<i>LBM</i> 1 yr 24%/2 yr 28% <i>Grip strength</i> 1 yr 26%/2 yr 23% <i>Calf area</i> 1 yr 16%/2 yr 13% <i>Forearm area</i> 1 yr 29%/2 yr 34%
Gava et al. [66]	$N=40$ TW 31 ± 10 yr	T suppression + E supplementation	<5 nmol/L at 6 mo and ≤ 1 nmol/L at 1 yr	<i>LBM</i> 1 yr – 2%	
Auer et al. [67]	$N=45$ TW 35 ± 1 (SE) yr	T suppression + E supplementation	<5 nmol/L at 1 yr	<i>LBM</i> 1 yr – 3%	<i>LBM</i> 1 yr 27%
Klaver et al. [68]	$N=179$ TW 29 (range 18–66)	T suppression + E supplementation	≤ 1 nmol/L at 1 yr	<i>LBM</i> 1 yr Total – 3% Arm region – 6% Trunk region – 2% Android region 0% Gynoid region – 3% Leg region – 4%	<i>LBM</i> 1 yr Total 18% Arm region 28% Leg region 19%
Figuera et al. [69]	$N=46$ TW 34 ± 10	E supplementation with or without T suppression	<5 nmol/L at 3 mo ≤ 1 nmol/L at 31 mo	<i>ALM</i> 31 mo – 4% from the 3 mo visit	
Scharff et al. [70]	$N=249$ TW 28 (inter quartile range 23–40)	T suppression + E supplementation	≤ 1 nmol/L at 1 yr	<i>Grip strength</i> 1 yr – 4%	<i>Grip strength</i> 1 yr 21%
Wiik et al. [71]	$N=11$ TW 27 ± 4	T suppression + E supplementation	≤ 1 nmol/L at 4 mo and at 1 yr	<i>Thigh volume</i> 1 yr – 5% <i>Quad area</i> 1 yr – 4% <i>Knee extension strength</i> 1 yr 2% <i>Knee flexion strength</i> 1 yr 3%	<i>Thigh volume</i> 1 yr 33% <i>Quad area</i> 26% <i>Knee extension strength</i> 41% <i>Knee flexion strength</i> 33%

Studies reporting measures of lean mass, muscle volume, muscle area or strength are included. Muscle/strength data are calculated in reference to baseline cohort data and, where reported, reference female (or transgender men before treatment) cohort data. Tack et al. [72] was not included in the table since some of the participants had not completed full puberty at treatment initiation. van Caenegem et al. [76] reports reference female values measured in a separately-published, parallel cohort of transgender men

N number of participants, TW transgender women, Yr year, Mo month, T testosterone, E estrogen. $\pm$ Standard deviation (unless otherwise indicated in text), *LBM* lean body mass, *ALM* appendicular lean mass

study has reported muscle loss exceeding the -12% found by Gooren and Bunck after 3 years of therapy. Notably, studies have found very consistent changes in lean body mass (using dual-energy X-ray absorptiometry) after 12 months of treatment, where the change has always been between -3 and -5% on average, with slightly greater reductions in the arm compared with the leg region [68]. Thus, given the large baseline differences in muscle mass between males and females (Table 1; approximately 40%), the reduction achieved by 12 months of testosterone suppression can reasonably be assessed as small relative to the initial superior mass. We, therefore, conclude that the muscle mass advantage males possess over females, and the performance implications thereof, are not removed by the currently studied durations (4 months, 1, 2 and 3 years) of testosterone suppression in transgender women. In sports where muscle mass is important for performance, inclusion is therefore only possible if a large imbalance in fairness, and potentially safety in some sports, is to be tolerated.

To provide more detailed information on not only gross body composition but also thigh muscle volume and contractile density, Wiik et al. [71] recently carried out a comprehensive battery of MRI and computed tomography (CT) examinations before and after 12 months of successful testosterone suppression and estrogen supplementation in 11 transgender women. Thigh volume (both anterior and posterior thigh) and quadriceps cross-sectional area decreased -4 and -5% , respectively, after the 12-month period, supporting previous results of modest effects of testosterone suppression on muscle mass (see Table 4). The more novel measure of radiological attenuation of the quadriceps muscle, a valid proxy of contractile density [74, 75], showed no significant change in transgender women after 12 months of treatment, whereas the parallel group of transgender men demonstrated a $+6\%$ increase in contractile density with testosterone supplementation.

As indicated earlier (e.g. Table 1), the difference in muscle strength between males and females is often more pronounced than the difference in muscle mass. Unfortunately, few studies have examined the effects of testosterone suppression on muscle strength or other proxies of performance in transgender individuals. The first such study was published online approximately 1 year prior to the release of the current IOC policy. In this study, as well as reporting changes in muscle size, van Caenegem et al. [53] reported that hand-grip strength was reduced from baseline measurements by -7% and -9% after 12 and 24 months, respectively, of cross-hormone treatment in transgender women. Comparison with data in a separately-published, parallel cohort of transgender men [76] demonstrated a retained hand-grip strength advantage after 2 years of 23% over female baseline measurements (a calculated average of

baseline data obtained from control females and transgender men).

In a recent multicenter study [70], examination of 249 transgender women revealed a decrease of -4% in grip strength after 12 months of cross-hormone treatment, with no variation between different testosterone level, age or BMI tertiles (all transgender women studied were within female reference ranges for testosterone). Despite this modest reduction in strength, transgender women retained a 17% grip strength advantage over transgender men measured at baseline. The authors noted that handgrip strength in transgender women was in approximately the 25th percentile for males but was over the 90th percentile for females, both before and after hormone treatment. This emphasizes that the strength advantage for males over females is inherently large. In another study exploring handgrip strength, albeit in late puberty adolescents, Tack et al. noted no change in grip strength after hormonal treatment (average duration 11 months) of 21 transgender girls [72].

Although grip strength provides an excellent proxy measurement for general strength in a broad population, specific assessment within different muscle groups is more valuable in a sports-specific framework. Wiik et al., [71] having determined that thigh muscle mass reduces only modestly, and that no significant changes in contractile density occur with 12 months of testosterone suppression, provided, for the first time, data for isokinetic strength measurements of both knee extension and knee flexion. They reported that muscle strength after 12 months of testosterone suppression was comparable to baseline strength. As a result, transgender women remained about 50% stronger than both the group of transgender men at baseline and a reference group of females. The authors suggested that small neural learning effects during repeated testing may explain the apparent lack of small reductions in strength that had been measured in other studies [71].

These longitudinal data comprise a clear pattern of very modest to negligible changes in muscle mass and strength in transgender women suppressing testosterone for at least 12 months. Muscle mass and strength are key physical parameters that constitute a significant, if not majority, portion of the male performance advantage, most notably in those sports where upper body strength, overall strength, and muscle mass are crucial determinants of performance. Thus, our analysis strongly suggests that the reduction in testosterone levels required by many sports federation transgender policies is insufficient to remove or reduce the male advantage, in terms of muscle mass and strength, by any meaningful degree. The relatively consistent finding of a minor (approximately -5%) muscle loss after the first year of treatment is also in line with studies on androgen-deprivation therapy in males with prostate cancer, where the annual loss

of lean body mass has been reported to range between -2 and -4% [77].

Although less powerful than longitudinal studies, we identified one major cross-sectional study that measured muscle mass and strength in transgender women. In this study, 23 transgender women and 46 healthy age- and height-matched control males were compared [78]. The transgender women were recruited at least 3 years after sex reassignment surgery, and the mean duration of cross-hormone treatment was 8 years. The results showed that transgender women had 17% less lean mass and 25% lower peak quadriceps muscle strength than the control males [78]. This cross-sectional comparison suggests that prolonged testosterone suppression, well beyond the time period mandated by sports federations substantially reduces muscle mass and strength in transgender women. However, the typical gap in lean mass and strength between males and females at baseline (Table 1) exceeds the reductions reported in this study [78]. The final average lean body mass of the transgender women was 51.2 kg, which puts them in the 90th percentile for women [79]. Similarly, the final grip strength was 41 kg, 25% higher than the female reference value [80]. Collectively, this implies a retained physical advantage even after 8 years of testosterone suppression. Furthermore, given that cohorts of transgender women often have slightly lower baseline measurements of muscle and strength than control males [53], and baseline measurements were unavailable for the transgender women of this cohort, the above calculations using control males reference values may be an overestimate of actual loss of muscle mass and strength, emphasizing both the need for caution when analyzing cross-sectional data in the absence of baseline assessment and the superior power of longitudinal studies quantifying within-subject changes.

4.3 Endurance Performance and Cardiovascular Parameters

No controlled longitudinal study has explored the effects of testosterone suppression on endurance-based performance. Sex differences in endurance performance are generally smaller than for events relying more on muscle mass and explosive strength. Using an age grading model designed to normalize times for masters/veteran categories, Harper [81] analyzed self-selected and self-reported race times for eight transgender women runners of various age categories who had, over an average 7 year period (range 1–29 years), competed in sub-elite middle and long distance races within both the male and female categories. The age-graded scores for these eight runners were the same in both categories, suggesting that cross-hormone treatment reduced running performance by approximately the size of the typical male advantage. However, factors affecting performances in the interim, including training and injury, were uncontrolled

for periods of years to decades and there were uncertainties regarding which race times were self-reported vs. which race times were actually reported and verified, and factors such as standardization of race course and weather conditions were unaccounted for. Furthermore, one runner improved substantially post-transition, which was attributed to improved training [81]. This demonstrates that performance decrease after transition is not inevitable if training practices are improved. Unfortunately, no study to date has followed up these preliminary self-reports in a more controlled setting, so it is impossible to make any firm conclusions from this data set alone.

Circulating hemoglobin levels are androgen-dependent [82] and typically reported as 12% higher in males compared with females [4]. Hemoglobin levels appear to decrease by 11–14% with cross-hormone therapy in transgender women [62, 71], and indeed comparably sized reductions have been reported in athletes with DSDs where those athletes are sensitive to and been required to reduce testosterone [47, 83]. Oxygen-carrying capacity in transgender women is most likely reduced with testosterone suppression, with a concomitant performance penalty estimated at 2–5% for the female athletic population [83]. Furthermore, there is a robust relationship between hemoglobin mass and VO_{2max} [84, 85] and reduction in hemoglobin is generally associated with reduced aerobic capacity [86, 87]. However, hemoglobin mass is not the only parameter contributing to VO_{2max} , where central factors such as total blood volume, heart size and contractility, and peripheral factors such as capillary supply and mitochondrial content also plays a role in the final oxygen uptake [88]. Thus, while a reduction in hemoglobin is strongly predicted to impact aerobic capacity and reduce endurance performance in transgender women, it is unlikely to completely close the baseline gap in aerobic capacity between males and females.

The typical increase in body fat noted in transgender women [89, 90] may also be a disadvantage for sporting activities (e.g. running) where body weight (or fat distribution) presents a marginal disadvantage. Whether this body composition change negatively affects performance results in transgender women endurance athletes remains unknown. It is unclear to what extent the expected increase in body fat could be offset by nutritional and exercise countermeasures, as individual variation is likely to be present. For example, in the Wiik et al. study [71], 3 out of the 11 transgender women were completely resistant to the marked increase in total adipose tissue noted at the group level. This inter-individual response to treatment represents yet another challenge for sports governing bodies who most likely, given the many obstacles with case-by-case assessments, will form policies based on average effect sizes.

Altogether, the effects of testosterone suppression on performance markers for endurance athletes remain

insufficiently explored. While the negative effect on hemoglobin concentration is well documented, the effects on $\text{VO}_{2\text{max}}$, left ventricular size, stroke volume, blood volume, cardiac output lactate threshold, and exercise economy, all of which are important determinants of endurance performance, remain unknown. However, given the plausible disadvantages with testosterone suppression mentioned in this section, together with the more marginal male advantage in endurance-based sports, the balance between inclusion and fairness is likely closer to equilibrium in weight-bearing endurance-based sports compared with strength-based sports where the male advantage is still substantial.

5 Discussion

The data presented here demonstrate that superior anthropometric, muscle mass and strength parameters achieved by males at puberty, and underpinning a considerable portion of the male performance advantage over females, are not removed by the current regimen of testosterone suppression permitting participation of transgender women in female sports categories. Rather, it appears that the male performance advantage remains substantial. Currently, there is no consensus on an acceptable degree of residual advantage held by transgender women that would be tolerable in the female category of sport. There is significant dispute over this issue, especially since the physiological determinants of performance vary across different sporting disciplines. However, given the IOC position that fair competition is the overriding sporting objective [14], any residual advantage carried by transgender women raises obvious concerns about fair and safe competition in the numerous sports where muscle mass, strength and power are key performance determinants.

5.1 Perspectives on Athletic Status of Transgender Women

Whilst available evidence is strong and convincing that strength, skeletal- and muscle-mass derived advantages will largely remain after cross-hormone therapy in transgender women, it is acknowledged that the findings presented here are from healthy adults with regular or even low physical activity levels [91], and not highly trained athletes. Thus, further research is required in athletic transgender populations.

However, despite the current absence of empirical evidence in athletic transgender women, it is possible to evaluate potential outcomes in athletic transgender women compared with untrained cohorts. The first possibility is that athletic transgender women will experience similar reductions (approximately -5%) in muscle mass and strength as untrained transgender women, and will thus

retain significant advantages over a comparison group of females. As a result of higher baseline characteristics in these variables, the retained advantage may indeed be even larger. A second possibility is that by virtue of greater muscle mass and strength at baseline, pre-trained transgender women will experience larger relative decreases in muscle mass and strength if they converge with untrained transgender women, particularly if training is halted during transition. Finally, training before and during the period of testosterone suppression may attenuate the anticipated reductions, such that relative decreases in muscle mass and strength will be smaller or non-existent in transgender women who undergo training, compared to untrained (and non-training) controls.

It is well established that resistance training counteracts substantial muscle loss during atrophy conditions that are far more severe than testosterone suppression. For example, resistance exercise every third day during 90-days bed rest was sufficient to completely offset the 20% reduction in knee extensor muscle size noted in the resting control subjects [92]. More relevant to the question of transgender women, however, is to examine training effects in studies where testosterone has been suppressed in biological males. Kvorning et al. investigated, in a randomized placebo-controlled trial, how suppression of endogenous testosterone for 12 weeks influenced muscle hypertrophy and strength gains during a training program (3 days/week) that took place during the last 8 weeks of the 3-month suppression period [93]. Despite testosterone suppression to female levels of 2 nmol/L, there was a significant $+4\%$ increase in leg lean mass and a $+2\%$ increase in total lean body mass, and a measurable though insignificant increase in isometric knee extension strength. Moreover, in select exercises used during the training program, 10RM leg press and bench press increased $+32\%$ and $+17\%$, respectively. While some of the training adaptations were lower than in the placebo group, this study demonstrates that training during a period of testosterone suppression not only counteracts muscle loss, but can actually increase muscle mass and strength.

Males with prostate cancer undergoing androgen deprivation therapy provide a second avenue to examine training effects during testosterone suppression. Testosterone levels are typically reduced to castrate levels, and the loss of lean mass has typically ranged between -2 and -4% per year [77], consistent with the findings described previously in transgender women. A recent meta-analysis concluded that exercise interventions including resistance exercise were generally effective for maintaining muscle mass and increasing muscle strength in prostate cancer patients undergoing androgen deprivation therapy [94]. It is important to emphasize that the efficacy of the different training programs may vary. For example, a 12-week training study of prostate cancer patients undergoing androgen deprivation therapy

included drop-sets to combine heavy loads and high volume while eliciting near-maximal efforts in each set [95]. This strategy resulted in significantly increased lean body mass (+3%), thigh muscle volume (+6%), knee extensor 1RM strength (+28%) and leg press muscle endurance (+110%).

In addition to the described effects of training during testosterone suppression, the effect of training prior to testosterone suppression may also contribute to the attenuation of any muscle mass and strength losses, via a molecular mechanism referred to as ‘muscle memory’ [96]. Specifically, it has been suggested that myonuclei acquired by skeletal muscle cells during training are maintained during subsequent atrophy conditions [97]. Even though this model of muscle memory has been challenged recently [98], it may facilitate an improved training response upon retraining [99]. Mechanistically, the negative effects of testosterone suppression on muscle mass are likely related to reduced levels of resting protein synthesis [100], which, together with protein breakdown, determines the net protein balance of skeletal muscle. However, testosterone may not be required to elicit a robust muscle protein synthesis response to resistance exercise [100]. Indeed, relative increases in muscle mass in men and women from resistance training are comparable, despite marked differences in testosterone levels [101], and the acute rise in testosterone apparent during resistance exercise does not predict muscle hypertrophy nor strength gains [102]. This suggests that even though testosterone is important for muscle mass, especially during puberty, the maintenance of muscle mass through resistance training is not crucially dependent on circulating testosterone levels.

Thus, in well-controlled studies in biological males who train while undergoing testosterone reduction, training is protective of, and may even enhance, muscle mass and strength attributes. Considering transgender women athletes who train during testosterone suppression, it is plausible to conclude that any losses will be similar to or even smaller in magnitude than documented in the longitudinal studies described in this review. Furthermore, pre-trained transgender women are likely to have greater muscle mass at baseline than untrained transgender women; it is possible that even with the same, rather than smaller, relative decreases in muscle mass and strength, the magnitude of retained advantage will be greater. In contrast, if pre-trained transgender women undergo testosterone suppression while refraining from intense training, it appears likely that muscle mass and strength will be lost at either the same or greater rate than untrained individuals, although there is no rationale to expect a weaker endpoint state. The degree of change in athletic transgender women is influenced by the athlete’s baseline resistance-training status, the efficacy of the implemented program and other factors such as genetic make-up and nutritional habits, but we argue that it is implausible that

athletic transgender women would achieve final muscle mass and strength metrics that are on par with reference females at comparable athletic level.

5.2 The Focus on Muscle Mass and Strength

We acknowledge that changes in muscle mass are not always correlated in magnitude to changes in strength measurements because muscle mass (or total mass) is not the only contributor to strength [103]. Indeed, the importance of the nervous system, e.g. muscle agonist activation (recruitment and firing frequency) and antagonist co-activation, for muscle strength must be acknowledged [104]. In addition, factors such as fiber types, biomechanical levers, pennation angle, fascicle length and tendon/extracellular matrix composition may all influence the ability to develop muscular force [105]. While there is currently limited to no information on how these factors are influenced by testosterone suppression, the impact seems to be minute, given the modest changes noted in muscle strength during cross-hormone treatment.

It is possible that estrogen replacement may affect the sensitivity of muscle to anabolic signaling and have a protective effect on muscle mass [106] explaining, in part, the modest change in muscle mass with testosterone suppression and accompanying cross-hormone treatment. Indeed, this is supported by research conducted on estrogen replacement therapy in other targeted populations [107, 108] and in several different animal models, including mice after gonadectomy [109] and ovariectomy [110].

In terms of other performance proxies relevant to sports performance, there is no research evaluating the effects of transgender hormone treatment on factors such as agility, jumping or sprint performance, competition strength performance (e.g. bench press), or discipline-specific performance. Other factors that may impact sports performance, known to be affected by testosterone and some of them measurably different between males and females, include visuospatial abilities, aggressiveness, coordination and flexibility.

5.3 Testosterone-Based Criteria for Inclusion of Transgender Women in Female Sports

The appropriate testosterone limit for participation of transgender women in the female category has been a matter of debate recently, where sports federations such as World Athletics recently lowered the eligibility criterion of free circulating testosterone (measured by means of liquid chromatography coupled with mass spectrometry) to <5 nmol/L. This was based, at least in part, on a thorough review by Handelsman et al. [4], where the authors concluded that, given the nonoverlapping distribution of circulating testosterone between males and females, and making an allowance

for females with mild hyperandrogenism (e.g. with polycystic ovary syndrome), the appropriate testosterone limit should be 5 rather than 10 nmol/L.

From the longitudinal muscle mass/strength studies summarised here, however, it is apparent that most therapeutic interventions result in almost complete suppression of testosterone levels, certainly well below 5 nmol/L (Table 4). Thus, with regard to transgender women athletes, we question whether current circulating testosterone level cut-off can be a meaningful decisive factor, when in fact not even suppression down to around 1 nmol/L removes the anthropometric and muscle mass/strength advantage in any significant way.

In terms of duration of testosterone suppression, it may be argued that although 12 months of treatment is not sufficient to remove the male advantage, perhaps extending the time frame of suppression would generate greater parity with female metrics. However, based on the studies reviewed here, evidence is lacking that this would diminish the male advantage to a tolerable degree. On the contrary, it appears that the net loss of lean mass and grip strength is not substantially decreased at year 2 or 3 of cross-hormone treatment (Table 4), nor evident in cohorts after an average 8 years after transition. This indicates that a plateau or a new steady state is reached within the first or second year of treatment, a phenomenon also noted in transgender men, where the increase in muscle mass seems to stabilise between the first and the second year of testosterone treatment [111].

6 Conclusions

We have shown that under testosterone suppression regimes typically used in clinical settings, and which comfortably exceed the requirements of sports federations for inclusion of transgender women in female sports categories by reducing testosterone levels to well below the upper tolerated limit, evidence for loss of the male performance advantage, established by testosterone at puberty and translating in elite athletes to a 10–50% performance advantage, is lacking. Rather, the data show that strength, lean body mass, muscle size and bone density are only trivially affected. The reductions observed in muscle mass, size, and strength are very small compared to the baseline differences between males and females in these variables, and thus, there are major performance and safety implications in sports where these attributes are competitively significant. These data significantly undermine the delivery of fairness and safety presumed by the criteria set out in transgender inclusion policies, particularly given the stated prioritization of fairness as an overriding objective (for the IOC). If those policies are intended to preserve fairness,

inclusion and the safety of biologically female athletes, sporting organizations may need to reassess their policies regarding inclusion of transgender women.

From a medical-ethical point of view, it may be questioned as to whether a requirement to lower testosterone below a certain level to ensure sporting participation can be justified at all. If the advantage persists to a large degree, as evidence suggests, then a stated objective of targeting a certain testosterone level to be eligible will not achieve its objective and may drive medical practice that an individual may not want or require, without achieving its intended benefit.

The research conducted so far has studied untrained transgender women. Thus, while this research is important to understand the isolated effects of testosterone suppression, it is still uncertain how transgender women athletes, perhaps undergoing advanced training regimens to counteract the muscle loss during the therapy, would respond. It is also important to recognize that performance in most sports may be influenced by factors outside muscle mass and strength, and the balance between inclusion, safety and fairness therefore differs between sports. While there is certainly a need for more focused research on this topic, including more comprehensive performance tests in transgender women athletes and studies on training capacity of transgender women undergoing hormone therapy, it is still important to recognize that the biological factors underpinning athletic performance are unequivocally established. It is, therefore, possible to make strong inferences and discuss potential performance implications despite the lack of direct sport-specific studies in athletes. Finally, since athlete safety could arguably be described as the immediate priority above considerations of fairness and inclusion, proper risk assessment should be conducted within respective sports that continue to include transgender women in the female category.

If transgender women are restricted within or excluded from the female category of sport, the important question is whether or not this exclusion (or conditional exclusion) is necessary and proportionate to the goal of ensuring fair, safe and meaningful competition. Regardless of what the future will bring in terms of revised transgender policies, it is clear that different sports differ vastly in terms of physiological determinants of success, which may create safety considerations and may alter the importance of retained performance advantages. Thus, we argue against universal guidelines for transgender athletes in sport and instead propose that each individual sports federation evaluate their own conditions for inclusivity, fairness and safety.

Compliance with Ethical Standards

Funding None. Open access funding provided by Karolinska Institutet.

Conflicts of interest Emma N Hilton and Tommy R Lundberg declare that they have no conflict of interest with the content of this review.

Authorship contributions Both authors (ENH and TRL) were involved in the conception and design of this paper, and both authors drafted, revised and approved the final version of the paper.

Ethics approval Not applicable.

Informed consent Not applicable.

Data availability Available upon request.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

- Suchomel TJ, Nimphius S, Bellon CR, Stone MH. The importance of muscular strength: training considerations. *Sport Med.* 2018;48:765–85.
- Coyle EF. Integration of the physiological factors determining endurance performance ability. *Exerc Sport Sci Rev.* 1995;23:25–63.
- Haizlip KM, Harrison BC, Leinwand LA. Sex-based differences in skeletal muscle kinetics and fiber-type composition. *Physiol.* 2015;30(1):30–9.
- Handelsman DJ, Hirschberg AL, Berman S. Circulating testosterone as the hormonal basis of sex differences in athletic performance. *Endocr Rev.* 2018;39(5):803–29.
- Sandbakk Ø, Solli GS, Holmberg HC. Sex differences in world-record performance: the influence of sport discipline and competition duration. *Int J Sports Physiol Perform.* 2018;13(1):2–8.
- Genel M. Transgender athletes: how can they be accommodated? *Curr Sports Med Rep.* 2017;16(1):12–3.
- Coggon J, Hammond N, Holm S. Transsexuals in sport—fairness and freedom, regulation and law. *Sport Ethics Philos.* 2008;2(1):4–17.
- Pitsiladis Y, Harper J, Betancourt JO, et al. Beyond fairness. *Curr Sports Med Rep.* 2016;15:386–8.
- Reeser JC. Gender identity and sport: is the playing field level? *Br J Sports Med.* 2005;39(10):695–9.
- Transgender Policy in Sport. A review of current policy and commentary of the challenges of policy creation. *Curr Sports Med Rep.* 2019;18(6):239–47.
- Harper J, Martinez-Patino MJ, Pigozzi F, Pitsiladis Y. Implications of a third gender for elite sports. *Curr Sports Med Rep.* 2018;17(2):42–4.
- Singh B, Singh K. The hermeneutics of participation of transgender athletes in sports—intensifying third force. *Phys Cult Sport Stud Res.* 2011;52(1):44–8.
- Bianchi A. Transgender women in sport. *J Philos Sport.* 2017;44:229–42.
- Harper J, Hirschberg AL, Jose M, et al. IOC consensus meeting on sex reassignment and hyperandrogenism. 2015. https://stillmed.olympic.org/Documents/Commissions_PDFfiles/Medical_commission/2015-11_ioc_consensus_meeting_on_sex_reassignment_and_hyperandrogenism-en.pdf. Accessed 28 Nov 2020
- Carré GA, Greenfield A. The gonadal supporting cell lineage and mammalian sex determination: the differentiation of sertoli and granulosa cells. In: Piprek R, editor. *Molecular mechanisms of cell differentiation in gonad development. Results and problems in cell differentiation*, vol 58. Cham: Springer; 2016. p. 47–66.
- Sobel V, Zhu YS, Imperato-McGinley J. Fetal hormones and sexual differentiation. *Obstet Gynecol Clin N Am.* 2004;31(4):837–xi.
- Hughes IA. Disorders of sex development: a new definition and classification. *Best Pract Res Clin Endocrinol Metab.* 2008;22(1):119–34.
- Tønnessen E, Svendsen IS, Olsen IC, et al. Performance development in adolescent track and field athletes according to age, sex and sport discipline. *PLoS ONE.* 2015;10(6):e0129014.
- Gershoni M, Pietrokovski S. The landscape of sex-differential transcriptome and its consequent selection in human adults. *BMC Biol.* 2017;15(1):7.
- Lanciotti L, Cofini M, Leonardi A, Penta L, Esposito S. Up-to-date review about minipuberty and overview on hypothalamic-pituitary-gonadal axis activation in fetal and neonatal life. *Front Endocrinol.* 2018;23(9):410.
- Becker M, Hesse V. Minipuberty: why does it happen? *Horm Res Paediatr.* 2020;93(2):76–84.
- Catley MJ, Tomkinson GR. Normative health-related fitness values for children: analysis of 85347 test results on 9–17-year-old Australians since 1985. *Br J Sports Med.* 2013;47(2):98–108.
- Tambalis KD, Panagiotakos DB, Psarra G, et al. Physical fitness normative values for 6–18-year-old Greek boys and girls, using the empirical distribution and the lambda, mu, and sigma statistical method. *Eur J Sport Sci.* 2016;16(6):736–46.
- Eiberg S, Hasselstrom H, Grønfelt V, et al. Maximum oxygen uptake and objectively measured physical activity in Danish children 6–7 years of age: the Copenhagen school child intervention study. *Br J Sports Med.* 2005;39(10):725–30.
- Bae YJ, Zeidler R, Baber R, et al. Reference intervals of nine steroid hormones over the life-span analyzed by LC-MS/MS: Effect of age, gender, puberty, and oral contraceptives. *J Steroid Biochem Mol Biol.* 2019;193:105409.
- Thibault V, Guillaume M, Berthelot G, et al. Women and men in sport performance: the gender gap has not evolved since 1983. *J Sport Sci Med.* 2010;9(2):214–23.
- Millard-Stafford M, Swanson AE, Wittbrodt MT. Nature versus nurture: have performance gaps between men and women reached an asymptote? *Int J Sports Physiol Perform.* 2018;13(4):530–5.
- Lee DH, Keum N, Hu FB, et al. Development and validation of anthropometric prediction equations for lean body mass, fat mass and percent fat in adults using the National Health and Nutrition Examination Survey (NHANES) 1999–2006. *Br J Nutr.* 2017;118(10):858–66.
- Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. *J Appl Physiol.* 2000;89:81–8.
- Bohannon RW, Wang YC, Yen SC, Grogan KA. Handgrip strength: a comparison of values obtained from the NHANES and NIH Toolbox studies. *Am J Occup Ther.* 2019;73(2):1–9.
- Neder JA, Nery LE, Shinzato GT, et al. Reference values for concentric knee isokinetic strength and power in nonathletic men and women from 20 to 80 years old. *J Orthop Sports Phys Ther.* 1999;29:116–26.

32. Jantz LM, Jantz RL. Secular change in long bone length and proportion in the United States, 1800–1970. *Am J Phys Anthropol*. 1999;110(1):57–67.
33. Brinckmann P, Hoefert H, Jongen HT. Sex differences in the skeletal geometry of the human pelvis and hip joint. *J Biomech*. 1981;14(6):427–30.
34. Lepley AS, Joseph MF, Daigle NR, et al. Sex differences in mechanical properties of the Achilles tendon: longitudinal response to repetitive loading exercise. *J Strength Cond Res*. 2018;32(11):3070–9.
35. Pate RR, Kriska A. Physiological basis of the sex difference in cardiorespiratory endurance. *Sports Med*. 1984;1(2):87–9.
36. Astrand PO, Cuddy TE, Saltin B, Stenberg J. Cardiac output during submaximal and maximal work. *J Appl Physiol*. 1964;19:268–74.
37. Best SA, Okada Y, Galbreath MM, et al. Age and sex differences in muscle sympathetic nerve activity in relation to haemodynamics, blood volume and left ventricular size. *Exp Physiol*. 2014;99(6):839–48.
38. Tong E, Murphy WG, Kinsella A, et al. Capillary and venous haemoglobin levels in blood donors: a 42-month study of 36 258 paired samples. *Vox Sang*. 2010;98(4):547–53.
39. Dominelli PB, Molgat-Seon Y, Sheel AW. Sex differences in the pulmonary system influence the integrative response to exercise. *Exerc Sport Sci Rev*. 2019;47(3):142–50.
40. Wingate S. Cardiovascular anatomy and physiology in the female. *Crit Care Nurs Clin N Am*. 1997;9(4):447–52.
41. Haugen T, Breitschädel F, Wiig H, Seiler S. Countermovement jump height in national team athletes of various sports: a framework for practitioners and scientists. *Int J Sports Physiol Perform*. 2020 (accessed 4 May 2020 from Researchgate)
42. Thomas JR, French KE. Gender differences across age in motor performance a meta-analysis. *Psychol Bull*. 1985;98(2):260–82.
43. Antti M, Komi PV, Korjus T, et al. Body segment contributions to javelin throwing during final thrust phases. *J Appl Biomech*. 1994;10:166–77.
44. Lassek WD, Gaulin SJC. Costs and benefits of fat-free muscle mass in men: relationship to mating success, dietary requirements, and native immunity. *Evol Hum Behav*. 2009;20(5):322–8.
45. Stoll T, Huber E, Seifert B, et al. Maximal isometric muscle strength: normative values and gender-specific relation to age. *Clin Rheumatol*. 2000;19(2):105–11.
46. Coleman DL. Sex in sport. *Law Contemp Probl*. 2017;80:63–126.
47. CAS 2018/O/5794 Mokgadi Caster Semenya v. International Association of Athletics Federation. https://www.tas-cas.org/fileadmin/user_upload/CAS_Award_-_redacted_-_Semenya_ASA_IAAF.pdf. Accessed 28 Nov 2020
48. Sparling PB. A meta-analysis of studies comparing maximal oxygen uptake in men and women. *Res Q Exerc Sport*. 1980;51(3):542–52.
49. Hubal MJ, Gordish-Dressman H, Thompson PD, et al. Muscle size and strength gain after unilateral resistance training. *Med Sci Sport Exerc*. 2005;37(6):964–72.
50. Morris JS, Link J, Martin JC, Carrier DR. Sexual dimorphism in human arm power and force: implications for sexual selection on fighting ability. *J Exp Biol*. 2020;223(Pt 2):jeb212365.
51. Thomas JR, Thomas KT. Development of gender differences in physical activity. *Quest*. 1988;40(3):219–29.
52. Wiepjes CM, de Jongh RT, de Blok CJM, et al. Bone safety during the first ten years of gender-affirming hormonal treatment in transwomen and transmen. *J Bone Miner Res*. 2019;34(3):447–54.
53. Van Caenegem E, Wierckx K, Taes Y, et al. Preservation of volumetric bone density and geometry in trans women during cross-sex hormonal therapy: a prospective observational study. *Osteoporos Int*. 2015a;26(1):35–47.
54. Singh-Ospina N, Maraka S, Rodriguez-Gutierrez R, et al. Effect of sex steroids on the bone health of transgender individuals: a systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2017;102(11):3904–13.
55. Figuera TM, Ziegelmann PK, da Silva TR, Spritzer PM. Bone mass effects of cross-sex hormone therapy in transgender people: updated systematic review and meta-analysis. *J Endocr Soc*. 2019;3(5):943–64.
56. Ruetsche AG, Kneubuehl R, Birkhaeuser MH, Lippuner K. Cortical and trabecular bone mineral density in transsexuals after long-term cross-sex hormonal treatment: a cross-sectional study. *Osteoporos Int*. 2005;16(7):791–8.
57. Rosen HN, Hamnvik OPR, Jaisarnarn U, et al. Bone densitometry in transgender and gender non-conforming (TGNC) individuals: 2019 ISCD official position. *J Clin Densitom*. 2019;22(4):544–53.
58. Khosla S, Melton LJ, Riggs BL. Estrogens and bone health in men. *Calcif Tissue Int*. 2001;69(4):189–92.
59. Sigward SM, Powers CM. The influence of gender on knee kinematics, kinetics and muscle activation patterns during side-step cutting. *Clin Biomech*. 2006;21(1):41–8.
60. Francis P, Whatman C, Sheerin K, et al. The proportion of lower limb running injuries by gender, anatomical location and specific pathology: a systematic review. *J Sport Sci Med*. 2019;18(1):21–31.
61. Elbers JM, Asscheman H, Seidell JC, Gooren LJ. Effects of sex steroid hormones on regional fat depots as assessed by magnetic resonance imaging in transsexuals. *Am J Physiol*. 1999;276(2):E317–25.
62. Gooren LJG, Bunck MCM. Transsexuals and competitive sports. *Eur J Endocrinol*. 2004;151(4):425–9.
63. Haraldsen IR, Haug E, Falch J, et al. Cross-sex pattern of bone mineral density in early onset gender identity disorder. *Horm Behav*. 2007;52(3):334–43.
64. Mueller A, Zollner H, Kronawitter D, et al. Body composition and bone mineral density in male-to-female transsexuals during cross-sex hormone therapy using gonadotrophin-releasing hormone agonist. *Exp Clin Endocrinol Diabetes*. 2011;119(2):95–100.
65. Wierckx K, Van Caenegem E, Schreiner T, et al. Cross-sex hormone therapy in trans persons is safe and effective at short-time follow-up: results from the European network for the investigation of gender incongruence. *J Sex Med*. 2014;11(8):1999–2011.
66. Gava G, Cerpolini S, Martelli V, et al. Cyproterone acetate vs leuprolide acetate in combination with transdermal oestradiol in transwomen: a comparison of safety and effectiveness. *Clin Endocrinol (Oxf)*. 2016;85(2):239–46.
67. Auer MK, Ebert T, Pietzner M, et al. Effects of sex hormone treatment on the metabolic syndrome in transgender individuals: focus on metabolic cytokines. *J Clin Endocrinol Metab*. 2018;103(2):790–802.
68. Klaver M, De Blok CJM, Wiepjes CM, et al. Changes in regional body fat, lean body mass and body shape in trans persons using cross-sex hormonal therapy: results from a multicenter prospective study. *Eur J Endocrinol*. 2018;178(2):163–71.
69. Figuera TM, da Silva E, Lindenau JDR, Spritzer PM. Impact of cross-sex hormone therapy on bone mineral density and body composition in transwomen. *Clin Endocrinol (Oxf)*. 2018;88(6):856–62.
70. Scharff M, Wiepjes CM, Klaver M, et al. Change in grip strength in trans people and its association with lean body mass and bone density. *Endocr Connect*. 2019;8:1020–8.
71. Wiik A, Lundberg TR, Rullman E, et al. Muscle strength, size, and composition following 12 months of gender-affirming

- treatment in transgender individuals. *J Clin Endocrinol Metab.* 2020;105(3):247.
72. Tack LJW, Craen M, Lapauw B, et al. Proandrogenic and antianandrogenic progestins in transgender youth: differential effects on body composition and bone metabolism. *J Clin Endocrinol Metab.* 2018;103(6):2147–56.
 73. Polderman KH, Gooren LJG, Asscheman H, et al. Induction of insulin resistance by androgens and estrogens. *J Clin Endocrinol Metab.* 1994;79(1):265–71.
 74. Aubrey J, Esfandiari N, Baracos VE, et al. Measurement of skeletal muscle radiation attenuation and basis of its biological variation. *Acta Physiol (Oxf).* 2014;210(3):489–97.
 75. Rasch A, Byström AH, Dalen N, Berg HE. Reduced muscle radiological density, cross-sectional area, and strength of major hip and knee muscles in 22 patients with hip osteoarthritis. *Acta Orthop.* 2007;78(4):505–10.
 76. Van Caenegem E, Wierckx K, Taes Y, et al. Body composition, bone turnover, and bone mass in trans men during testosterone treatment: 1-year follow-up data from a prospective case-controlled study (ENIGI). *Eur J Endocrinol.* 2015b;172(2):163–71.
 77. Storer TW, Miciek R, Travison TG. Muscle function, physical performance and body composition changes in men with prostate cancer undergoing androgen deprivation therapy. *Asian J Androl.* 2012;14(2):204–21.
 78. Lapauw B, Taes Y, Simoens S, et al. Body composition, volumetric and areal bone parameters in male-to-female transsexual persons. *Bone.* 2008;43(6):1016–21.
 79. Imboden MT, Swartz AM, Finch HW, et al. Reference standards for lean mass measures using GE dual energy x-ray absorptiometry in Caucasian adults. *PLoS ONE.* 2017;12(4):e0176161.
 80. Bohannon RW, Peolsson A, Massy-Westropp N, et al. Reference values for adult grip strength measured with a Jamar dynamometer: a descriptive meta-analysis. *Physiotherapy.* 2006;92(1):11–5.
 81. Harper J. Race times for transgender athletes. *J Sport Cult Identities.* 2015;6(1):1–9.
 82. Coviello AD, Kaplan B, Lakshman KM, et al. Effects of graded doses of testosterone on erythropoiesis in healthy young and older men. *J Clin Endocrinol Metab.* 2008;93(3):914–9.
 83. Berman S. Androgens and athletic performance of elite female athletes. *Curr Opin Endocrinol Diabetes Obes.* 2017;24(3):246–51.
 84. Joyner MJ. VO₂MAX, blood doping, and erythropoietin. *Br J Sports Med.* 2003;37(3):190–1.
 85. Eklblom B, Goldbarg AN, Gullbring B. Response to exercise after blood loss and reinfusion. *J Appl Physiol.* 1972;33(2):175–80.
 86. Kanstrup IL, Eklblom B. Blood volume and hemoglobin concentration as determinants of maximal aerobic power. *Med Sci Sports Exerc.* 1984;16(3):256–62.
 87. Otto JM, Montgomery HE, Richards T. Haemoglobin concentration and mass as determinants of exercise performance and of surgical outcome. *Extrem Physiol Med.* 2013;2(1):33.
 88. Joyner MJ, Lundby C. Concepts about VO_{2max} and trainability are context dependent. *Exerc Sport Sci Rev.* 2018;46(3):138–43.
 89. T'Sjoen G, Arcelus J, Gooren L, et al. Endocrinology of transgender medicine. *Endocr Rev.* 2018;40(1):97–117.
 90. Klaver M, Dekker MJHJ, de Mutsert R, et al. Cross-sex hormone therapy in transgender persons affects total body weight, body fat and lean body mass: a meta-analysis. *Andrologia.* 2017. <https://doi.org/10.1111/and.12660>.
 91. Muchicko MM, Lepp A, Barkley JE. Peer victimization, social support and leisure-time physical activity in transgender and cisgender individuals. *Leis Loisir.* 2014;3–4:295–308.
 92. Alkner BA, Tesch PA. Knee extensor and plantar flexor muscle size and function following 90 days of bed rest with or without resistance exercise. *Eur J Appl Physiol.* 2004;93:294–305.
 93. Kvorning T, Andersen M, Brixen K, Madsen K. Suppression of endogenous testosterone production attenuates the response to strength training: a randomized, placebo-controlled, and blinded intervention study. *Am J Physiol Metab.* 2006;291:E1325–32.
 94. Chen Z, Zhang Y, Lu C, et al. Supervised physical training enhances muscle strength but not muscle mass in prostate cancer patients undergoing androgen deprivation therapy: a systematic review and meta-analysis. *Front Physiol.* 2019;10:843.
 95. Hanson ED, Sheaff AK, Sood S, et al. Strength training induces muscle hypertrophy and functional gains in black prostate cancer patients despite androgen deprivation therapy. *J Gerontol A Biol Sci Med Sci.* 2013;68(4):490–8.
 96. Gundersen K. Muscle memory and a new cellular model for muscle atrophy and hypertrophy. *J Exp Biol.* 2016;219:235–42.
 97. Bruusgaard JC, Johansen IB, Egner IM, et al. Myonuclei acquired by overload exercise precede hypertrophy and are not lost on detraining. *Proc Natl Acad Sci.* 2010;107:15111–6.
 98. Murach KA, Dungan CM, Dupont-Versteegden EE, et al. “Muscle Memory” not mediated by myonuclear number?: secondary analysis of human detraining data. *J Appl Physiol.* 2019;127(6):1814–6.
 99. Staron RS, Leonardi MJ, Karapondo DL, et al. Strength and skeletal muscle adaptations in heavy-resistance-trained women after detraining and retraining. *J Appl Physiol.* 1991;70:631–40.
 100. Hanson ED, Nelson AR, West DWD, et al. Attenuation of resting but not load-mediated protein synthesis in prostate cancer patients on androgen deprivation. *J Clin Endocrinol Metab.* 2017;102(3):1076–83.
 101. Roberts BM, Nuckols G, Krieger JW. Sex differences in resistance training. *J Strength Cond Res.* 2020;34(5):1448–60.
 102. Morton RW, Oikawa SY, Wavell CG, et al. Neither load nor systemic hormones determine resistance training-mediated hypertrophy or strength gains in resistance-trained young men. *J Appl Physiol.* 2016;121:129–38.
 103. Balshaw TG, Massey GJ, Maden-Wilkinson TM, et al. Changes in agonist neural drive, hypertrophy and pre-training strength all contribute to the individual strength gains after resistance training. *Eur J Appl Physiol.* 2017;117:631–40.
 104. Balshaw TG, Massey GJ, Maden-Wilkinson TM, et al. Neural adaptations after 4 years vs. 12 weeks of resistance training vs. untrained. *Scand J Med Sci Sports.* 2018;29(3):348–59.
 105. Maden-Wilkinson TM, Balshaw TG, Massey GJ, Folland JP. What makes long-term resistance-trained individuals so strong? A comparison of skeletal muscle morphology, architecture, and joint mechanics. *J Appl Physiol.* 2020;128:1000–11.
 106. Chidi-Ogbolu N, Baar K. Effect of estrogen on musculoskeletal performance and injury risk. *Front Physiol.* 2019;9:1834.
 107. Sørensen MB, Rosenfalck AM, Højgaard L, Ottesen B. Obesity and sarcopenia after menopause are reversed by sex hormone replacement therapy. *Obes Res.* 2001;9(10):622–6.
 108. Greising SM, Baltgalvis KA, Lowe DA, Warren GL. Hormone therapy and skeletal muscle strength: a meta-analysis. *J Gerontol A Biol Sci Med Sci.* 2009;64(10):1071–81.
 109. Svensson J, Movérare-Skrtic S, Windahl S, et al. Stimulation of both estrogen and androgen receptors maintains skeletal muscle mass in gonadectomized male mice but mainly via different pathways. *J Mol Endocrinol.* 2010;45(1):45–57.
 110. Kitajima Y, Ono Y. Estrogens maintain skeletal muscle and satellite cell functions. *J Endocrinol.* 2016;229(3):267–75.
 111. Elbers JMH, Asscheman H, Seidell JC, et al. Long-term testosterone administration increases visceral fat in female to male transsexuals. *J Clin Endocrinol Metab.* 1997;82(7):2044–7.

Fit Transitioning: When Can Transgender Airmen Fitness Test in Their Affirmed Gender?

*Maj Elvira Chiccarelli, Medical Corps, USAF, MD; Jay Aden, PhD; Dale Ahrendt, MD;
Lt Col Joshua Smalley, DO, Medical Corps, USAF*

ABSTRACT

Introduction:

Transgender individuals have served openly in the U.S. Military since 2016. Official policies for transgender service-members continue to evolve, including approaches to physical fitness testing of transgender servicemembers. There is a paucity of scientific data regarding the effects of gender affirming hormone therapy (GAHT) on athletic performance for the past 24 months of treatment. Identification of expected trends in performance during and after gender transition is essential to allow for the development of appropriate military policy regarding when to assess servicemembers' fitness by standards of their affirmed gender.

Materials and Methods:

We identified Department of the Air Force transgender patients using the Transgender Health Medical Evaluation Unit database and recorded dates of GAHT initiation through a retrospective chart review. We recorded performance values for the Air Force physical fitness test components 1 year before and up to 4 years after GAHT initiation. Performance measures were maximum sit-ups in 1 minute, push-ups in 1 minute, and 1.5-mile run time. Pre- and post-GAHT scores were compared using one-sample *T*-test to mean scores of Air Force-wide cisgender averages to assess for significant difference between affirmed transgender and cisgender airmen. We then performed the two one-sided test (TOST) procedure for equivalence with upper and lower bounds set at 1 SD from the means for cisgender airmen. Finally, using Z-scores, average transgender group scores were assigned a percentile rank with their respect to affirmed gender throughout the transition process.

Results:

Following initiation of GAHT, transgender males demonstrated statistically significant worse performance than cisgender males in all events until 3 years of GAHT. Their average scores would have attained a comfortable passing score within 1 year of GAHT. Transgender females' performance showed statistically significantly better performance than cisgender females until 2 years of GAHT in run times and 4 years in sit-up scores and remained superior in push-ups at the study's 4-year endpoint. TOST confirmed equivalence at all points where statistical difference was not demonstrated. Servicemembers approximate their pre-GAHT assigned gender percentile ranking in their affirmed gender in a manner consistent with hypothesis and TOST testing in the push-up event for both transgender males and females and in the 1.5-mile run event for transgender males.

Conclusions:

In a sample of Air Force adult transgender patients, athletic performance measures demonstrate variable rates of change depending on the patients' affirmed gender and differ by physical fitness test component. Based on this study, transgender females should begin to be assessed by the female standard no later than 2 years after starting GAHT, while transgender males could be assessed by their affirmed standard no earlier than 3 years after initiating GAHT.

INTRODUCTION

In 2016, U.S. DoD policy changed to allow open service by transgender servicemembers.^{1,2} Since then, many transgender individuals have served honorably in all DoD institutions

and proven their suitability for military service. The military health system has facilitated these policy changes by ensuring appropriate healthcare delivery for transgender members.

When patients transition from one gender to another, they are prescribed hormonal medication regimens to facilitate alignment with their affirmed gender, known as gender affirming hormone therapy (GAHT). For transgender males, this is a regimen of testosterone to facilitate masculinizing changes. For transgender females, this is typically medication to block natural testosterone in addition to taking estrogen to facilitate feminization. Many transgender patients also seek surgical procedures in support of their transition including facial plastic surgeries, mastectomy or breast augmentation, genital surgery, or voice surgery.^{3,4} The Department of the Air Force provides this care through centralized medical

Department of Adolescent Medicine, San Antonio Uniformed Services Health Education Consortium, San Antonio, TX 78234, United States

Preliminary findings from this research have been previously presented in short abstract form at the Society for Adolescent Health and Medicine Annual Meeting 2022.

The views expressed in this material are those of the authors and do not reflect the official policy or position of the U.S. Government, the DoD, or the Department of the Army.

doi:<https://doi.org/10.1093/milmed/usac320>

Published by Oxford University Press on behalf of the Association of Military Surgeons of the United States 2022. This work is written by (a) US Government employee(s) and is in the public domain in the US.

multidisciplinary care team known as the Transgender Health Medical Evaluation Unit (THMEU). This approach ensures access to care for transgender servicemembers, adherence to Air Force policies, and a standardized approach to transgender care.

DoD policy currently states that fitness standards applied to transgender members should align with their gender marker in the Defense Enrollment Eligibility Reporting System.^{5,6} Exceptions to policy (ETPs) are also available, but obtaining individual ETPs creates additional administrative burdens to command and individual airmen. The ongoing appropriate evolution of Air Force policy remains the ultimate standard in military operations.⁷

Under 2021 guidance, all transgender servicemembers starting hormone therapy may seek a fitness exemption for a period of 6 months with re-evaluation every 6 months.⁵ These policies, while flexible, lend unnecessary confusion and paperwork to the already complex transition process and are based on scarce evidence of the true impact of hormone therapy on a member's ability to perform their fitness assessment. They also add the concern that a member's overall health and conditioning may be impacted if they are not being held to any physical fitness test (PFT) standard at all for that period.⁷ It is prudent for policymakers to ensure that servicemembers have a gender marker change when they have fully transitioned but also at the time that they are fit to pass the fitness assessment in their affirmed gender. The right balance with this policy will maintain maximum force fitness with minimal unnecessary medical reviews and waivers for a transgender patient who is fit to serve.

Transgender athletics research thus far has focused on documenting physiological changes. Transgender males improve in most aspects of physical performance on GAHT, while transgender females experience deteriorating performance.⁸ Transgender females experience increases in fat mass on GAHT.⁹ While transgender males experience gains in lean mass, transgender females will have less lean body mass after 4 years of GAHT.¹⁰ There are also changes in muscle cross-sectional area, with transgender males making gains and transgender females demonstrating losses.¹¹ Maximal strength tests show mixed results depending on the modality used.^{8,11,12} It is impossible to say how these changes translate to real-life athletic performance over time given the lack of research on this topic. The precise timing of when performance approximates that of an individual's affirmed, rather than assigned, gender is poorly understood.^{13–15} The military's fitness testing programs offer an opportunity to better understand this because of the standardized process through which it is administered at specific intervals and the advantage of a cisgender comparison group.

This article expands on previously published data by Roberts et al. which documented a cohort of 75 transgender airmen's fitness testing following up to 2 years of GAHT.¹ The focus of this previous analysis was to examine when transgender athletes might gain (in the case of transgender males)

or lose (in the case of transgender females) a competitive advantage relative to the field of their affirmed gender during the follow-up period. Using simple hypothesis testing, they found that transgender males retained no advantage after 1 year of GAHT compared to cisgender males and transgender females retained a significant athletic advantage compared to cisgender females after 1 year of GAHT.

With continuing follow-up, we were able to establish a larger cohort of 374 patients followed for up to 4 years of GAHT to discuss in this article. Our focus is not to discuss competitive advantage but to address the question of unified and evidence-based fitness testing policy for a growing number of transgender servicemembers. We seek to provide evidence to guide commanders and policymakers about transgender airmen's fitness assessments during gender transition. This is a fundamentally different question as military fitness testing aims to set a standard above which individuals demonstrate basic physical performance capabilities and maximize medical readiness, rather than quantifying the ceiling of human performance in a cohort.

Additionally, readers will note that the resulting performance timelines when servicemembers initiate GAHT differ between transitioning genders. There are several reasons for this. First, the parameters between genders differ in that transgender females should be assessed by the female standard once they are likely to fail the male standard including the failure of any single event, whereas transgender males should be assessed by the male standard once they are likely to be able to pass that standard.⁷ Second, limited prospective evidence has shown that advantageous increases to muscle mass and hemoglobin are mostly induced in the first 12 months of testosterone initiation for transgender males, whereas the time course of reduction in muscle bulk among transgender females has shown progressive loss for up to 36 months.^{13–15}

METHODS

For this study, we identified Air Force transgender patients using the Air Force's centralized THMEU case management database. GAHT initiation date was recorded, as well as scores for the Air Force PFT (AFPFT) components in the year before and up to 4 years following GAHT initiation. Scores were categorized by year after GAHT initiation. Additional data gathered for this study included the servicemember's military rank and duty status, GAHT regimen, as well as the dates of any gender-affirming surgical procedures performed during the study's follow-up period.

The AFPFT performance measures at the time of the study were maximum number of push-ups and maximum number of sit-ups in 1 minute and a 1.5-mile run time.⁶ PFT tests are administered in a standardized fashion at the individual unit level across the Air Force. Testing is required biannually for performers who score from 75 to 90 and annually in the case of an "excellent" score over 90. Failing scores require retesting in 3 months. Servicemembers may receive waivers from their physicians not to test

TABLE I. Mean Scores by Component with Estimate Total Test Scores

Transgender males						
	Male cisgender	Pre-GAHT	1-year GAHT	2-year GAHT	3-year GAHT	4-year GAHT
Number of scores		292	93	50	17	17
Number of subjects		131	63	46	25	5
Push-ups (SD)	54 (9)	37.5 (9) ^a	45.5(13)	48.4 (14)	56.6 (9)	62.1 (14)
Sit-ups (SD)	52 (8)	50 (8)	54.2 (7)	54.4 (8)	58.5 (10)	59 (8)
1.5-mile run (SD)	11:59 (1:33)	13:50 (2:08)	13:14 (2:15)	12:48 (1:48)	11:29 (1:39)	12:33 (1:02)
Total score, male standard	90.9	80.2	87.2	89.5	93.9	94
Total score, female standard	97.5	93	95.6	96.5	98.5	97
Transgender females						
	Female cisgender	Pre-GAHT	1-year GAHT	2-year GAHT	3-year GAHT	4-year GAHT
Number of scores		456	106	42	26	11
Number of subjects		223	93	61	40	15
Push-ups (SD)	30 (10)	49.9 (10)	43.4 (10)	39.3 (9)	38.5 (13)	35.3 (7)
Sit-ups (SD)	41 (8)	52.6 (7)	49.4 (8)	48.1 (8)	45.6 (10)	44.4 (10)
1.5-mile run (SD)	14:36 (1:51)	12:00 (4:38) ^a	13:15 (1:52)	13:51 (1:53)	13:51 (3:12)	14:34 (2:13)
Total score, female standard	86	97.5	94.2	92.4	91	70.6
Total score, male standard	66	90.1	83.5	80.4	78	54

This table shows mean scores of each component at each phase of GAHT with standard deviations, as well as aggregate scores from these means calculated using the 2022 AFPFT standards for airmen aged 25-29. Bolded scores denote that no statistical difference was noted when compared with affirmed cisgender means using one-tailed *T*-test with $P < .05$.

^adenote those scores that were considered non-equivalent to affirmed cisgender means by TOST analysis with upper and lower bounds set at 1 SD around the mean. The number of scores and number of individuals tested is analyzed is also noted at each endpoint. When multiple scores were attained in each period they were averaged for analysis. A score of 75 is a passing score.

specific components of the fitness test due to injury. We calculated aggregate scores using scoring tables released for testing on January 1, 2022, for ages 25-29 (Table I).⁷

Mean pre- and post-GAHT scores were separated by affirmed gender and categorized by year after initiation. If multiple scores were available in a given year, they were averaged for analysis. These were then compared by one-sample *T*-test to mean scores of Air Force-wide cisgender averages for servicemembers aged 20-30 to demonstrate where no significant difference could be found between affirmed transgender and cisgender airmen.¹⁶ This analysis evaluated the data sets for the prevalence or absence of a statistical difference—and where a difference is not found—it is not appropriate to conclude that equivalence between score groups exists.¹⁷

Additional analysis for equivalence was performed using the two one-sided test (TOST) procedure with upper and lower bounds for comparison set at 1 SD from the mean for cisgender average scores to assess for equivalence between affirmed gender and cisgender scores to capture the middle 50% of cisgender performances. This type of statistical analysis allows us to appropriately reject the presence of a statistically significant effect of difference between groups. The analysis allows us to set upper and lower equivalence bounds based on the smallest effect size of interest, which are chosen as above to adequately represent 50% of the comparison sample size and provide a confirmatory test for initial hypothesis testing (Table I).¹⁷

Finally, to illustrate progression with respect to peer airmen, we utilized a Z-score calculation using the normally

distributed Air Force-wide cisgender averages to identify the percentile ranking of the transgender mean among those of their assigned gender before GAHT. This percentile is then compared with a percentile ranking among those in their affirmed gender at different time points following the initiation of GAHT (Fig. 3).

RESULTS

The sample included 374 patients, 146 transgender males and 228 transgender females, with a mean age of 26 at GAHT initiation (Supplemental Table S1). Twenty-eight patients completed follow-up to 4 years of GAHT (Table I, Supplemental Table S1).

Transgender Males

Before GAHT, transgender males demonstrated better performance compared to cisgender females in push-ups, sit-ups, and run times. Compared with cisgender males, they performed inferiorly in all events. Following initiation of GAHT, transgender men showed no statistical difference from cisgender men in the sit-up event at 1 year while push-ups and run times took 3 years to cease demonstrating statistically significant difference (Table I). This is demonstrated graphically in Fig. 1.

For percentile rankings, transgender males approach their pre-GAHT percentile ranking among cisgender females in their affirmed gender in a time pattern consistent with hypothesis testing in the push-up and 1.5-mile run time (Fig. 3). This can be appreciated as these airmen reach their pre-GAHT

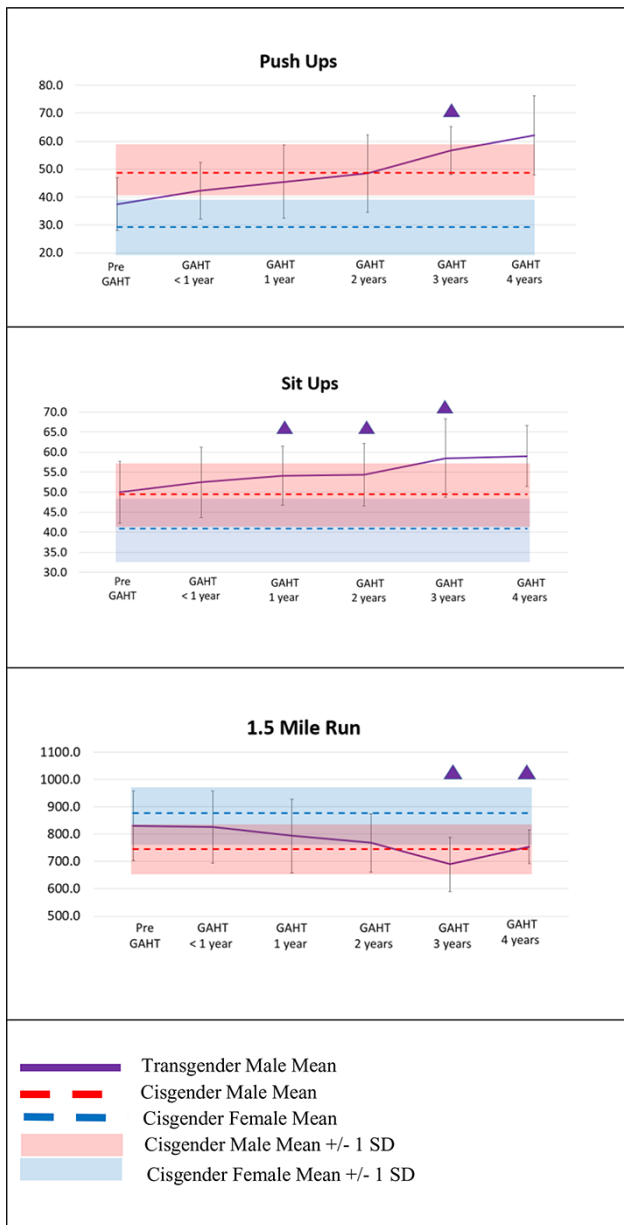


FIGURE 1. Transgender male performance after GAHT initiation.

ranking at the same point as hypothesis testing ceases to demonstrate a difference between transgender and cisgender athletes in a particular event. In the sit-up event, the analogous percentile was reached 2 years after hypothesis testing initially failed to demonstrate a significant difference.

Using mean PFT component scores, we calculated the hypothetical average score on an entire test by each gender standard (Table I). Transgender males are high athletic performers before GAHT, and their hypothetical average score before therapy was a very low passing score in their affirmed gender. This includes no individual component failures by the male standards. There were increases in performance thereafter.



FIGURE 2. Transgender female performance after GAHT initiation.

For transgender males, results of TOST analysis showed non-equivalence to cisgender females only in the push-up event before GAHT because of superior performance.

Transgender Females

Before GAHT, transgender females demonstrated poorer performance in push-ups compared to cisgender males but were not significantly different in sit-ups or run times. Compared with cisgender females, they demonstrated better performance in all events. Following initiation of GAHT, transgender females performed significantly better than cisgender females at 1 year in all tested events (Table I). Mean performances over time are noted in Fig. 2.

Transgender female's performance showed almost no statistical difference from cisgender females at 4 years of GAHT

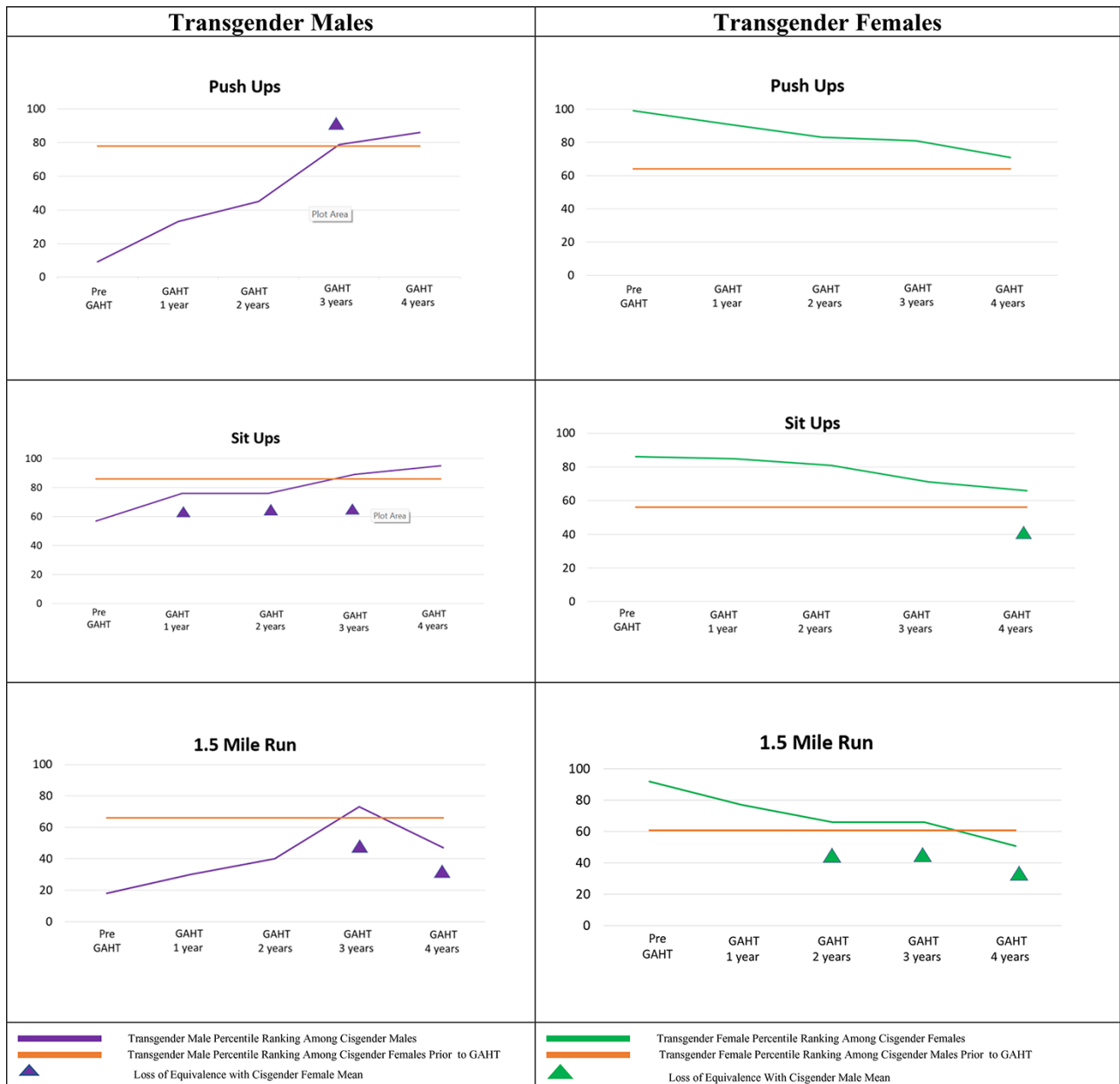


FIGURE 3. Transgender percentile ranked performance.

in the sit-up event. They did continue demonstrate statistical superiority in maximum push-ups during the study's 4-year follow-up period. In run times, transgender females were no longer statistically different from cisgender females after 2 years of hormone therapy (Table I).

With respect to overall PFT scores, transgender females demonstrate an immediate decline in performance at the initiation of GAHT and demonstrate a very low passing score on the male standard after 2 years of therapy. This includes no individual component failures by the female standards. Scores and performance continue to decline thereafter (Table I, Fig. 2).

For transgender females, results of TOST analysis showed non-equivalence with cisgender females only in the run event before GAHT, demonstrating superior performance. In all other events and time points, transgender females demonstrated equivalence with cisgender females.

When assessing percentile ranking, transgender females do not arrive at their pre-GAHT cisgender percentile ranking in the push-up event, and this is consistent with hypothesis testing. They also do not arrive at their ranking in the sit-up event, and this differs from hypothesis testing which shows no significant difference between cisgender and transgender athletes at the 4-year mark. In the 1.5-mile run event, transgender

females achieved their pre-GAHT ranking only after 4 years of therapy, which is a later time point compared to hypothesis testing.

DISCUSSION

Statistical Methods: Establishment of Equivalence with Affirmed Gender

The combined methods of hypothesis and equivalence testing as noted above create a superior analytical model to demonstrate performance equivalence where it may exist between two groups that goes beyond hypothesis testing. As noted in Figs. 1-2, performance scores for 50% of the cisgender populations show overlap in many events. In our study, the combination of null hypothesis testing with equivalence testing can help clarify incremental changes in performance when transgender athletes are compared with both their assigned and transitioning gender groups.¹⁷

Where transgender athletes are found to be statistically equivalent to as well as not statistically different from the performance of their affirmed gender, we can confidently state that transgender performance has approximated that of the cisgender group. This occurs for transgender males in the sit-up event at 1 year, run event, and push-up events at 3 years of GAHT and for transgender females in the 1.5-mile run event at 2 years of therapy and sit-ups at 4 years. Transgender females did not demonstrate equivalence in the push-up event during the study's follow-up period. Further consideration must be given with respect to total PFT scoring to determine fitness testing timelines.

Additional confirmatory analysis using percentile rankings is demonstrated in Fig. 3. This allows another aspect of consideration for when performance was equivalent as an assessment of percentile ranking among an affirmed gender's peers. In some events, this analysis acts as confirmatory to the previous tests: both push-up events and the transgender male run time. Yet, in other events, we note that percentile rank equivalence is achieved more slowly than hypothesis testing.

Transgender Males

Transgender males showed improvements in performance across all PFT events after initiation of GAHT. This is an expected result given the known anabolic and performance-enhancing effects of testosterone.^{13,14,18} Of the 146 transgender males in our study, the most common regimen utilized was injected testosterone cypionate by 106 participants, injected testosterone ethanoate by three participants, with the other 37 utilizing topical testosterone gel or patch. We surmise that this may be a higher rate of topical testosterone use than the civilian population, as this formulation is more costly, but this regimen is preferred for servicemembers to remain deployable. We also note that this group had a high rate of gender-affirming surgical procedures during the study follow-up, with mastectomy being the most performed procedure in 65 participants. This may slow gains in performance over time

as individuals are unable to complete training regimens or fitness tests while recovering from surgery.

An important finding is also that transgender males have a high level of fitness with respect to cisgender females before transition; i.e., they perform better in all events than cisgender females before transition. However, the model does suggest that most transgender males undergoing in-service transition should be capable of comfortably passing the male standard PFT after 3 years of masculinizing hormone therapy based on demonstrating a loss of significant difference with cisgender males in all events and indicating equivalence with cisgender males in two of three events. Aggregate scores noted in Table I comfortably support this conclusion. Furthermore, the percentile rankings wherein transgender males are likely to attain similar ranking relative to their peers within 3 years support this conclusion in the push-up and run events (Fig. 3).

Transgender Females

Transgender females demonstrate declining performance following initiation of GAHT. This is consistent with previous studies documenting loss of muscle mass and aerobic endurance.^{8,15} However, the timing of individual changes to different PFT components illustrates the heterogeneous nature of changes that transgender females undergo over time.

At the 2-year mark, they cease demonstrating statistically different performance to females in the 1.5-mile run event—a marker for aerobic fitness. After 4 years, the sit-up event also lost significant difference as a marker of core strength and endurance, around when muscle area changes are maximized.^{11,15} In this study, push-ups never stopped demonstrating a significant difference. This may illustrate innate anthropometric changes that occur because of assigned gender puberty such as larger upper body muscle mass and smaller lower body fat mass. These may change more slowly or not at all. The percentile ranking model is confirmatory in this event.

Transgender females only approximate cisgender female performance in two of three events, the run and the sit-up event, at 4 years. Percentile ranking adaptation lags in both of these events compared with hypothesis testing (Fig. 3). However, declines in performance following GAHT initiation prevent transgender women from obtaining a passing score on the male standard throughout their transition (Table I). A failure in any single event results in a failure of the entire test. Transgender females are likely to fail the male PFT standard around 2 years of therapy, suggesting a fitness ETP or change of gender marker to ensure use of female standards should occur by then.

Military-Specific Considerations

There are a few additional considerations unique to this data set. First, we recognize that all fitness testing in the study was completed before scoring standard changes in 2022. These changes included lower minimum component and total scores, smaller age group brackets, higher point values for similar

performances, as well as the option to complete alternative testing components.⁶ It is difficult to say how these changes would motivate performance on the individual level. We recognize that we have used a previous performance compared to a current metric and the effect of this change is unknown.

In competitive athletics, some have suggested creating a separate transgender category, and the THMEU has considered this possibility for transitioning servicemembers. There are several flaws with this model. First, transition timelines differ significantly between individual depending on the number and type of surgical procedures required for transition. These surgeries also impact a servicemember's ability to complete fitness testing during their transition. There are not yet enough data to create normative scores for transgender patients. Finally, the current ETP model allows commanders of fitness-exempted servicemembers to keep a close eye on their servicemembers during the transition process and provide optimal support.

Limitations

It is important to recognize the limitations of this study and analysis. First, this analysis does not contribute to the ongoing discussion of the inclusion criteria for transgender athletes in cisgender sporting competition, and that is not the aim of this paper. The question of retained advantage relative to the field in transitioning transgender female athletes is an exceedingly difficult one to answer with available statistical data, as demonstrated by the intricacy of results in this article regarding transgender females' fitness changes over time.

This analysis, like many in the transgender literature, suffers from many methodological issues including a small sample size and uncontrolled for lifestyle variables that could affect physical fitness such as different exercise regimens, body mass index, and access to fitness equipment during Coronavirus lockdowns of 2020. Recent literature regarding transgender individuals' fitness practices shows mixed factors contributing consistent physical training including an overall lack of trans-inclusive spaces but also individual's desire for gender-specific body changes that can be achieved in the gym, and these criteria should be considered in future analyses without specific training programs.¹⁹

In this design, there is also concern for survivorship bias. Most of our subjects did not complete 4-year follow-up because of recent start dates of GAHT, but many of them had also left the military before receiving 4 years of GAHT. We are unable to account for the performance of dropout subjects because they were no longer in the military or receiving care within the military health system. This might skew our data in several ways. For example, perhaps, individuals who continue military service display a higher level of physical fitness or have better access to healthcare than those who leave. Our data are unable to distinguish between the career servicemember who might have more external motivation to stay fit versus the young airman wanting to separate after an initial enlistment. Number of scores analyzed at each data

point is noted in Table I. Servicemembers with poor scores are also tested more frequently, but data points achieved within a single analysis timeframe were averaged for analysis.⁷

Improvements to a future design might include a longitudinal control group without GAHT or more standardized GAHT and exercise regimens, both of which would contribute well to a randomized controlled trial model but whose methods may be unethical or unfeasible.

CONCLUSIONS

As transgender individuals receive more opportunities to serve, policy development regarding fitness testing should consider their unique physiology. Commanders can advocate for their transgender troops at the unit level as well. Currently, the process of obtaining individual fitness ETPs can be burdensome and a unified policy would better support both troops and command. To this end, our data support that transgender males should be held to the male standard no earlier than 3 years after GAHT initiation and transgender females should be afforded the female standard no later 2 years after GAHT initiation.

ACKNOWLEDGMENTS

None.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *Military Medicine* online.

FUNDING

This study received no funding.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

CLINICAL TRIAL REGISTRATION

None.

INSTITUTIONAL REVIEW BOARD

This study was approved by the Wilford Hall Ambulatory Surgical Center's Institutional Review Board.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

Not applicable.

DATA AVAILABILITY

The data that support the findings of this study are available on request from the corresponding author.

INSTITUTIONAL CLEARANCE

Institutional clearance approved.

REFERENCES

1. Roberts TA, Smalley J, Ahrendt D: Effect of gender affirming hormones on athletic performance in transwomen and transmen: implications for sporting organisations and legislators. *Br J Sports Med* 2021; 55(11): 577–83. [10.1136/bjsports-2020-102329](https://doi.org/10.1136/bjsports-2020-102329).

2. Office of the Undersecretary of Defense for Personnel and Readiness: *DoD Instruction 1300.28: In-Service Transition for Transgender Servicemembers*. United States Department of Defense; 2016.
3. World Professional Association for Transgender Health. 2012. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People [7th Version]. Available at <https://www.wpath.org/publications/soc>; accessed 1 August, 2022.
4. Hembree WC, Cohen-Kettenis PT, Gooren L, et al: Endocrine treatment of gender-dysphoric/gender-incongruent persons: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2017; 102(11): 3869–903. [10.1210/je.2017-01658](https://doi.org/10.1210/je.2017-01658).
5. Office of the Undersecretary of Defense for Personnel and Readiness: *DoD Instruction 1300.28: In-Service Transition for Transgender Servicemembers*. United States Department of Defense; 2021.
6. The Secretary of the Air Force: AFPM2016-36-101: Air Force Policy Memorandum for In-Service Transition for Airmen Identifying as Transgender. United States Air Force; 2016.
7. The Secretary of the Air Force: *DAFMAN 36-2905: Department of the Air Force Physical Fitness Program*. United States Air Force; 2022.
8. Harper J, O'Donnell E, Sorouri Khorashad B, et al: How does hormone transition in transgender women change body composition, muscle strength and haemoglobin? Systematic review with a focus on the implications for sport participation. *Br J Sports Med* 2021; 55(15): 865–72. [10.1136/bjsports-2020-103106](https://doi.org/10.1136/bjsports-2020-103106).
9. Klaver KM, Daan VV, Christel DB, et al: Change in visceral fat and total body fat and the effect on cardiometabolic risk factors during transgender hormone therapy. *J Clin Endocrinol Metab* 2022; 107(1): e153–64. [10.1210/clinem/dgab616](https://doi.org/10.1210/clinem/dgab616).
10. Klaver M, de Blok CJM, Wiepjes CM, et al: Changes in regional body fat, lean body mass and body shape in trans persons using cross-sex hormonal therapy: results from a multicenter prospective study. *Eur J Endocrinol* 2018; 178(2): 163–71. [10.1530/EJE-17-0496](https://doi.org/10.1530/EJE-17-0496).
11. Wiik A, Lundberg TR, Rullman E, et al: Muscle strength, size, and composition following 12 months of gender-affirming treatment in transgender individuals. *J Clin Endocrinol Metab* 2020; 105(3): dgz247. [10.1210/clinem/dgz247](https://doi.org/10.1210/clinem/dgz247).
12. Alvares LAM, Santos MR, Souza FR, et al: Muscle strength in transgender women after long-term hormone therapy: a cross-sectional study. *J Endocr Soc* 2021; 5(Suppl 1): A792–3. [10.1210/jendso/bvab048](https://doi.org/10.1210/jendso/bvab048).1612.
13. Hilton EN, Lundberg TR: Transgender women in the female category of sport: perspectives on testosterone suppression and performance advantage. *Sports Med* 2021; 51(2): 199–214. [10.1007/s40279-020-01389-3](https://doi.org/10.1007/s40279-020-01389-3).
14. Handelsman DJ, Hirschberg AL, Bermon S: Circulating testosterone as the hormonal basis of sex differences in athletic performance. *Endocr Rev* 2018 39(5): 803–29. [10.1210/er.2018-00020](https://doi.org/10.1210/er.2018-00020).
15. Gooren LJ, Bunck MC: Transsexuals and competitive sports. *Eur J Endocrinol* 2004; 151(4): 425–9. [10.1530/eje.0.1510425](https://doi.org/10.1530/eje.0.1510425).
16. Griffith JR: The Air Force fitness test: creating new fitness assessment charts using waist to height ratios. Theses and Dissertations. Air Force Institute of Technology; 2017.
17. Lakens D: Equivalence tests: a practical primer for t tests, correlations, and meta-analyses. *Soc Psychol Personal Sci* 2017; 8(4): 355–62. [10.1177/1948550617697177](https://doi.org/10.1177/1948550617697177).
18. Bardin CW: The anabolic action of testosterone *N Engl J Med* 1996 335(1): 52. [10.1056/NEJM199607043350111](https://doi.org/10.1056/NEJM199607043350111).
19. Oliveira J, Frontini R, Jacinto M, Antunes R: Barriers and motives for physical activity and sports practice among trans people: a systematic review. *Sustainability* 2022; 14(9): 5295. [10.3390/su14095295](https://doi.org/10.3390/su14095295).



E-Alliance

*Centre de recherche
pour l'équité des
genres+ en sport*

*Research hub for
gender+ equity
in sport*

Transgender Women Athletes and Elite Sport: A Scientific Review

Table of Contents

<i>Executive Summary</i>	1
Methods	3
Key Biomedical Findings	4
Key Sociocultural Findings	6
Conclusion	9
<i>Introduction</i>	11
Methods	12
The Structure of This Report	13
<i>Biological Considerations</i>	15
Sedentary Adults Versus Elite Athletes	17
Population-Level Comparison Groups	18
Erroneous Information and Flawed Measurement Techniques	21
Testosterone Effects on the Body	22
Effects of Testosterone Suppression for Trans Women	23
Evidence of Other Biological Markers	27
<i>Sociocultural Context and Framing of Trans Women’s Sport Participation</i>	31
History of Gender Categorization in Elite Sport	32
Continuing a Long History of Exclusion: The Women’s Category of Sport	34
Social Factors in Keeping Women’s Sport Inferior to Men’s	35
Discrimination and Violence Against Trans Women	36
Myths About Trans Women Circulated in Sport	37
Experiences of Systematic Discrimination in Sport	38
Knowledge Production and Impact	38
Approaches to Balancing Biological and Sociological Considerations	39
<i>Conclusion</i>	40
<i>Bibliography</i>	43
<i>Appendix A: Detailed Tables of Reviewed Academic and Grey Literature</i>	53
Academic Literature	53
Grey Literature	79
<i>Appendix B: Scoping Review Yield</i>	83
<i>Appendix C: List of Some Canadian Organizations Who Have Trans Inclusion Policies at Competitive/Elite Levels</i>	84



Executive Summary

Transgender Women Athletes and Elite Sport: A Scientific Review is an in-depth review of scientific literature on transgender athlete participation in competitive sport. The inclusion criteria for this report were research articles published in the English language between 2011 and 2021 inclusive. Only peer-reviewed articles or syntheses of academic literature (e.g., meta-analyses) in reputable academic journals were included. Grey literature, or non-academic literature, was included if it provided a summary of empirical data or if it described rules currently in place worldwide to include/exclude trans athletes. The resulting report is divided into two sections reflecting the primary perspectives by which the question of trans inclusion has been addressed - one that encompasses biomedical studies and a second that encompasses sociocultural studies. While there are questions of inclusion for non-binary and intersex athletes, this report focused on the population of trans women athletes in the context of elite sport.

The biomedical perspective views the physiology of trans women's bodies as the source of perceived unfairness, with medicalized interventions (such as estrogen supplementation and testosterone suppression) as the resolution. More specifically, this perspective holds that sexual dimorphism between those assigned male at birth (AMAB) and those assigned female at birth (AFAB) is the reason for athletic differences. Testosterone measures and boundaries are typically chosen as defining characteristics of manhood and womanhood in the context of sport and are used as the predominant marker to predict and level sex-related athletic advantage and the means for inclusion criteria.

The research findings in the biomedical area are inconclusive. Studies which make conclusions on pre- and post-hormone replacement therapy (HRT) advantage held by trans women athletes have used either cis men or sedentary trans women as proxies for elite trans women athletes. These group references are not only inappropriate for the context but produce conclusions that cannot be applied to elite trans women athletes. Further, there is little scientific understanding about the attributes or properties of HRT, namely testosterone suppression and estrogen supplementation, on the physiology and athletic ability of trans women athletes. This ignores the potential for estrogen supplementation to reduce Lean Body Mass (LBM), and for testosterone suppression to produce holistic health disadvantages.

The second perspective is a sociocultural one. Researchers in the sociocultural field of study argue that social factors contribute to performance advantages to a far greater extent than does testosterone and that assessing testosterone levels is another way to perpetuate the long history of policing women's bodies in sport. Researchers highlight the many social factors that contribute to differences in athletic performance, including, for example: discriminations, disparate resource allocations, inequities, and violence against women in sport in the forms of sexism and sexual violence in sport contexts, arbitrary differences in rules and equipment between men's and women's sport, as well as histories of barring women from certain sports. This body of work also highlights the foundational histories of anti-Blackness, anti-Global Southness, and misogyny which maintain inequities in sport. Arguments are made that the use of testosterone to exclude trans women athletes represents another phase in the long history of policing women's bodies in sport. Once women were allowed into competitive sport in the early 20th century, those whose athletic ability was on par with their male counterparts, or whose physique was too manly, were disqualified from competition as deviants of the gender order. Through the history of women's sport, female athletes have been exposed to intrusive gender verification processes including medical inspection of external genitalia and chromosome testing that produced many false positives and had catastrophic impacts on athletes' careers. The current climate is one that focuses on testosterone levels of those athletes whose gender is deemed to be 'suspicious.'

In the context of sport policy development, biomedical and physiological data have to-date been privileged over other aspects such as social factors. Many policies cite biomedical studies to explain their conditions of inclusion, or their exclusion.

Methods

The findings of this report result from a thorough literature scan in May/June 2021. Academic (i.e., peer-reviewed primary or synthesized secondary research journal articles) and grey (not peer reviewed, reports, policy documents, do not follow a scientific process) literature were included.

Inclusion Criteria:

- Published between **2011** and **2021**;
- English language;
- **Primary research** or **syntheses** (e.g., meta-analyses, reviews);
- **Grey literature** was included if it was a **final evaluation** or report on empirical data;
- **Grey literature** was included if it was about **rules currently in place** worldwide for the inclusion/exclusion of trans women in high-performance sport.

Excluded: discussion articles, opinion pieces, or commentaries not presenting empirical or theoretical research.

Key Biomedical Findings

1. Biological data are severely limited, and often methodologically flawed.

- Most studies do not adequately adjust for factors such as height or lean body mass;
- Almost no studies examining the effects of testosterone suppression on trans women do so among trained athletes;
- Most studies on the effects of testosterone on sport performance involve examination of individuals who use performance-enhancing drugs.

2. There is limited evidence regarding the impact of testosterone suppression (through, for example, gender-affirming hormone therapy or surgical gonad removal) on transgender women athletes' performance.

- Most of these studies had small sample sizes, imperfect measurement techniques, poor reference group comparisons, and studied a sedentary/non-athletic/untrained sample population;
- Some significant studies used misleading data sources and actively ignored contradictory evidence.

3. Available evidence indicates trans women who have undergone testosterone suppression have no clear biological advantages over cis women in elite sport.

- The higher levels of red blood cell count experienced by cis men is removed within the first four months of testosterone suppression;
- There is no basis for athletic advantage conferred by bone size or density, other than advantages achieved through height. Elite athletes tend to have higher than average height across genders, and above-average height is not currently classified as an athletic advantage requiring regulation;
- On average, trans women who are pre-testosterone suppression still have lower Lean Body Mass (LBM), Cross Section Area (CSA), and strength than cis males. This indicates that the performance benefit experienced by these individuals cannot be generalized by examining cis male athletes;
- Non-athletic trans women experience significant reduction in LBM, CSA, and strength loss within 12 months of hormonal suppression. It is important to note that this 12-month threshold is arbitrarily defined, and no significant studies examine the rate of LBM, CSA or strength reduction over time;
- When adjusting for height and fat mass, LBM, CSA, and strength after 12 months of testosterone suppression, trans women still retained statistically higher levels than sedentary cis women. However, this difference is well within the normal distribution of LBM, CSA, and strength for cis women (Jassen et al., 2000);
- LBM, CSA, and strength loss continues for trans women after the 12-month initial testosterone suppression;
- The limited available evidence examining the effect of testosterone suppression as it directly affects trans women's athletic performance showed no athletic advantage exists after one year of testosterone suppression (Harper, 2015; Roberts et al., 2020; Harper, 2020);
- Post gonad removal, many trans women experience testosterone levels far below that of pre-menopausal cis women.

Key Sociocultural Findings

1. Biomedical studies are overvalued in sports policies in comparison to social sciences studies.

- The literature on trans sport policies, their implementation, people who write them and apply them, consequences for athletes, and the debates they frame is constitutive of the social hierarchy of knowledge, within which some sciences are discredited to the benefit of others;
- Excluding certain types of knowledge from the restricted definition of 'scientific' makes it possible for sport governing bodies to obscure the power relations at play in the creation, maintenance, and legitimization of regulations;
- There are troubling links between some researchers, sport organizations, and third organizations with anti-trans agenda;
- Some sport organizations use science strategically, drawing solely and uncritically on data which appears to support their claims;
- Only certain biomedical factors are policed under a mandate of 'fairness' in elite sport, despite strong evidence that financial material resources (such as access to infrastructure and equipment, nutrition, time to train, higher salaries) are associated with advantage in sport.

2. Policies that impact trans women's participation in elite sport are the continuation of a long history of exclusion of women from competitive sport – an exclusion that resulted in the introduction of a 'women's' category of sport in the first place.

- Since the early 20th century, elite sport policies worked to pathologize and control women's bodies and enforce dimorphic sex. There is, however, a significant overlap in all sexual characteristics. 'Male' and 'female' are not mutually exclusive categories and should not be treated as such;

- Many social factors continue to keep women's sport less valued than men's: fewer resources, lack of access to sport spaces or equipment, fewer coaches and teams, sexist discrimination, having to quit sports due to sexual violence, lesbophobia, classism, racism and/or transphobia;
- There are examples of competitive sport events that have changed sporting structures or put restrictions on particular athletes as women began to excel;
- The literature largely ignores areas where cis women have an athletic advantage over cis men (long-distance swimming, for example), as well as the ways in which trans women's participation in elite sport elevates sport for all women.

3. Many trans “inclusion” sport policies use arbitrary bounds that are not evidence based.

- Elite sport federations often apply none, one, two, three, or more of the following criteria based mostly on their own perspectives / ideologies: gender declaration (gender marker, letter, or just during registration), stable gender identification of two years or four years, hormonal level (not specified, 5 nmol / L or 10 nmol / L), request for Therapeutic Use Exemption (TUE), physical and morphological criteria, medical file or medical appointment;
- Many sport organizations circulate myths about trans women that are transphobic, harmful, and violent. For example, that trans women will overwhelm women's sport, when trans women are in fact under-represented in sport and especially elite sport; or that trans women are cis men in women's clothes, a dangerous misunderstanding of trans women's identities and experiences directly linked to trans women's decreased safety especially in such highly gendered spaces as sport.

4.

Cissexism, transphobia, transmisogyny and overlapping systems of oppression need to be recognized and addressed for trans women to participate in elite sport.

- Despite unavailability of the exact prevalence of trans women in the population, we can reliably conclude trans women are systematically underrepresented in elite athletics both in terms of participation and results;
- On a population level, trans women experience living conditions which are the result of downward social mobility and discrimination, including restricted access to and/or experiences of discrimination in vital spaces (i.e., housing, health care, work, public space including sports facilities);
- In qualitative studies, trans women have reported facing significant barriers to returning to sport after they transition;
- Trans women are not a monolith. Racism, classism, ableism, and overlapping systems of oppression must be addressed for trans women to be able to participate in elite sport. Trans women's diversity is also reflected in their transition journeys – diverse incomes, access, and desires affect in what medical gender affirmation processes a trans woman might participate and at what stage in her life course.

Conclusion

There is no firm basis available in evidence to indicate that trans women have a consistent and measurable overall performance benefit after 12 months of testosterone suppression. While an advantage in terms of Lean Body Mass (LBM), Cross Section Area (CSA) and strength may persist statistically after 12 months, there is no evidence that this translates to any performance advantage as compared to elite cis-women athletes of similar size and height. This is contrasted with other changes, such as hemoglobin (HG), which normalize within the cis women range within four months of starting testosterone suppression. For pre-suppression trans women it is currently unknown when during the first 12 months of suppression that any advantage may persist. The duration of any such advantage is likely highly dependent on the individual's pre-suppression LBM which, in turn varies, greatly and is highly impacted by societal factors and individual circumstance.

Any policy developed should carefully consider the current lack of participation of trans athletes (in many sport organizations there is a complete absence or outright exclusion) and balance the value of fairness with inclusion. Policies should be crafted in ways which clarify and highlight administrators' duty to prevent and actively attend to barriers, carefully considering the administration of any such policy in ways which do not further discourage participation through the creation of unnecessary barriers, or unnecessarily infringe on the individual's privacy (including their right to not openly identify as transgender). Additionally, these individuals should not be excluded during any non-competition periods from participating with a team through training, exhibition matches or social activities.

Further research is needed to ensure a foundation in sound evidence, a foundation which does not currently exist. Specifically, additional research is needed with sample populations of trained trans women and trained cis women as a comparison group, as current studies tend to focus on sedentary populations. These studies ought to include large populations, make comparisons with equivalent population groups (i.e., adjust for height and weight), and avoid using measures which are empirically proven to be unreliable outside of population-level analysis (i.e., handgrip strength).

Political, historical, and sociocultural contexts must also be intentionally considered in implementation, the framing of 'trans inclusion' policies, defining 'fairness' in sport, and participation in the hierarchy of knowledge and scientific processes.



Introduction

The Canadian Centre for Ethics in Sport (CCES) commissioned this literature review with a mandate to review the scientific and grey literature regarding trans women athletes' participation in elite or otherwise high-performance sport (herein shortened to 'elite sport'), with a special focus on the state of scientific literature around the science of testosterone and its impact on sport performance.



There is a triple bind for this research project: part of the challenge of this review is in responding to questions about the relationship between testosterone levels and athletic advantage while also accounting for scientific findings that risk reducing the question of trans women's inclusion in elite sport to one of (a) biology and (b) solely testosterone, while obscuring the highly relevant socio-historic-cultural contexts that render scientific and evidence-sharing processes vulnerable. While the current mandate understandably engages with discourse on trans women's participation in elite sport, this report features findings relating to both the mandated research question about testosterone and the assumptions layered in the discourses and framing of the mandated research question itself.

It is also important to emphasize the limits to the scope of this report before engaging with the findings: the findings of the current review should not be applied on community, recreational, school, or levels/contexts of sport other than elite, where the evidence overwhelmingly supports the inclusion of cis and trans athletes of all genders. Nor does it review evidence regarding the full range of trans identities (i.e., transmasculine athletes, non-binary trans athletes, or the full range of transfeminine athletes) or athletes who transition at different stages of their life course (e.g., trans youth). The findings of this review are specific to trans women's participation in elite, high-performance sport and are not necessarily applicable to these alternative contexts or populations. For more specific research questions regarding non-elite contexts and the full range of trans identities in sport, different evidence ought to be pursued.

Methods

The findings of this report result from an analysis and synthesis of the existing literature. Academic (i.e., peer-reviewed primary or synthesized secondary research journal articles, scholarly book chapters, other materials that follow conventional scientific and peer review processes) and grey (not peer reviewed, reports, policy documents, do not follow a scientific process) literature were included.

Researchers studying trans identities and sport in Canada and internationally were consulted to build a list of key search terms and literature. Articles were also hand-searched to identify further relevant materials. This process took place in May 2021.

In order to be included, materials had to fit the following criteria:

- Published between 2011 and 2021;
- English language;
- Primary research or syntheses (e.g., meta-analyses, reviews);
- Grey literature was included if it was a final evaluation or report on empirical data;
- Grey literature was included if it was about rules actually in place worldwide for the inclusion/exclusion of trans women in high-performance sport.

Discussion articles, opinion pieces, or commentaries not presenting empirical or theoretical research were excluded.

Approximately 50 academic articles, books, and grey literature materials were identified. The researchers entered articles they reviewed into tables (see Appendix A). In addition to this initial yield, researchers conducted searches for further academic articles with regards to particular issues, claims, or arguments through consultations with leading scholars, previous work, and library searches. These articles are included in analysis and referenced, but not included on the expanded review tables in Appendix A.

At the same time, a university librarian conducted a systematic search in June 2021 (see Appendix B for summary of yield and databases). A scoping review process was unable to be fully completed due to time constraints, however, the authors intend to publish the full scoping review results in future. The authors reviewed abstracts of the biomedical yield of the systematic review (n=360) to ensure no major biomedical articles were missed. (In fact, the systematic search was refined and benefitted from the articles identified through the present search methodology.)

The Structure of This Report: Biological and Sociocultural Approaches to Knowledge Production

What is apparent through public discourse and supported through analysis of the reviewed research materials is that there are competing ways of conceptualizing (“epistemologies”) trans women’s participation in elite sport.

This report is therefore organized by two main conceptualizations. For the purposes of this report, they have been broadly characterized by the way ‘fairness’ in sport is understood. One conceptualization, shorthand to a sociocultural perspective, understands ‘fairness’ in sport as a sociocultural, embodied phenomenon, wherein sport systems need to change to fully welcome the embodied diversities of humans. This conceptualization questions the control elite sport exerts over definitions of gender and the long, ongoing history of sexism, cissexism, transmisogyny, and other forms of systemic discrimination trans women athletes face. The other conceptualization, shorthand to a biological perspective, focusses narrowly on ‘fairness’ as a practice and/or enforcement of biological parity and on testosterone in particular (though, the discourses seem to be evolving to all manner of biological phenomena, and without consensus about what form ‘biological parity’ might or should take). This biological perspective of fairness in elite sport requires trans women’s bodies to conform to yet unidentified biological measures.

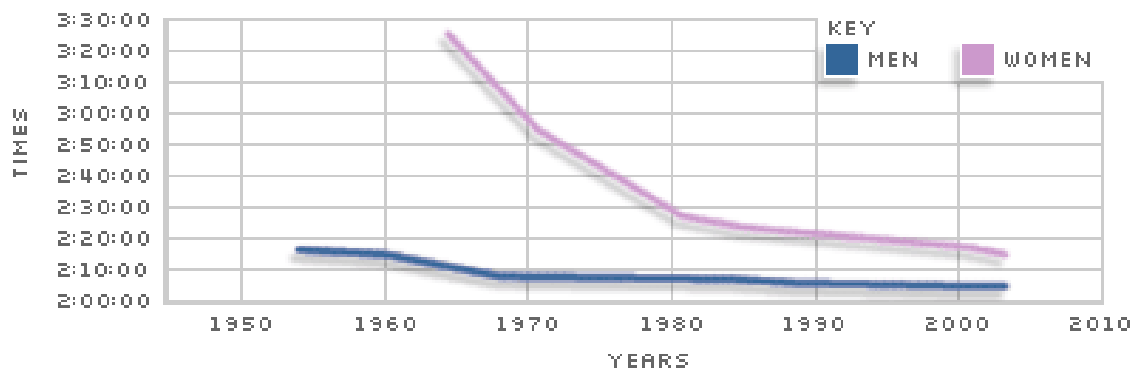
These conceptualizations and the research available in each differ in reliability and impact, with elite sport often prioritizing biological framing and studies over the sociocultural. They also apply differently to different populations of trans women and transfeminine people, who are not a monolith. Because of these competing epistemologies, questions about trans women's participation in elite sport are often reduced to the question of the impact of prior exposure to higher levels of testosterone on athletic performance. Throughout this report, however, the authors will show that there are more salient and more appropriate gaps in biological evidence to consider, and more salient sociocultural considerations towards trans women's inclusion in elite sport. Therefore, despite the mandate of the report to speak to the up-to-date science of the impact of prior exposure to higher levels of testosterone on trans women's athletic performance, it is important to speak to the research in each epistemology. This report offers findings from both, which are presented together, but not equated to each other.

Biological Considerations

Biological data in this area are severely limited. In fact, an illuminating place to start is to note that, “to date, there have been no prospective studies investigating the changes in athletic performance in transgender athletes after hormonal transition” (Harper et al., 2021, p. 1), and many pertinent biological questions remained unexplored. The data that do exist often come with methodological concerns, and/or are limited in their ability to generalize to elite transgender athletes. Many studies employ a false biological equivalency between the role of testosterone in doping to the role of testosterone among trans populations, including trans women. Most available studies do not include placebo controlled or blinded sample groups of trans women, cis women control groups, or even cis men control groups. Height and Lean Body Mass (LBM) are rarely adjusted for as a fair assessment would require. When adjusting for height and fat-free mass, relative differences in strength between cis men and cis women largely disappear (Harms et al., 2011) making this a critical step in conducting population level comparisons. To illustrate this, the average 5’10” cis woman carries significantly higher muscle mass than a 5’4” cis woman. As we do not currently consider height to be an eligibility criterion (no threshold exists which would limit participation in sport), significant as in many men and women’s elite sport, participants tend to be taller than population averages. Unless sporting organizations put limits on height for competition, a fair comparison would use height-adjusted cis women (i.e., comparing the muscular mass and strength of a 5’10” trans women to a 5’10” cis women). Without this comparison, the standard of fairness would be set such that trans women would be required to have lower LBM, strength, and muscle mass than cis women of equivalent height. LBM is similarly useful as a measure, as it includes the total mass of muscles, bones, ligaments, tendons, and essential fat. As skeletal mass is an approximate function of height^2 and sex, height-adjusted LBM can be used to compare total muscle mass the primary driver of performance. Similarly, these studies do not make adequate adjustments for other population-level artifacts such as participation rates (known to reduce elite-level performance levels), availability of training resources, social body image. or other sociological artifacts that affect performance. A practical implication that illustrates this effect is the shrinking of the athletic performance gap between men and women as some of these socio-culturally-driven barriers are alleviated, as seen in Figure 1 below.

Figure 1 Progression of men's and women's world marathon records as reported in BBC Sport (14 April 2003).

Progression of Men's and Women's World Marathon records



Note: Reproduced from BBC Sport (14 April 2003).

The content of this report will demonstrate the irrelevance of the following finding to trans women's inclusion in sport; none-the-less, the report might be incomplete without it: the distribution of testosterone levels among elite athletes overlaps between cis men and cis women, with different exact hormonal profiles and descriptions of the overlaps across various sports described by Sonksen et al. (2018). While some women are considered to have high testosterone in the so-called male range, there are many elite male athletes with testosterone in the so-called normal female range. Bermon et al. (2014) additionally found that testosterone levels were not predictive of sporting success, with no demonstrated higher performance impact of testosterone among cis women track athletes (excluding confirmed or suspected athletes with doping violations and athletes Bermon et al. describe as having Differences of Sexual Development (DSD)). The following sub-sections outline the available research on testosterone, methodological concerns with research on testosterone in sport, and additional biological markers employed.

Sedentary Adults Versus Elite Athletes

As studies in this area rarely use trained athletic women as a representative group, we must also give consideration to what differences exist in sedentary adults versus elite athletes, in particular how total muscle mass (which can be approximated from LBM) increases with physical activity. To start, labour markets have significant gender divides, particularly in jobs with high physical demand where men are far more likely to hold these positions, such as construction or the military (Bureau of Labour Statistics (BLS), 2020). The Euro Barometer (2010, pp. 12) found youth (aged 15-24) participation in sport heavily favoured men (71% male, 50% female). This gap extended for heavily active youth participating in sport at least five times a week (19% male vs. 8% female). Further, there are significant differences between genders for non-sedentary adults and trained athletes due to social pressures and sports preference. Findings also establish that type of sporting activities is highly gendered, where women seek physical activities that emphasize slimness, muscle tone, and other standards of post-modern femininity (Pfister, 2011). This suggests that population level LBM, Cross Section Area (CSA), and strength are not representative of the athletic potential that cis women could achieve if these gendered social expectations did not exist. Not only do cis women have lower participation rates in physical activities which limit their muscle production, when they do participate in physical activities, they further de-emphasize the production of muscle mass by selecting roles which do not prioritize strength and muscle mass. This has been reported in dance where men tend towards mesomorphy (athletic and muscular body type) and females towards ectomorphy (thin, minimal muscle mass, low body fat; Ferrari et al., 2013). Notably, women dancers had significantly lower values for LBM, body fat percentage, and overall lower Body Mass Index (BMI) (Ferrari et al., 2013; Matthew et al., 2014). Similar differences in body compositions have been seen in elite athletes across many sports, going as far back as 1955 (Krawczyk et al., 1955). These sociological pressures result in cis women having lower LBM and strength than their biological potential would allow for.

It is important to note that participation rates also dramatically impact likely performance of elite athletes. This is due to statistical artifacts whereby the larger a study population, the more likely outliers will develop to maximally perform a task. There also were no studies that examine areas that, as a population, cis women outperform cis men. These areas include women having higher levels of endurance and quicker recovery as a result of a higher proportion of type 1 muscle fibers (Haizlip. et al., 2015), increased glycogen-sparing fat oxidation during endurance exercise (Tarnopolsky, 2008), higher myocardial perfusion, extracellular volume and myocardial perfusion stress (Nickander et al., 2020), and at a population level of untrained individuals, higher performance in balance (Torres et al., 2014). It should not be assumed that men outperform women in all elite sports; this is currently not considered in any of the research examining trans populations in elite sport.

Along with using sedentary adults as proxies for elite athletes, these studies also tend to have very small sample sizes, regularly use imperfect measurement techniques, measure sex differences that are poor proxies for performance, and use inappropriate reference group comparisons to establish their conclusions, all of which limits the applicability of the research for policymaking. More concerning, there exists significant evidence that some highly impactful articles in this area are selectively included, manipulated, or used misleading data sources to create support for their conclusions while ignoring all evidence that contradicted these conclusions. Specifically, Hilton and Lundberg (2020) have written what is best described as an argumentative essay in the form of original scientific research (see Appendix A for detailed methodological concerns).

Population-Level Comparison Groups

Research investigating the potential for athletic advantage conferred onto transgender athletes tends to be centered on relative changes to LBM, CSA, strength, and hemoglobin as a result of testosterone suppression. It is important to note that no one biological marker can be used as a proxy for the complex set of advantages and disadvantages that is attributed to individual performance. As a result, bodies (both cis and trans) must be looked at in a holistic way, and that their performance is a result of many interactive social and biological systems and not just the sum of discrete biological components. We must also examine what bias we have when examining biologic advantage, especially as it relates to transgender women. In sports, athletes are regularly praised as talented for having physical attributes which gain them significant athletic advantage compared to population averages. An example of this is Michael Phelps who is notably reported to have a longer torso, shorter legs, hyperextended joints, double jointed elbows and ankles, size 14 feet, and he produces less lactic acid than other athletes. All of these attributes create a significant performance advantage, yet his biological advantages are not considered unfair. Rather than examining individual variations of LBM, CSA, strength, and hemoglobin, we should instead examine the total impact of HRT on an athlete's performance. In this, we should also note that outside of sports with defined weight categories, weight and height are not considered to be an unfair advantage, rather taking positions as examples of tolerable unfairness (Devine, 2018). This is despite height being highly predictive of not just lean body mass, but also in measuring maximal torque. The increased lever length attributed to skeletal frame (height) accounts for significant levels of the variation measured for both men and women (Harbo et al., 2011). It is important to note that both male and female muscle mass are the same strength when comparing equivalent cross section size or mass (Costill et al., 1976) and total mass and cross section size, both increase with height for both cis men and cis women (Forbes, 1974). When adjusting for height and weight, cis men still have higher LBM than cis women, largely as a result of being able to achieve a lower body fat percentage, a direct performance advantage due to having less non-contractile tissue to carry. It is unsafe for cis women to attempt to

achieve cis men levels of body fat (Nazem & Ackerman, 2012). Despite this, we could find no studies that examined the effect of HRT on body fat percentage or performance. This is despite the fact that a widely used part of HRT is estrogen supplementation which impacts body fat retention (Handelsman et al., 2018).

Population Differences

Many studies in this area often use cis men as a reference group to trans women. This is highly flawed, as the typical pre-medical transition woman does not exhibit a body that is comparable to that of a cis man. These flawed assumptions lead to an under reporting of the effect of testosterone suppression in individuals who were assigned male at birth due to a lower starting muscle mass pre-suppression.

Table 1 below illustrates the average height and weight of trans women participants.

Table 1 Average height and weight of trans women participants.

Article	Height (cm)	Weight (Kg)	Country	Trans Women Participants (n)
Wiik et al., (2019)	180	73	Sweden	11
Defrayne et al., (2018)	179	72.8	Netherlands and Belgium	239
Gava et al., (2016)	180	73.0	Italy	40

Table 2 Height and weight among cis men and cis women (as presented by Harper, 2020).

Country	Height (cm)/Weight (Kg) (cis men)	Height (cm)/Weight (Kg) (cis women)
Sweden	180/86.8	166/70
Netherlands	183/87.4	169/72.3
Belgium	181/87.8	165/70.0
Italy	177/83.6	166/70.0

Note: Reproduced from Harper (2020).

The data in Tables 1 and 2 show that pre-testosterone suppression trans women cannot be compared to cis men (while closer to cis men for height, weight is lower and seemingly closer to cis women's). It may follow that trans women as a population have lower BMI than cis women, and therefore lower height-adjusted muscle mass than cis women. This is important to note as the majority of studies examining the effect of testosterone suppression in trans women assume that their starting muscle mass is equivalent to cis men.

This finding is also supported by cross-section studies measuring the baseline differences between pre-testosterone suppression trans women and cis men. These data clearly show that it is erroneous to assume trans women and cis men are synonymous. Therefore, in order to examine if any advantage exists, we must compare the observed reduction in LBM, CSA, and strength with height-adjusted cis women and not cis men. This is largely not done in the available literature and leads to misleading conclusions of any retained advantage. An equivalent facetious argument using height would be that the average child grows 70 cm by the age of 18 but the average adolescent only grows 30 cm at the age of 18, therefore children who have turned 18 have an unfair advantage due to a 40 cm height gap. Table 3 below shows the relative change between pre-suppression transwomen and post-suppression transwomen, both of whom have lower LBM, CSA, and strength than cis men.

Table 3 Relative changes between pre- and post-suppression trans women among various markers.

Category	Difference
LBM	6.4% (Van Caenegem et al., 2015), 17.2% (Lapauw et al., 2008) 8.0% (Haraldsen et al., 2007)
CSA	6.0% (Van Caenegem et al., 2015), 11.4% (Van Caenegem et al., 2015)
Handgrip strength	14.3% (Van Caenegem et al., 2015)

Neither of these options provides a robust framework by which trans athletes' performances should be assessed. Without making appropriate adjustments in height and LBM, and without consideration of other performance advantages or disadvantages, the standard set for fairness would require trans women to underperform or be at a demonstratable disadvantage compared to cis women. There must therefore be critical examination of the few existing studies that examine the direct impact on trans athletes' performances as a result of testosterone suppression through either HRT or surgical gonad removal.

Erroneous Information and Flawed Measurement Techniques

Several studies allude to performance advantages which are derived from testosterone exposure during key periods of development (i.e., puberty). However, while these advantages - such as q-angle, lung size and bone density - are commonly thought to confer a performance advantage, there is no support in the literature that these factors confer any such advantage. The q-angle - defined as the angle between a line drawn from the anterior superior iliac spine (ASIS) to the center of the patella and a second line from the patella to the tibial tubercle - has often been assumed to play a role in generating power during acceleration and efficiency of a running stride. However, under investigation there appears to be no performance advantage conferred in sport as a result of q-angle, further increased risk of injury attributed to q-angle can be entirely removed with training (Bruton et al., 2013; Kernozek & Greer, 1993; Thomas et al., 1998; Nguyen et al., 2009; Sigward & Powers, 2006; Hertel & Braham, 2004). Arguments based on bone density derive from systematically racist arguments first introduced in the 1920's while attempting to ignore this background, black women and women of color have higher bone density than white men (Leslie, 2012) removing any potential for bone density to be considered a factor for unfairness in trans athletes. Lung size is also commonly attributed as performance enhancing; however, it is never adjusted for height (taller individuals naturally have larger lungs on average) nor is it a good predictor of sport performance (Hopkins et al., 2018; Degens et al., 2019; Åstrand et al., 1964). To clarify, on the topic of Maximum Breathing Capacity (MBC), "MBC is not likely to be an adequate physiological measure of the competence of the respiratory system in strenuous work and should be regarded rather as the biomechanical limit of the possibilities of the ventilatory apparatus," (Breslav et al., 2000, pp. 485) and, "After differences in lung volume are accounted for there is no intrinsic sex difference in the DLco [diffusion capacity], Vc [pulmonary capillary blood volume, or Dm [membrane diffusing capacity] response to exercise ... together, these data suggest that the pulmonary capillary blood volume response is proportional to lung size and is adequate to meet individual oxygen demand during exercise," (Bouwsema et al., 2017). As such, lung size should not be used as a proxy for an individual's endurance capacity.

Beyond using misleading physiological traits, studies often use measurement techniques with poor accuracy and generalizability. Handgrip strength, for example, is often used for broad population level analysis, however handgrip strength should not be used as a proxy for overall muscle strength (Yeung et al., 2018). In fact, due to ease of gripping the testing device, grip strength is largely correlated with hand size and therefore height (Alahmari et al., 2019). Additionally, some studies do not include cis female control groups, which leads to poor accuracy and confounding attributions. One example of this can be found in Wiik et al., (2020), in which the authors' results ignore that cis women are also able to maintain or increase muscle mass while undergoing intense training cycles and that untrained females have a high capacity to build muscle mass, particularly upper body strength (Roberts et al., 2020). Without a cis women comparison group, the results are misleading. Moreover, many strength studies ignore

that untrained individuals can quickly gain strength independent of muscle gain due to neural mechanisms (Chilibeck et al., 1997). This ability to quickly gain muscle is in addition to higher performance on strength tests that can be attributed to comfort and familiarity with testing devices after repeated use. As such, sedentary adults should not be used as a proxy for elite athletes when determining the ability to gain or retain muscle mass. Additional studies need to be made which appropriately control for these factors. This requires studies to use appropriate control groups of height-adjusted elite athletes and measure muscle and strength from appropriate tests which can be used as a proxy for overall strength and adequately control for artifacts such as training familiarity and neural adaptations which give inaccurate measurement results.

Testosterone Effects on the Body

The general effects of testosterone on the body presented below must be further explored and ought to be taken as guideposts rather than definitive. Many methodologies in these research projects relied on treating serum testosterone levels and doping as similar functions, but current science demonstrates that doping is not the same as serum testosterone levels.

Table 4 below summarizes the evidence on the generalized effects of testosterone on the body.

Table 4 Summary of evidence of the generalized effects of testosterone on the body.

Effect	Supporting Citation(s)
Increases muscle fibre diameter by increasing muscle protein synthesis	Griggs et al., 1989
Increases cardiac muscle	Thum & Borlak, 2002
Induces red blood cell production	Bachman et al., 2014
Increases height during puberty	Bourguignon et al., 1986
Bone formation is affected	Tuck & Francis, 2009

It is important to note that for some of these traits there is little or no research evidence that effectively and directly links them to athletic performance, and some of these references are notably older. Many of these claims are a result of directly comparing male and female sports performance, which has many notable flaws (as previously discussed). Many of the claims about the benefits of testosterone in athletics have gone unchecked since they are often taken for granted in biological research papers and do not include citations. For the sake of this report and providing a review of the most up-to-date evidence on testosterone, we entertained the presumptions - which many researchers have taken for granted without sufficient evidence - that there are links to performance to explore, despite the 'taken-for-granted,' unsubstantiated, and refuted natures of this claim.

Effects of Testosterone Suppression for Trans Women

As we are attempting to examine the maximum potential of the human body for elite athletes, we must examine the extreme and untested case: an individual whose body is indistinguishable from a trained, elite male athlete prior to testosterone suppression/estradiol supplementation. With a lack of trained, elite male athletes undergoing HRT, we must hypothesize what performance effects this individual would undergo as a result of HRT. While this is the case scenario presupposed within nearly every trans-focussed sport policy, no cases of this exist, to the best of our knowledge. Rather, most athletically untrained trans women have lower muscular mass and strength than elite female athletes. In order to hypothesize the performance effects of HRT on a trained, elite male athlete, we must look at the available evidence and consider whether the research as it currently stands (without a population of, or even a single, trained elite male athlete undergoing HRT) can be used to make effective comparisons through:

1. Comparing trained athlete cohorts.
2. Including body composition (fat-free mass %) affected by testosterone.
3. Using height-matched control groups.
4. Comparing participation rates between populations.

Metrics Used to Predict Elite Sport Performance:

Testosterone Level

Muscle Mass

Red Blood Cell Count

Body Fat

Strength

Bone Density



Athletes should be looked at holistically, that they are a sum of all their advantages and disadvantages which result in performance.

Additional possible metrics of performance could include direct LBM measurement through a dEXA MRI scan.

It is important to note that no one metric can be used to predict performance. Further, the metrics reported do not account for the population-level differences that exist between trans women and cis men. Therefore, we must look at the absolute height adjusted values and compare these values with values produced by cis women. In this, athletes should be looked at holistically, that they are a sum of all their advantages and disadvantages which results in performance. Existing studies often do not continuously measure muscle mass during the 12 months of testosterone suppression, nor do they continue after the 12 months of suppression to see if any persisting trend exists. This is significant for policy creation, as a 12-month testosterone suppression requirement may be excessive to achieve practical performance equivalence. This also holds true for studies examining hemoglobin and red blood cell count where levels normalize within 4 months (See Table 5). As a result, it is impossible to say exactly when any potential individual athletes' performance advantage has been mitigated. It is likely that the majority of any advantage is erased prior to the 12-month arbitrary timeline. In addition, flawed conclusions are often drawn from these studies as they notably ignore any significant disadvantages that affect trans women during and after testosterone suppression. These disadvantages can include: the diuretic effects of suppressive medications, speed, endurance, or recovery as a result of reduced muscle mass while maintaining a larger body along with reduced aerobic capacity as well as sociological disadvantages. When examining the normal distribution of LBM, CSA, and strength for cis women (Jassen et al., 2000) sedentary trans women appear to be well within the normal distribution of cis women, which is suggestive that no residual effect on these traits exist once variations in height, weight, participation rates and social factors are accounted for. Additionally, it has been reported that for trans women who have undergone gonad removal, their serum testosterone levels can often be below that of pre-menopausal cis women leading to additional performance and health factors (Genel, 2016). However, the majority of studies reviewed examine the effects of testosterone suppression on non-athlete trans women and have reported decreases in hemoglobin levels, LBM, muscle CSA, and strength loss (see Tables 5 - 8). Of particular note, hemoglobin levels after testosterone suppression reach cis woman levels within 4 months (see Table 5 examining non-athletes HCT (hematocrit) or HG variance).

Table 5 Hemoglobin levels after testosterone suppression.

Article (by date)	Suppression effect	Time Frame	Participants (n)
Wiik et al., (2020)	10.5%	4 months	9
Wiik et al., (2020)	11.7%	12 months	10
Defrayne et al., (2018)	8.9%	3 months	239
Defrayne et al., (2018)	8.7%	6 months	239
Defrayne et al., (2018)	9.6%	24 months	239
Olson-K (2018)	8.3%	24 months	23
Vita (2018)	10.5%	6-30 months	21
Auer (2016)	5.5%	12 months	20
Wierchx (2014)	7.0%/4.6% *	12 months	52

*oral oestrogen vs transdermal oestrogen

Table 6 Muscle loss in non-athletes using LBM.

Article (by date)	Suppression effect	Time Frame	Participants (n)
Klaver (2018)	3.0%	12 months	179
Tack (2018)	4.7%	12 months	21
Gava et al., (2016)	3.5%	12 months	40
Auer (2018)	3.4%	12 months	45
Wierckx (2014)	5.4%/4.6% *	12 months	52
Van Caenegem (2014)	4.0%	12 months	49
Mueller (2011)	4.0%	12 months	84
Haroldsen et al., (2007)	4.0%	12 months	12

*oral oestrogen vs transdermal oestrogen

Table 7 Reduction in muscle CSA in non-athletes.

Article (by date)	Suppression Effect	Time Frame	Participants (n)
Wiik et al., (2019)	4.2% quadricep	12 months	11
Tack et al., (2018)	8.9% calf, 4.1% forearm	12 months	21
Van Caenegem (2015)	8.6% forearm, 4.4% tibia	12 months	49
Gooren (2004)	9.5% quadricep	12 months	19
Elbers et al., (1999)	9.5% thigh	12 months	20
Elbers et al., (1999)	11.7% thigh	36 months	20
Lapauw et al., (2008)	23.9% forearm, 24.1% tibia	48 months	69
Van Caenegem (2015)	11.4% forearm, 6.0% tibia	Baseline	98

Table 8 Strength losses in non-athletes.

Article (by date)	Suppression Effect	Time Frame	Participants (n)
Wiik et al., (2019)	0% quadriceps	12 months	11
Scharff (2019)	4.5% handgrip	12 months	249
Auer (2016)	0% handrip	12 months	20
Van C (2015)	7.1% handgrip	12 months	49

Direct evaluation of performance is currently the most reliable method of assessing the impact of testosterone reduction on athletic ability, which in turn is used as a basis for fairness. However, limited evidence currently exists in this area. Harper (2015) used 200 self-reported race times from 8 trans women runners. Runners were at least 10% slower after transition and achieved World Masters Athletics (WMA) age-grade equivalence before and after transition. Similarly, Roberts et al., (2021) used one-minute maximal push-up count from a standardized army fitness test to determine the effect of medical transition on strength. This type of activity is critical to understand how performance is impacted not only by upper body strength, but also muscular endurance, cardiovascular

endurance, and technique. Through this study they saw that trans women lost all performance advantage during 12 months on HRT, making it highly indicative of the impact on performance in sports where strength is but one component that is required for success.

Harper (2020) presented additional preliminary evidence (Table 9) that comes from ongoing research on the topic of retrospective performance declines of athletes after medical transition.

Table 9 Retrospective evidence from trans-athletes, preliminary data presented by Harper (2020).

Trans woman sprinter (100m)			
Race Times	Age	Athletic Gender	Age Group Percentile
10.95	31	male	89.4%
12.54	39	female	86.6%
Trans Women Cyclist			
Power Output	Age	Athletic Gender	
338	32	male	
300	36	female	
Trans Woman Rower (2km)			
Race Time	Age	Athletic gender	
7:01	18	Male	
7:25	20	Female	

Note: Reproduced from Harper, 2020.

This evidence is highly suggestive that any potential performance advantage is negated through effective testosterone suppression. Additional studies led by Joanna Harper are currently underway prospectively examining the impact of HRT on performance. It is important to note that some organizations have claimed safety as a value which may merit the discrimination of trans athletes. However, this appears to be an illogical position given the performance data. If there exists no policy regulating height and weight of athletes, and no performance advantage exists in terms of strength, LBM, CSA, or hemoglobin, then no basis exists for a safety concern. There currently exists no studies which examine transgender athletes posing a realized or potential safety risk to cis women in sport. The only available comparisons use population data for measuring potential impacts of cis men against cis women. As mentioned above, this should not be considered an equivalent comparison.

Evidence of Other Biological Markers

There seems to be agreement among biologically based studies that we do not have the appropriate data or research to make evidence-based recommendations or decisions. Hamilton et al., (2021) suggests that, in absence of the research needed to make informed decisions, testosterone is an imperfect but most actionable proxy. This latter point is not consensual. There are many biological markers used in studies that are inadequate as biomarkers. There are also some additional biomarkers that may show promise if taken into account, all described in Table 10 below (Level of evidence for biological markers). It is important to re-emphasize here that bodies are systems, and there is not one discrete biomarker that allows easy comparison of athletes' bodies to each other in terms of performance.

Table 10 Level of evidence for biological markers.

Biological Marker	Notes	References	Used As Marker In
Handgrip strength	Not a reliable biological proxy; more related to hand size than gender.	Yeung et al., 2018; Alahmari et al., 2019	Yeung et al., 2018; Alahmari et al., 2019
Muscle mass	A potentially reliable biological proxy but must be controlled for height and weight.	Dual energy X-ray absorption (DEXA or DXA) is considered a reference standard for muscle mass measurement (Buckinx et al., 2018), though evaluation of the technology seems mostly centred on diagnosis and care for sarcopenia. The technology has yet to be evaluated in studies of gender and athleticism.	Several studies used muscle mass as a biomarker, with significant methodological/ analytical concerns.
Testosterone receptors	Should be considered/ measured along with testosterone levels, if pursuing testosterone as a marker.	As far as our research can tell, there exists no non-invasive, cost-effective way of determining the level of testosterone reception in an individual, but some studies mention receptor measurement might be helpful/ complementary.	None found.
Osteology – q-angle	Not reliable biological proxy; more related to height.	Grelsamer, Dubey & Weinstein, 2005	Sutherland, Wassersug, & Rosenberg, 2017
Osteology – Bone density	Not reliable biological proxy; not related only to sex/gender but also link socio-economic position. Can't be understood as strictly sex dimorphic.	Fausto-Sterling, 2005 Ritz, 2017 : 321	Sutherland, Wassersug, & Rosenberg, 2017
Red Blood Cell Count	Affects endurance and recovery.	(See Table 5)	



Bodies are systems, and there is not one discrete biomarker that allows easy comparison of athletes' bodies to each other in terms of performance.



Through examining the available literature, we have significant confidence with the following statements:

1. There is no clear scientific evidence that high levels of naturally produced serum testosterone was predictive of athletic performance among cis women.
2. Female participation in elite athletics is significantly lower than male participation. This leads to a significant statistical artifact in performance data where statistical sampling results in a larger gap in performance than would otherwise exist if participation rates between sexes were equal. This issue is compounded by training advantage conferred by additional resources typically given to male programs over female programs.
3. Women with high serum testosterone levels well above the expected range of cis women as a result of natural variations in their sex-linked development (referred to also as 'DSD', 'Difference of Sexual Development', or 'Disorder of Sexual Development' - terms rejected by many in the intersex community as pathologizing) are overrepresented in some athletic events. However, selection bias may account for much of this discrepancy, as well as the global variation in responses to women with high testosterone (i.e., in the Global North the number of women in the broader population who could present with high testosterone is artificially suppressed because of aggressive medical responses to children with intersex variation).
4. The higher levels of red blood cell count experienced by cis men is removed within the first four months of testosterone suppression. This suggests a rapid decrease in athletic performance particularly in sports with an endurance requirement.
5. There is no basis for athletic advantage conferred by bone size or density, other than advantages achieved through height. Elite athletes tend to have higher than average height across genders, there is overlap in height distributions among genders, and this is not currently considered an athletic advantage.
6. Trans women who are pre-testosterone suppression still have lower LBM, CSA, and strength than cis males. This indicates that the performance benefit experienced by these individuals cannot be generalized by examining cis male athletes.

- 7.** Non-athletic trans women experience significant reduction in LBM, CSA, and strength loss within 12 months of hormonal suppression. It is important to note that this 12-month threshold is arbitrarily defined, and no significant studies examine the rate of LBM, CSA, or strength reduction over time.
- 8.** When adjusting for height and fat mass, LBM, CSA, and strength after 12 months of testosterone suppression, trans women still retained statistically higher levels than sedentary cis women. However, this difference is well within the normal distribution of LBM, CSA, and strength for cis women (Jassen et al., 2000).
- 9.** LBM, CSA, and strength loss continues after the 12-month initial testosterone suppression.
- 10.** Evidence directly examining the effect of testosterone suppression as it directly affected trans women's athletic performance showed no athletic advantage exists after one year of testosterone suppression (Harper, 2015, 2021).
- 11.** Despite unavailability of the exact prevalence of trans women in the population, we can reliably conclude trans women are systematically underrepresented in elite athletics both in terms of participation and results.
- 12.** Post gonad removal, many trans women experience testosterone levels far below that of pre-menopausal cis women.
- 13.** The literature largely ignores areas where cis women have an athletic advantage over cis men.
- 14.** Estradiol likely plays a role in athletic performance as trans women undergoing HRT increase their average body fat percentage (Handelsman et al., 2018). This in turn reduces performance through increasing body mass for the equivalent LBM.

Sociocultural Context and Framing of Trans Women's Sport Participation

The evidence reviewed in this section provides clear indication that the questions cisgender sportspeople have about trans women competing in elite sport and policies that govern trans women's participation in elite sport policies are founded in transmisogynist, misogynoir, racist, geopolitical cultural norms. The literature reviewed here can provide an excellent foundation for forward movement with regards to trans women competing in elite sport, help differentiate claims from empirical evidence, and help guide policymakers in building safer and inclusive competitive sporting environments.



It is worth noting that trans women athletes are a distinct group from intersex athletes. In elite sport, these groups are often combined because each of their existences is seen in elite sport as a challenge to the current structures of oppression. Sports administrators' drives for what they frame as some kind of biological parity affect both of these athlete populations and act to forcibly exclude them from competition, locating 'fairness' in women's and intersex peoples' bodies. In this section, the authors review literature which instead locates 'fairness' in unjust systems within sport. Therefore, while the authors focus on the impacts on trans women athletes, some factors in this section may also have bearing on intersex athletes' participation.

History of Gender Categorization in Elite Sport

A brief history of gender categorization policies and ongoing evolutions in elite sport is catalogued below. This timeline and the experiences of trans athletes are provided to illustrate the thinking around gender in elite sport as well as some experiences of athletes who lived through these policies. The long history of gender policies in elite sport is often used uncritically as reasoning that questioning transgender athletes' participation in elite sport is a natural, neutral part of long-standing questions of gender and gender categorization, but there is a rich body of literature on the racist, sexist, eugenicist, geopolitical origins and ongoing evolutions of such policies that provides relevant context.

- 1930's** - Muscle Moll - (see Cahn, 1993)
- 1936** 100 m sweep (intersex athletes) and Heinrich Ratjen
- 1937** International Association of Athletics Federations (IAAF), now World Athletics, Gender Protest Policy
- 1946** IAAF Medical Certificate
- 1948** International Olympic Committee (IOC) Medical Certificate
- 1966** European Athletics Championship – “Nude parades” / morphological and gynecological examination
- 1967** European Athletics Championship – “Barr body test” / chromosomes
- 1991** IAAF – Recommendation to end systematic sex/gender testing
- 1992** IOC – PCR-SRY / chromosomes
- 2004** Stockholm Consensus
- 2011** IAAF and 2012 IOC Consensus Statement on Hyperandrogenism
- 2015** IOC Consensus Meeting on Sex Reassignment and Hyperandrogenism
- 2015** Suspension of Hyperandrogenism Rules/2018 Testosterone Level Modification
- 2020** World Rugby Ban on the Participation of Transgender Women

The USGA [United States Golf Association] has done nothing to develop a policy to include transitioned women on tour. Rather, they have explicitly, through their policy, excluded transitioned women from competing on tour. They request a signed waiver by the entrant giving the USGA complete and unrestricted access to one's medical records and pre-operative and post-operative psychiatric records. And I just find that horrendous. We are treated as a complete freak, and we are treated so differently to any other competitor with complete disregard to the real facts and medical conditions involved in our treatment and the person who we are. It's an obvious policy developed based on emotion and fear.

-- Mianne Bagger about the USGA policy on trans athletes in Love et al. (2009)



*A few years ago
I was hospitalized. When I told
the doctor that I play basketball she
told me: "but if you play on a women's
team you are a cheater."*

**-- 40-year-old woman, non-elite athlete
(Interview: 1h50, February 2019) Pavlenko
(2019, 2021)**

Continuing a Long History of Exclusion: The Women's Category of Sport

Policies that impact trans women's participation in elite sport are the continuation of a long history of exclusion of women from competitive sport.

The women's sports category is the result of the historical exclusion of women from competitive sport, which was underpinned by pathologizing discourses about their bodies and the harms of their participation in physical activities. Policies that impact the practice of trans women in competitive sport emanate from the parallel history of efforts to define the female category in ways that excluded those women whose bodies were deemed to not conform to normative standards of femininity.

Forbidden to take part explicitly in sports from the end of the 19th century, women organized their own competitions during the 20th century and gained some access to sports that were prohibited to them (Prudhomme-Poncet, 2003; Rosol, 2004; Vilain et al., 2017); for example, the Women's World Games in 1922 by the International Women's Sports Federation (FSFI) occurred in response to the ban on participation for women in many Olympic events (Castan-Vicente et al., 2019). Throughout this period, women athletes were subjected to a "virilization trial" (Bohuon, 2008): the accusation of not sufficiently meeting the socially expected criteria of femininity, not being enough of a woman by society standards because of traits like having muscles, wearing sportswear deemed masculine, or because of their hairstyle or body hair (Bohuon, 2008; Vilain et al., 2017).

This virilization trial, which is found in discourses, and the exclusion by sports organizations from allowing some women to compete in their competitions gradually became systematized by the femininity test (Bohuon, 2012; Sullivan, 2011). Behind the pretext of protecting the women's category from potential impostors, sports federations sought to establish sex/gender control to police femininity and performances (Bohuon, 2012; Hargie, 2017; Sullivan, 2011; Vilain et al., 2017). In this context, being a woman is understood as having physical capacities inferior to men as evidenced by the sex controls. At the 1966 European Athletics Championship, the athletes were subjected to an anatomical and physical test attesting that they were women. Therefore, if their body matched medical expectations and if their performances were lower than men's, they were cleared as women for the event (Bohuon, 2012; Sullivan, 2011).

Since 1966 we have witnessed different waves of femininity tests implemented by sports organizations (Bohuon, 2012; Hargie, 2017; Sullivan, 2011; Vilain et al., 2017). Anatomical at first, then genetics, and now hormonal. All tests were inconclusive because contrary to the medical assumption that led to these tests, men and women are not dimorphic and show overlap in all those areas (Pape, 2017). Instead of considering non-dimorphic data as part of the diversity of human bodies, these findings (when they are related to women's bodies) are pathologized, excluded from scientific studies results, and policed in sport regulations (Pape, 2019). Today, in line with

medicalization and control of women's bodies by sports institutions, policymakers still (erroneously) assume and insist that human bodies are dimorphic, testosterone is a male hormone, testosterone is the key to winning competitions, and women are inherently weaker than men. These assumptions are implemented without tangible evidence as a way of maintaining patriarchy and the domination of men over women. (Erikainen, 2020; Karkazis and Jordan-Young, 2018; Pieper, 2016; Sanchez et al., 2013; Sullivan, 2011).

Systematic gender testing was canceled in 2000 (Sullivan, 2011), but the controversy around Caster Semenya's victory at the 2011 Athletics World championship re-actualized the debate about medical regulation of women athletes. "Visual" doubts, therefore, external criteria of racialized cis-heterosexist femininity have been used to enforce gender testing, resulting in the fact that almost all women targeted by those tests in the 21st century are racialized women from the Global South (Bohuon, 2012; Karkazis and Young, 2018). Making gender testing a way of maintaining power on the geopolitical and racial organization of women athletes' bodies (Bohuon, 2012; Karkazis and Jordan-Young, 2018).

With a regulation like the 2012 IAAF Statement on Hyperandrogenism, racialized athletes from the Global South are sent to the Global North to be "treated," "saved" and taken in charge for their "diseases" (namely having a testosterone level above the expected average by women) which are created by Western medicine and do not present any danger for the athletes (Karkazis et Young, 2018). Sex/gender regulation policies are produced by sport organizations in the name of fairness without taking into account the living conditions of marginalized women (racialized and/or trans) that actually constitute the opposite of an unfair advantage given the lack of access to resources to train (Erikainen, 2020; Karkazis and Jordan-Young, 2018).

Social Factors in Keeping Women's Sport Inferior to Men's

There are many social factors involved in keeping the women's category of sport inferior to the men's category.

Women are banned from sports competitions. For example, women's marathon was absent from the Olympics Games for 84 years (Vilain et al., 2017). Women were excluded from Olympic boxing until 2012 and they were not allowed to take part in the Olympic ski jumping event until 2014. The Olympic skeet event was originally mixed gender but, in 1992, after the victory of a woman named Shan Zhang, women were banned from this event at the 1996 Olympics. The possibility for women to participate was reinstated in 2000 with a women-only category and with different shooting criteria, making it so the performance of men and women were not directly comparable. During the 2021 Olympic canoe-kayak championship, women did not have races longer than 500 m, while men's races are 1000 m long - another example of differences between

men's and women's elite sport which have the effect of maintaining the positioning of men's and women's elite sport.

Other social factors have been forgotten in most articles about competitive differences between men and women: lack of women's teams depending on sports and geographical positions, disparities in access to sports facilities for women's teams, lack of financial resources (gender pay gap), and lack of staff (including medical staff). Sexism in sport impacts women's participation at each step, including restrictions in strengthening exercises because of the social representation of what women should look like. Women have had to quit sport, change clubs/trainers, and practice in deteriorated conditions due to sexual violence (Ohlert, 2020), lesbophobia (Griffin, 1998), classism, racism, and intersex phobia (Karkazis & Jordan-Young, 2018), or transphobia (Cohen et Semerjian, 2008; Hargie et al., 2017; Ivy, 2020; Jones et al., 2017; Lenskyj, 2018; Tagg, 2012). Faulty and/or absent data about trans women's performances makes transphobia especially present and prominent in this context of scarcity and scrutiny for women in elite sport.

Discrimination and Violence Against Trans Women

Trans women are subjected to discrimination and violence.

The living conditions of trans women are the result of downward social mobility and the many cissexist discriminations they experience in this context. Surveys on the living conditions of trans women in Canada show a strong limitation and discrimination in access to vital spaces (housing, health care, work, public space including sports facilities, etc.) meaning that they can be subjected to violence in every aspect of their life. Trans women are disproportionately affected by unemployment and homelessness (Rotondi et al., 2011). Almost half of trans people who responded to the Trans Pulse Survey earned less than \$15,000 annually (Rotondi et al., 2011). Trans women are disproportionately remote from salaried employment (Rotondi et al., 2011). Discrimination at work encompasses harassment and physical and mental violence, including sexual violence (Grant et al., 2011). More than half of trans women say they feel uncomfortable going to see a doctor (Bauer et al., 2015). Discriminations in this context include refusal to provide care by a medical professional (Bauer et al., 2015). Transphobia impacts access to public spaces. In fact, 97% of trans people in the Ontarian studies reported to have avoided at least one type of public space because of their trans status (gyms were the second space most avoided after public washrooms) (Scheim et al., 2014).

These discriminations are incredibly salient to the question of 'fairness' regarding trans women athletes' inclusion in elite sport. There are some ways discrimination impacts trans women's access to sport directly (such as administrators' varying or absent standards of safety and/or availability of necessary sport spaces such as change rooms, training facilities, and washrooms), and others which are a bit more complex but

relevant (for example, the impacts of lower income or availability of secure shelter on participation and/or excellence in sport). All of these factors ought to be taken into account when thinking through the questions of what makes sport 'fair' and are important to understand the context of trans women's participation. This evidence suggests there needs to be more focus on all discrimination against trans women as it appears in elite sport.

Myths About Trans Women Circulated in Sport

There are myths surrounding trans women in sport.

It is a myth perpetuated by and through sport that trans women are akin to cis men. Biomedical studies that inform trans sport policies have cis men as a proxy to trans women in comparison with cis women and use terms like "biological male" or "transitioning males" (Hilton and Lundberg, 2020; Sutherland, 2017). In other words, trans women are assimilated to cis men. The debate is framed not with the concern of trans women's participation in sport, but with the supposed place of a man in the women's category even though trans women's bodies and living conditions are not comparable to cis men's (Ivy and Friedlaender, 2020).

Trans women are assimilated to the stereotype of the cheater who would enter women's competitions with the sole aim of exploiting a single-sex space reserved for women (Hilton and Lundberg, 2020; Sutherland, 2017) – another myth with deep impacts. This fear is unsubstantiated and completely ignores the material living conditions of trans women and the conditions in which women participate in sport. Transitioning, and/or trans women's status as trans, is often utterly misunderstood in sport discourse as a deliberate choice rather than a necessity for an individual's survival, despite strong evidence that affirming one's gender identity is important to health and well-being. These kinds of presumptions and misunderstandings play into the same unsubstantiated transphobic fears that cis men choose to transition solely to gain advantage in elite sports. However, the discrimination and violence experienced by cis and trans women in sport and everyday life expose the dangerous dismissive attitudes towards trans identities as well as some of the contradictions, ignorance, and violence imposed in requiring trans women to adhere to specific medical transition guidelines in order to participate in sport competitions.

It is a myth that trans women dominate (i.e., win) all sports. In response to the literature review on trans athlete's participation in sport by Jones and al. (2017), Richardson and Chen (2020) report a lot of false information without scientific precautions. For example, the fact that several trans women have been the subject of media coverage is used to argue that there are frequent and massive occurrences of trans women athletes winning sport competitions when, in fact, the literature shows that no trans woman has ever won an Olympic medal ever since they have been allowed to compete in 2004 (Ivy

and Friedlaender, 2020). Trans women are over-sensationalized in media due to the moral gender panic that surrounds their experience (Espiniera, 2015).

Experiences of Systematic Discrimination in Sport

Qualitative studies with trans women athletes show that trans women face a lot of discrimination while participating in sport.

Negative experiences and exclusion of sport participation for trans women are highly reported in the academic literature (Cohen and Semerjian, 2008; Barras, 2021; Devis-Devis et al, 2020; Elling-Machartzki, 2017; Hargie, 2017; Jones et al., 2017; Tagg, 2012). Studies with trans women athletes reveal the anxiety-provoking climate and constant surveillance with which trans athletes must contend at all stages of practice: locker rooms, teammates, opponents, staff, dress codes, supporters, obtaining a license, physical and verbal violence (Jones et al., 2017). This leads to a phenomenon of disengagement from the practice of physical activity and sports in the trans population (Cohen and Semerjian, 2008; Devis-Devis et al, 2020; Elling-Machartzki, 2017; Hargie, 2017; Jones et al., 2017; Tagg, 2012). Discriminatory policies also have a role to play in maintaining the climate of violence that trans women experience (Jones et al., 2017), as well as being outed (McClearen, 2015), violence from staff, the public, and being pushed out of sport (Cohen, 2008) and having to choose between continuing to play or transitioning (Lucas-Carr et al., 2012). Discrimination shapes sport participation making the trans population proportionally and on average less engaged in sports activities than cis people (Muchicko et al., 2014). We might imagine that these kinds of experiences have negative consequences for their athletic ability and athletic development, though they are not typically factored into scientific studies of testosterone.

Knowledge Production and Impact

Different depth, weight, and levels of consideration of scientific knowledge and political factors are imbedded in the framing of trans policies in sport.

The literature on trans sport policies, their implementation, people who write them and apply them, consequences for athletes, and the debates they frame is constitutive of the social hierarchy of knowledge and the discrediting of some sciences for the benefit of others (Pape, 2019). Biomedical studies are overvalued in sports policies in comparison to social sciences studies (Pape, 2019). Research in science and gender, and in particular the work of Anne Fausto-Sterling, have shown that sex is gender-dependent and that the gender system modifies so-called biological sex (Ritz, 2017). The exclusion of certain types of knowledge from the restricted definition of scientific by the sport's governing bodies makes it possible to obscure the power relations at play in the creation, maintenance, and legitimization of regulations (Pape, 2017, 2019). Thus, the literature insists on looking at regulations not only at a biological scale, but on the

social and political climate that creates them. This analytical framework makes it possible to highlight the links between some sports organizations, studies in biomedical sciences, and groups with an anti-trans agenda.

Scientists working in this field have organizational ties that suggest particular ideological commitments (Itani 2020, Pape, 2019, Pearce et al. 2020). Moreover, some biomedical scientists that publish academic papers on trans women participation in sport to advise sport organizations are part of anti-trans activism. For example, in the United Kingdom (UK) since 2017 and the plan to reform the 2004 Gender Recognition Act (very expensive, invasive, medicalized, and long process to change the gender marker on the birth certificate), some women's trans-exclusionary organizations, such as Fair Play for Women, expanded their movement (Itani, 2020; Pearce et al., 2020). The science is used by this group strategically (using only the data that suit their view) to assist their essentialist agenda that sex is immutable. These organizations use sports as a strategy because preconceived ideas about trans individuals can spread quickly through sport due to the sensationalist medical treatment. Sports are used as a strategy because it emulates strong debate. This allows them to quickly spread their agenda as their target does not look at how the science they used is constructed (Lefebvre, 2019) and rely on misinformation regarding the implementation of sport policies (Pape, 2000). For example, we can see that there is data that is systematically overlooked, like the diversity advantages that one can have while playing sport. These include financial material resources such access to infrastructure, equipment, nutrition, time to train, salary, etc. Yet these resources are not subjected to regulations and are not framed by sports organizations to ensure fairness (Karkazis and Jordan-Young, 2018). It is therefore important to consider the differences in considerations by the governing sports organization between all the sports advantages that may exist and the fact that only biological factors are policed on women's bodies. While Michael Phelps is celebrated for his physical advantages that allow him to compete and be successful at the highest level of sport, women (cis, trans, and intersex) are scrutinized and have their performance medically restricted (Jones et al., 2020; Karkazis and Jordan-Young, 2012, 2018).

Approaches to Balancing Biological and Sociological Considerations

As the grey literature revealed, some sport organizations have produced regulations that take into account social issues, discrimination experienced by trans women, and the discourse surrounding their participation in sport competitions. For example, the rules of the UK Roller Derby Association (UKRDA), a collective sport with important and violent contacts, allow trans women to compete in the women category with no restrictions by taking into account the diversity of women's bodies (cis, intersex, and/or trans) and the many factors of sports performance other than physical capacities, namely technical, tactical, and strategic intelligence: "The UKRDA do not believe that we can prove that transgender skaters experience a physical advantage or disadvantage over cis-gendered (non-trans) skaters. To maintain fairness and equality, and as well as

to avoid legal challenge, the UKRDA feel that we cannot categorically state that skaters who identify as a different gender than that which they were assigned at birth experience a physical advantage and we cannot, therefore, utilize the legal exceptions. The legislation states that evidence is required to claim an 'unfair advantage.' In a roller derby team, there exists a spectrum of heights, weights, natural abilities, and existing or gained fitness levels. Each skater on a team utilizes the strengths they have – whether it be a speedy, explosive jammer compared to a more powerful, offensive style jammer, or a super-agile blocker compared to a powerhouse blocker. It is not therefore relevant to deem a transgender skater ineligible for inclusion in roller derby based on what stage of gender transition they are at or how their physical body presents.”

The statement from the Australian Human Rights Commission Regarding Testosterone and Competitive Advantage notably draws to sport organizations in process of policy-making's attention that knowledge on testosterone is restricted and debated, and many factors outside testosterone influence sport performance and capacities. Further, the statement reminds affected parties that there have been no cases of people transitioning solely to gain advantage in a sport, and that, “for transgender athletes, as for all athletes, sport is about the physical, social and mental health benefits of participation” (p.37). There are, regrettably, also problematic clauses in the statement which permit Australian sport governing bodies to make their own decisions at the elite level and continue with exclusionary practices. More work needs to be done to act, and to seam these acknowledgements closer to implementation.

For a list of some of the sport organizations in Canada who have trans inclusion policies, please see Appendix C.

Conclusion

There is currently no substantial research evidence of any biological advantages that would impede the fairness of trans women competing in elite women's sport. There currently exists no evidence to suggest that trans women who elect to suppress testosterone (through, for example, gender affirming hormone therapy and/or surgical gonad removal) maintain disproportionate advantages over cis women indefinitely. More specifically, current evidence suggests any biological advantages trans women have in sport performance do not fall outside the range observed among cis women after testosterone suppression. Red blood cell count is well within cis women's range after four months of testosterone suppression. Strength is a possible exception, a topic on which research is limited/non-existent. Available related research seems to suggest strength decreases over time after suppression, demonstrated through significant decreases in strength (LBM, CSA) after 12 months of suppression and ongoing decreases after the arbitrary one-year mark. Even so, the cut-off levels of testosterone for trans women and of the length of time after testosterone suppression in current sport policies are not currently evidence based. Most biologically based studies

focused on the question of appropriate levels of testosterone for testosterone-suppressed trans women for fair competition among women (cis and trans) and did not arrive at a consensus about (a) whether the question of testosterone is a and/or the most salient biological marker, nor (b) assuming testosterone is an imperfect proxy of heightened and/or unfair advantage in performance, at what levels such advantages are incurred. Further, there is currently no existing evidence on the measurable difference testosterone has on lean muscle mass for active (versus sedentary) individuals, and no research in the context of high-performance athletes that would help understand, for example, testosterone uptake capacities among cis and trans women athletes. There are also questions which remain about what length of time gender-affirming hormone therapies are appropriate to be comparable to cis women on various factors, as well as questions about the definitions of what can be celebrated as a biological gift versus condemned as an 'unfair advantage' and where the boundaries of those are.

Additional biomarkers (such as handgrip strength, hip angle, bone density) have been used uncritically in positivist biological studies to demonstrate cis men's purported biological advantages over cis women, but there is not sufficient evidence these measures are salient to the question of trans women's participation. In fact, studies often use these measures without examining appropriate comparison populations (often resulting in an uncritical comparison of cis men to trans women, which additional evidence suggests is not apt), possible confounding factors, controls for weight and height, controls for hand size, or other methodological concerns. Some study authors also selectively reported on measures (for example, one review left out the results of a primary study whose conclusion ran counter to their claims), did not include important conflicts of interest (such as funding from groups who support the exclusion of trans women from sport and/or society), and relied on 'common knowledge' claims that were not scientifically supported as foundational assumptions.

There are also key areas of positivist biological research that remain unexplored. For example, the ways in which trans women are biologically disadvantaged in elite sport, and the ways in which cis women tend to outperform cis men on a population level in some sport-relevant attributes (e.g., endurance, recovery, perfusion, balance).

In this dearth of positivist evidence (evidence which anticipates one objective truth), research indicates that people not only fall back to socio-cultural, historical, geopolitical systems, but are actively engaged in political practices of non-knowledge and active ignorance within these systems when it comes to the topics of gender, sex, and trans women's participation in elite sport. It is within this absence of biological evidence and within these systems that current arbitrary boundaries, policies, limits, and levels are formed.

There is strong evidence that elite sport policy is made within transmisogynist, misogynoir, racist, geopolitical cultural norms. There is evidence that the fears that cis women need be protected from trans women in elite sport are unsubstantiated and

misplaced. What threatens women's elite sport, for cis and trans women, is not trans women, but is rather misogyny in the form of underfunding, non-parity in participation and leadership, inequitable sport space allocation/access, and a range of sporting opportunities not afforded to women (cis women and trans women) in equitable ways. Counter to these misplaced fears and in addition to the limited opportunities for women in sport, trans women also face overlapping systems of cissexism and transmisogyny (among others) in accessing sporting opportunities.

To answer the positivist question of what biological factors would make sport 'fair' among cis and trans women, more research needs to be funded and conducted using appropriate, ethical methods and populations. The critical question of what sociocultural factors would make sport 'fair' among cis and trans women can already be adequately answered but requires transformations and more actions towards equitable sport at the elite level. Many current trans inclusion policies at high-performance levels in Canada act as trans exclusion policies or have arbitrary criteria that trans women must meet to compete (Re-creation Collective, 2021). Sport organizers need better education, dedicated resources, and high-quality research to confront, disrupt or transform gendered systems.

Bibliography

- Alahmari, K. A., Kakaraparthi, V. N., Reddy, R. S., Silvian, P. S., Ahmad, I., & Rengaramanujam, K. (2019). Percentage difference of hand dimensions and their correlation with hand grip and pinch strength among schoolchildren in Saudi Arabia. *Nigerian Journal of Clinical Practice*, 22(10), 1356-1364.
- Åstrand, P. O., Cuddy, T. E., Saltin, B., & Stenberg, J. (1964). Cardiac output during submaximal and maximal work. *Journal of Applied Physiology*, 19(2), 268-274.
- Bachman, E., Travison, T. G., Basaria, S., Davda, M. N., Guo, W., Li, M., & Bhasin, S. (2014). Testosterone induces erythrocytosis via increased erythropoietin and suppressed hepcidin: evidence for a new erythropoietin/hemoglobin set point. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, 69(6), 725-735.
- Barras, A., Frith, H., Jarvis, N., & Lucena, R. (2021). Timelines and transitions: Understanding transgender and non-binary people's participation in everyday sport and physical exercise through a temporal lens. In *Temporality in Qualitative Inquiry* (pp. 57–71). Routledge.
- Bauer, G., & Scheim, A. (2016). *Transgender people in Ontario, Canada: Statistics from the Trans PULSE Project to inform human rights policy*. University of Western Ontario.
- BBC Sport. (14 April 2003). Radcliffe raises the standard. BBC Online. http://news.bbc.co.uk/sport2/hi/athletics/london_marathon_2003/2945709.stm
- Bermon, S., & Garnier, P. Y. (2017). Serum androgen levels and their relation to performance in track and field: Mass spectrometry results from 2127 observations in male and female athletes. *British Journal of Sports Medicine*, 51, 1309–1314.
- Bohuon, A. (2008). Sport et bicatégorisation par sexe: Test de féminité et ambiguïtés du discours médical. *Nouvelles Questions Féministes*, 27(1), 80–91. Cairn.info.
- Bohuon, Anaïs. (2012). *Le test de féminité dans les compétitions sportives: Une histoire classée X ?* Editions iXe.
- Bourguignon, J. P., Vandeweghe, M., Vanderschueren-Lodeweyckx, M., Malvaux, P., Wolter, R., Caju, M. D., & Ernould, C. (1986). Pubertal growth and final height in hypopituitary boys: a minor role of bone age at onset of puberty. *The Journal of Clinical Endocrinology & Metabolism*, 63(2), 376-382.
- Bouwsema, M. M., Tedjasaputra, V., & Stickland, M. K. (2017). Are there sex differences in the capillary blood volume and diffusing capacity response to exercise? *Journal of Applied Physiology*, 122(3), 460-469.

- Breslav, I. S., Segizbaeva, M. O., & Isaev, G. G. (2000). Does the respiratory system limit the aerobic working capacity of humans? *Human Physiology*, 26(4), 481-487.
- Bruton, M. R., O'Dwyer, N., & Adams, R. (2013). Sex differences in the kinematics and neuromuscular control of landing: Biological, environmental and sociocultural factors. *Journal of Electromyography and Kinesiology*, 23(4): 747-758.
- Buckinx, F., Landi, F., Cesari, M., Fielding, R.A., Visser, M., Engelke, K., Maggi, S., Dennison, E., Al-Daghri, N.M., Allepaerts, S., Bauer, J., Bautmans, I., Brandi, M.L., Bruyère, O., Cederholm, T., Cerreta, F., Cherubini, A., Cooper, C., Cruz-Jentoft, A. & Kanis, J.A. (2018). Pitfalls in the measurement of muscle mass: A need for a reference standard. *J Cachexia Sarcopenia Muscle*, 9(2): 269-278.
- Cahn, S.K. (1993). From the “Muscle Moll” to the “Butch” Ballplayer: Mannishness, Lesbianism and Homophobia in U.S. Women’s Sport. *Feminist Studies*, 19(2), 343-368.
- Castan-Vicente, F., Bohuon, A., Henaff-Pineau, P., & Chanavat, N. (2019). Les pionnières françaises du sport international des femmes: Alice Milliat et Marie-Thérèse Eyquem, entre tutelle médicale et non-mixité militante? *Staps*, 3, 31–47.
- Castro, M. J., McCANN, D. J., Shaffrath, J. D., & Adams, W. C. (1995). Peak torque per unit cross-sectional area differs between strength-trained and untrained young adults. *Medicine and science in sports and exercise*, 27(3), 397-403.
- Caudwell, J. (2014). [Transgender] young men: Gendered subjectivities and the physically active body. *Sport, Education and Society*, 19(4), 398–414.
- Chilibeck, P. D., Calder, A. W., Sale, D. G., & Webber, C. E. (1997). A comparison of strength and muscle mass increases during resistance training in young women. *European journal of applied physiology and occupational physiology*, 77(1), 170-175.
- Cohen, J. H., & Semerjian, T. Z. (2008). The Collision of Trans-Experience and the Politics of Women’s Ice Hockey. *International Journal of Transgenderism*, 10(3–4), 133–145.
- Costill, D. L., Daniels, J., Evans, W., Fink, W., Krahenbuhl, G., & Saltin, B. (1976). Skeletal muscle enzymes and fiber composition in male and female track athletes. *Journal of applied physiology*, 40(2), 149-154.
- Degens, H., Stasiulis, A., Skurvydas, A., Statkeviciene, B., & Venckunas, T. (2019). Physiological comparison between non-athletes, endurance, power and team athletes. *European journal of applied physiology*, 119(6), 1377-1386.

- Devine, J. W. (2019). Gender, steroids, and fairness in sport. *Sport, Ethics and Philosophy*, 13(2), 161-169.
- Devis-Devis, J., Valencia-Peris, A., Pereira-García, S., Fuentes-Miguel, J., & Pérez-Samaniego, V. (2020). Physical activity and sport in trans persons before and after gender disclosure: Prevalence, frequency, and type of activities. *Journal of Physical Activity and Health*, 17(6), 650–656.
- Elling-Machartzki, A. (2017). Extraordinary body-self narratives: Sport and physical activity in the lives of transgender people. *Leisure Studies*, 36(2), 256–268.
- Erikainen, S. (2020). *Gender verification and the making of the female body in sport: A history of the present*. Routledge.
- Espineira, K. (2015). *Médiacultures: La transidentité en télévision*. L'Harmattan.
- Euro barometer (2010). Sport and Physical Activity. European Commission Eurobarometer, 72.3.
- Ferrari E.P., Santos Silva D.A., Martins R.C., Fidelix Y.L., Petroski E.L. (2013) Morphological Characteristics of Professional Ballet Dancers of the Bolshoi Theater Company. *Collegium Antropologicum*, Vol. 37 s.2 no.2
- Figuera, T. M., da Silva, E., Lindenau, J. D. R., & Spritzer, P. M. (2018). Impact of cross-sex hormone therapy on bone mineral density and body composition in transwomen. *Clinical endocrinology*, 88(6), 856-862
- Foddy, B., & Savulescu, J. (2011). Time to re-evaluate gender segregation in athletics?. *British Journal of Sports Medicine*, 45(15), 1184-1188.
- Fomin, Å., Ahlstrand, M., Schill, H. G., Lund, L. H., Ståhlberg, M., Manouras, A., & Gabrielsen, A. (2012). Sex differences in response to maximal exercise stress test in trained adolescents. *BMC pediatrics*, 12(1), 1-8.
- Forbes, G. B. (1974). Stature and lean body mass. *The American journal of clinical nutrition*, 27(6), 595-602.
- Genel, M. (2017). Transgender athletes: how can they be accommodated?. *Current sports medicine reports*, 16(1), 12-13.
- Gill-Peterson, J. (2014). The technical capacities of the body: Assembling race, technology, and transgender. *Transgender Studies Quarterly*, 1(3), 402-418.

- Grant, J.M., Mottet, L., Tanis, J.E., Harrison, J., Herman, J., Keisling, M. (2011). *Injustice at every turn: A report of the national transgender discrimination survey*. National Center for Transgender Equality.
- Grelsamer, R. P., Dubey, A., & Weinstein, C. H. (2005). Men and women have similar Q angles: a clinical and trigonometric evaluation. *The Journal of bone and joint surgery. British volume*, 87(11), 1498-1501.
- Griffin, Pat. (1998). *Strong women, deep closets: Lesbians and homophobia in sport*. Human Kinetics.
- Griggs, R. C., Kingston, W., Jozefowicz, R. F., Herr, B. E., Forbes, G. & Halliday, D. (1989). Effect of testosterone on muscle mass and muscle protein synthesis. *Journal of Applied Physiology*, 66(1), 498-503.
- Haizlip, K. M., Harrison, B. C., & Leinwand, L. A. (2015). Sex-based differences in skeletal muscle kinetics and fiber-type composition. *Physiology*, 30(1), 30-39.
- Hamilton, B. R., Lima, G., Barrett, J., Seal, L., Kolliari-Turner, A., Wang, G., ... & Pitsiladis, Y. P. (2021). Integrating Transwomen and female athletes with differences of sex development (DSD) into elite competition: the FIMS 2021 consensus statement. *Sports Medicine*, 51(7), 1401-1415.
- Handelsman, D. J., Hirschberg, A. L., & Berman, S. (2018). Circulating testosterone as the hormonal basis of sex differences in athletic performance. *Endocrine reviews*, 39(5), 803-829.
- Harbo T. Brincks J. & Andersen H. (2011) Maximal isokinetic and isometric muscle strength of major muscle groups related to age, body mass, height, and sex in 178 healthy subjects. *European Journal of Applied Physiology*, 112, 267-275.
- Hargreaves, J. (2012). Chapter 9-Olympic women: A struggle for recognition: Chapter taken from *Sporting Females: Critical Issues in the History and Sociology of Women's Sport* ISBN: 978-0-415-07028-7. *Routledge Online Studies on the Olympic and Paralympic Games*, 1(12), 209-234.
- Harms, C. A., Cooper, D., & Tanaka, H. (2011). Exercise physiology of normal development, sex differences, and aging. *Comprehensive Physiology*, 1(4), 1649-1678.
- Hargie, O. D. W., Mitchell, D. H., & Somerville, I. J. A. (2017). 'People have a knack of making you feel excluded if they catch on to your difference': Transgender experiences of exclusion in sport. *International Review for the Sociology of Sport*, 52(2), 223–239.

- Harper, J. (2015). Race Times for Transgender Athletes. *Journal of Sporting Cultures and Identities*, 6(1), 1-9.
- Harper, J., Lima, G., Kolliari-Turner, A., Malinsky, F. R., Wang, G., Martinez-Patino, M. J., ... & Pitsiladis, Y. P. (2018). The fluidity of gender and implications for the biology of inclusion for transgender and intersex athletes. *Current sports medicine reports*, 17(12), 467-472.
- Harper, J. (2020). Equality and Access: *The Importance and Complexity of Transgender and Intersex Inclusion in Sports*. Online presentation sponsored by Georgia College on Oct 21, 2020.
- Harper, J., O'Donnell, E., Khorashad, B. S., McDermott, H., & Witcomb, G. L. (2021). How does hormone transition in transgender women change body composition, muscle strength and haemoglobin? Systematic review with a focus on the implications for sport participation. *British Journal of Sports Medicine*, 55(15), 865-872.
- Heggie, V. (2010). Testing sex and gender in sports; reinventing, reimagining and reconstructing histories. *Endeavour*, 34(4), 157-163.
- Henne, K. (2014). The “science” of fair play in sport: Gender and the politics of testing. *Signs: Journal of Women in Culture and Society*, 39(3), 787-812.
- Hertel, J., Dorfman, J. H., & Braham, R. A. (2004). Lower extremity malalignments and anterior cruciate ligament injury history. *Journal of sports science & medicine*, 3(4), 220.
- Hilton, E. N., & Lundberg, T. R. (2021). Transgender Women in the Female Category of Sport: Perspectives on Testosterone Suppression and Performance Advantage. *Sports Medicine*, 51(2), 199–214.
- Hopkins, S. R., Kubo, K., Moon, Y. S., Darquenne, C. J., & Theilmann, R. J. (2018). Athlete Lungs: Bigger and Better or Just Bigger?. In *C29. LUNG STRUCTURE AND FUNCTION: NEW INSIGHTS FROM MEASUREMENT AND MODELING* (pp. A4670-A4670). American Thoracic Society.
- Ingram, B. J., & Thomas, C. L. (2019). Transgender policy in sport, a review of current policy and commentary of the challenges of policy creation. *Current sports medicine reports*, 18(6), 239-247.
- Itani, S. (2020). The ‘Feminist’ Discourse on Trans Exclusion from Sports. ジェンダー研究: お茶の水女子大学ジェンダー研究所年報, (23), 27–46.
- Ivy, V., & Friedlaender, B. (2020). A Defense of Intentional Microaggressions and Microaggressive Harassment: The Fundamental Attribution Error, Harassment, and

- Gaslighting of Transgender Athletes. In J. Weekes Schroer & L. Freeman, *Microaggressions and Philosophy* (1st Edition, pp. 184–204). Routledge.
- Janssen, I., Heymsfield, S.B., Wang, Z.M., & Ross, R. (2000). Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. *Journal of Applied Physiology*, 89(1).
- Jefferson Lenskyj, H. (2018). *Gender, Athletes' Rights, and the Court of Arbitration for Sport*. Emerald Publishing Limited.
- Jones, B. A., Arcelus, J., Bouman, W. P., & Haycraft, E. (2017). Sport and Transgender People: A Systematic Review of the Literature Relating to Sport Participation and Competitive Sport Policies. *Sports Medicine*, 47(4), 701–716.
- Jones, B.A., Arcelus, J., Bouman, W.P. *et al.* (2020). Authors' Reply to Richardson and Chen: Comment on "Sport and Transgender People: A Systematic Review of the Literature Relating to Sport Participation and Competitive Sport Policies". *Sports Medicine*, 50, 1861–1862.
- Karkazis, K., & Jordan-Young, R. (2015). Debating a testosterone "sex gap". *Science*, 348(6237), 858-860.
- Karkazis, K., & Jordan-Young, R. M. (2018). The Powers of Testosterone: Obscuring Race and Regional Bias in the Regulation of Women Athletes. *Feminist Formations*, 30(2), 1–39.
- Kernozek, T. W., & Greer, N. L. (1993). Quadriceps angle and rearfoot motion: relationships in walking. *Archives of physical medicine and rehabilitation*, 74(4), 407-410.
- Klein, A., Krane, V., & Paule-Koba, A. L. (2018). Bodily changes and performance effects in a transitioning transgender college athlete. *Qualitative Research in Sport, Exercise and Health*, 1(5).
- Krawczyk B., Sklad M., & Majle B. (1955). Body Components of Male and Female Athletes Representing Various Sports. *Biology of Sport*, 12, 243-250.
- Leslie, W. D. (2012). Ethnic differences in bone mass—clinical implications. *The Journal of Clinical Endocrinology & Metabolism*, 97(12), 4329-4340.
- Ljungqvist, A. (2018). Sex segregation and sport. *British Journal of Sports Medicine*, 52(1), 3–3.
- McClearn, J. (2015). The Paradox of Fallon's Fight: Interlocking Discourses of Sexism and Cissexism in Mixed Martial Arts Fighting. *New Formations*, 86(1), 74–88.
- Nazem, T. G., & Ackerman, K. E. (2012). The female athlete triad. *Sports health*, 4(4), 302-311.

- Nguyen, A. D., Boling, M. C., Levine, B., & Shultz, S. J. (2009). Relationships between lower extremity alignment and the quadriceps angle. *Clinical journal of sport medicine: official journal of the Canadian Academy of Sport Medicine*, 19(3), 201.
- Nickander, J., Themudo, R., Sigfridsson, A., Xue, H., Kellman, P., & Ugander, M. (2020). Females have higher myocardial perfusion, blood volume and extracellular volume compared to males—an adenosine stress cardiovascular magnetic resonance study. *Scientific Reports*, 10(1), 1-9.
- Ohlert, J., Rau, T., Rulofs, B., & Allroggen, M. (2020). Comparison of elite athletes' sexual violence experiences in and outside sport. *German Journal of Exercise and Sport Research*, 50(4), 435–443.
- Pape, M. (2017). The Fairest of Them All: Gender-Determining Institutions and the Science of Sex Testing. *Gender Panic, Gender Policy*, 24, 177–200.
- Pape, M. (2019). Expertise and Non-binary Bodies: Sex, Gender and the Case of Dutee Chand. *Body & Society*, 25(4), 3–28.
- Pavlenko, F. (2021, June 11). *Santé et genre: Incidence sur le désengagement et les barrières à la reprise du sport pour les personnes trans* [Communication]. Colloque du Réseau des stagiaires de recherche sur le sexe et le genre de l'Institut de la santé des femmes et des hommes des Instituts de recherche en santé du Canada, En ligne.
- Pavlenko, F. (2019). *Faire du sport en tant que personne trans: Redéfinitions, violences et négociations* [Mémoire de Master 2 Egal'APS- Dirigé par Aurélie Olivesi et Muriel Salle]. Université Claude Bernard Lyon 1.
- Pearce, R., Erikainen, S., & Vincent, B. (2020). TERF wars: An introduction. *The Sociological Review*, 68(4), 677-698.
- Pérez-Samaniego, V., Fuentes-Miguel, J., Pereira-García, S., López-Cañada, E., & Devís-Devís, J. (2019). Experiences of trans persons in physical activity and sport: A qualitative meta-synthesis. *Sport Management Review*, 22(4), 439–451.
- Pfister G. (2011) Gender equality and (elite) sport. EPAS (2011) INF 25. Department of Exercise and Sport Sciences, University of Copenhagen. Enlarged Partial Agreement on Sport (EPAS). Strasbourg, 28 November 2011.
- Pieper, L. P. (2016). *Sex testing gender policing in women's sports*. University of Illinois Press.
- Pike, J. (2021). Safety, fairness, and inclusion: transgender athletes and the essence of Rugby. *Journal of the Philosophy of Sport*, 48(2), 155-168.

- Pitsiladis, Y., Harper, J., Betancurt, J. O., Martinez-Patino, M.-J., Parisi, A., Wang, G., & Pigozzi, F. (2016). Beyond Fairness: The Biology of Inclusion for Transgender and Intersex Athletes. *Current Sports Medicine Reports*, 15(6), 386–388.
- Prudhomme-Poncet, L. (2003). Mixité et non-mixité: L'exemple du football féminin. *Clio. Femmes, Genre, Histoire*, 18, 167–175.
- Re-creation Collective (2021, June 4). *Hedging, Erasing, Absolving, and Other "EDI" Pitfalls: Recreating Equity, Diversity and Inclusion Policies, and Praxis* [conference session]. Canadian Sociological Association Annual Conference, virtual/Edmonton, Canada.
- Rene, K. (1984, October). Sex Differences in Joint Mobility. In Proceedings of the Human Factors Society Annual Meeting (Vol. 28, No. 11, pp. 1006-1006). Sage CA: Los Angeles, CA: SAGE Publications.
- Richardson, A., & Chen, M. A. (2020). Comment on: "Sport and Transgender People: A Systematic Review of the Literature Relating to Sport Participation and Competitive Sport Policies." *Sports Medicine*, 50(10), 1857–1859.
- Ritz, S. A. (2017). Complexities of Addressing Sex in Cell Culture Research. *Signs: Journal of Women in Culture and Society*, 42(2), 307–327.
- Roberts, B. M., Nuckols, G., & Krieger, J. W. (2020). Sex differences in resistance training: a systematic review and meta-analysis. *The Journal of Strength & Conditioning Research*, 34(5).
- Roberts, T. A., Smalley, J., & Ahrendt, D. (2021). Effect of gender affirming hormones on athletic performance in transwomen and transmen: Implications for sporting organisations and legislators. *British Journal of Sports Medicine*, 55(11), 577–583.
- Rosol, N. (2004). « Le sport vers le féminisme ». L'engagement du milieu athlétique féminin français au temps de la FSFSF (1917-1936). *Staps*, 4, 63–77.
- Rotondi, N. K., Bauer, G. R., Travers, R., Travers, A., Scanlon, K., & Kaay, M. (2011). Depression in Male-to-Female Transgender Ontarians: Results from the Trans PULSE Project. *Canadian Journal of Community Mental Health*, 30(2), 113–133.
- Sánchez, F. J., Martínez-Patiño, M. J., & Vilain, E. (2013). The New Policy on Hyperandrogenism in Elite Female Athletes is Not About "Sex Testing." *The Journal of Sex Research*, 50(2), 112–115.
- Schantz, P., RANDALL-FOX, E., Hutchison, W., Tydén, A., & Åstrand, P. O. (1983). Muscle fibre type distribution, muscle cross-sectional area and maximal voluntary strength in humans. *Acta Physiologica Scandinavica*, 117(2), 219-226.

- Scheim, A., Bauer, G., & Pyne, J. (2014). Avoidance of public spaces by trans Ontarians: The impact of transphobia on daily life. *Trans PULSE E-Bulletin*, 4(1).
- Sigward, S. M., & Powers, C. M. (2006). The influence of gender on knee kinematics, kinetics and muscle activation patterns during side-step cutting. *Clinical biomechanics*, 21(1), 41-48.
- Sönksen, P., Holt, R.I.G., Bohning, W., Guha, N., Cowan, D.A., Bartlett, C. & Bohning, D. (2018). Why do endocrine profiles in elite athletes differ between sports?. *Clinical Diabetes and Endocrinology*, 4(1), 1-16.
- SoRelle, J. A., Jiao, R., Gao, E., Veazey, J., Frame, I., Quinn, A. M., & Patel, K. (2019). Impact of hormone therapy on laboratory values in transgender patients. *Clinical chemistry*, 65(1), 170-179.
- Sullivan, C. F. (2011). Gender Verification and Gender Policies in Elite Sport: Eligibility and “Fair Play.” *Journal of Sport and Social Issues*, 35(4), 400–419.
- Sutherland, M. A., Wassersug, R. J., & Rosenberg, K. R. (2017). From transsexuals to transhumans in elite athletics: The implications of osteology (and other issues) in leveling the playing field. In *Transgender Athletes in Competitive Sport* (pp. 173–193). Routledge.
- Tagg, B. (2012). Transgender Netballers: Ethical Issues and Lived Realities. *Sociology of Sport Journal*, 29(2), 151–167.
- Tannenbaum, C., & Bekker, S. (2019). Sex, gender, and sports. *BMJ (Clinical Research Ed.)*, 364.
- Tarnopolsky, M. A. (2008). Sex differences in exercise metabolism and the role of 17-beta estradiol. *Medicine and science in sports and exercise*, 40(4), 648-654.
- Teetzel, S. (2017). Athletes’ perceptions of transgender eligibility policies applied in high-performance sport in Canada. In *Transgender athletes in competitive sport* (pp. 68-79). Routledge.
- Thomas, J. S., Corcos, D. M., & Hasan, Z. (1998). The influence of gender on spine, hip, knee, and ankle motions during a reaching task. *Journal of motor behavior*, 30(2), 98-103.
- Thum, T., & Borlak, J. (2002). Testosterone, cytochrome P450, and cardiac hypertrophy. *The FASEB Journal*, 16(12), 1537-1549.
- Torres, S. F., Reis, J. G., & Abreu, D. C. C. D. (2014). Influence of gender and physical exercise on balance of healthy young adults. *Fisioterapia em Movimento*, 27(3), 399-406.

- Travers, A. (Ed.). (2017). *Transgender athletes in competitive sport*. Taylor & Francis Limited.
- Tuck, S., & Francis, R. (2009). Testosterone, bone and osteoporosis. *Advances in the management of testosterone deficiency*, 37, 123-132.
- Van Caenegem, E., Wierckx, K., Taes, Y., Schreiner, T., Vandewalle, S. A. R. A., Toye, K., & T'Sjoen, G. (2015). Preservation of volumetric bone density and geometry in trans women during cross-sex hormonal therapy: a prospective observational study. *Osteoporosis International*, 26(1), 35-47.
- Vilain, E., Betancurt, J. O., Bueno-Guerra, N., & Martinez-Patiño, M. J. (2017). Transgender athletes in elite sport competitions: Equity and inclusivity. In *Transgender Athletes in Competitive Sport* (pp. 156–170). Routledge.
- Wiik, A., Lundberg, T. R., Rullman, E., Andersson, D. P., Holmberg, M., Mandić, M., Brismar, T. B., Dahlqvist Leinhard, O., Chanpen, S., Flanagan, J. N., Arver, S., & Gustafsson, T. (2019). Muscle strength, size and composition following 12 months of gender-affirming treatment in transgender individuals. *The Journal of Clinical Endocrinology and Metabolism*, 105(3), e805-e813.
- Wyon, M. A., Hutchings, K. M.; Wells, A., & Nevill, A. M. (2014). Body Mass Index, Nutritional Knowledge, and Eating Behaviors in Elite Student and Professional Ballet Dancers. *Clinical Journal of Sport Medicine*, 24(5): p. 390-396.
- Yeung, S. S., Reijnierse, E. M., Trappenburg, M. C., Hogrel, J. Y., McPhee, J. S., Piasecki, M., & Maier, A. B. (2018). Handgrip strength cannot be assumed a proxy for overall muscle strength. *Journal of the American Medical Directors Association*, 19(8), 703-709.

Appendix A: Detailed Tables of Reviewed Academic and Grey Literature

HRT = hormone replacement therapy
HST = hormonal-surgical treatments

Academic Literature

The first eight articles in the table below are primary studies (i.e., individual original research studies) and syntheses (i.e., systematic reviews, meta-analyses, other syntheses) which the authors considered especially important to highlight given their prominence in literature, policy, and/or media. The rest of the articles listed are presented in order of review.

Table 11 Detailed review table, syntheses and primary literature.

Author(s)	Year	Kind of Study and/or Sample	Methods/ Study design (PICO where relevant: Population, Intervention, Comparator, Outcome)	Self-identified trans researcher(s) lead and/or trans research team members?	Key Conclusions	Key Reviewer Criticisms	Other notes
Jones, B. A., Arcelus, J., Bouman, W. P., & C Haycraft, E.	2021	Literature review	Systematic literature review Research papers: between 1966 and 2015 with keywords - gender dysphoria, gender identity disorder, trans people, trans individual, transgender and transsexual AND physical activity, exercise and sport Regulations: google search	Unknown	In this paper, the authors conducted a literature review of 8 research articles looking at the social and biological conditions affecting trans people's participation in sport and looking at 31 sport regulations governing trans people's participation in sport. The results show that the majority of trans people have had a negative experience within the sports space. A scientific void is observed surrounding the biological issue of trans people having a supposed physical advantage. Thus, sports governing bodies do not rely on any tangible medical evidence to construct their rules, leading to the exclusion of an already marginalized population from competitive sport in this space. Moreover, this logic leads to the reinforcement of the exclusion process that is already in place.	It is important to note that the regulations are not based on medical evidence but rather on an assumption that stems from cissexism and oppositional sexism (Serano, 2007). Namely, the idea that the women's category and the men's category are mutually exclusive and that trans women are in fact men. Under this assumption, federations do not need medical evidence on trans athletes to implement their rules. This is precisely what is denounced in this article. The literature review on qualitative research conducted with trans athletes attests to the violence used against this population in the sports space. Trans athletes have to deal with an anxiety-provoking climate at all stages when competing in sports, whether on the field, in the locker room, or through dress codes. Clubs and federations also take part in this institutional violence: athletes need to obtain a license, and sport organizations maintain discriminatory rules. Finally, this violence can manifest as physical and/or verbal violence from teammates, opponents, staff, supporters. The 31 regulations named in the article have not been fairly studied. The article focuses on the criticism of IOC rules. The inclusive rules of quidditch or roller derby are not presented (although listed in a table).	711-712: conclusion of the analysis of the regulations "Currently, the majority of sport policies unfairly exclude transgender people from competitive sport, as the requirements they place on them are not underpinned by evidence-based medicine. Until (and if) there is consistent and direct evidence to demonstrate transgender people have an athletic advantage, it seems unreasonable to exclude them on any basis." 713: Difference in consideration of biological vs. social advantage factors "At the current time, this is a difficult issue to address considering that there is a lack of direct and consistent physiological performance-related data with transgender people, which is preventing a consensus from being made as to whether transgender people (especially trans-gender female individuals) do or do not have an athletic advantage. It may be sensible to suggest that until there are direct and consistent scientific data to suggest that transgender competitors have an advantage, transgender people should be allowed to compete in accordance with their gender identity with no restrictions (e.g., no requirement to have cross-sex hormones, gender-confirming surgery). The athletic advantage transgender female individuals are perceived to have (based on

							indirect and ambiguous evidence) may be no greater than widely accepted physiological (e.g., large hands) and financial (e.g., training opportunities) advantages that some cisgender people possess in competitive sport."
Hilton, E., & Lundberg, T.	2020	Analysis of Hilton & Lundberg (2020) Transgender Women in the Female Category of Sport: Perspectives on Testosterone Suppression and Performance Advantage	Presented as a scientific review but more accurately is an argumentative essay	No		Hilton & Lundberg do not appropriately review the available literature and draw false comparisons between men and women athletes. The assumptions employed and conclusion posed by the authors is therefore not supported by evidence found in the literature. The authors systematically use adjustment for mass instead of fat-free mass which leads to significant errors when comparing population groups. This argument is of key importance as transgender women athletes undergoing HRT increase their estradiol, affecting total body fat percentage, and also significantly reduces testosterone, reducing muscle mass, red blood cell count and other factors important for athletic performance. In Table 4 of their article, Hilton & Lundberg (2020) summarize their findings from available literature, categorizing differences between men's and women's athletic performance. This table has many errors and omissions including as some examples: 1. The reference group employed compares "average cis women" to cis men, without adjustment for height or weight. This is significant since cis men are, as a population, taller than cis women, and we would expect to see similar results in comparing any taller group to a shorter group (for example, comparing five foot four inches tall cis women to five foot ten inches tall cis women). 2. Authors state that "grip strength provides an excellent proxy measurement for general strength in a broad population." However, this is incorrect (Yeung et al., 2018). Grip strength is largely correlated with hand size rather than strength due to gripping testing device easier (Alahmari et al., 2019). 3. The authors cite a study whereby testosterone-suppressed untrained transgender women see an increase of lean mass (4% leg and 2% overall) after an intense 8-week training cycle. However, they omit Roberts, Nuckols, & Krieger's (2020) findings that untrained females also show high capacity to build muscle mass especially in upper body strength. The authors also do not show the relative strength compared to	

						trained female competitors - a more appropriate comparison group - nor do they include that their control group without testosterone suppression gained significantly more mass and a 400% greater increase to isometric strength. The authors additionally omit that trans women participants failed to gain any noticeable gains to isometric strength. Yet despite these observations, the authors conclude “endogenous testosterone is of paramount importance for the muscular adaptation to strength training.” 4. They claim the 12 months hormone suppression as determined by the IOC is insufficient by using data where hormone suppression was present for less than two months. 5. Pelvic width comparison is used as a measure, but studies show that pelvic width difference, including q-angle, does not have any benefit for athletic ability (such as moving or jumping); gait differences, lift ability and risk to injury also are not meaningful as a result of q-angle (Bruton, O'Dwyer & Adams, 2013; Hertel, Dorfman & Braham, 2004; Kernozek & Greer, 1993; Thomas, Corcos & Hasan, 1998; Nguyen et al., 2009; Sigward & Powers, 2006). This includes a study by Sigward & Powers which was referenced by the authors as leading to increased injury in athletics, but the original paper states, “No differences in kinematics were found.” 6. Bone density was used extensively as evidence of the advantage trans women retain. The claims were unsubstantiated, with no citations to demonstrate bone density as a performance enhancer. 7. The authors argue that larger lung size is a retained advantage. However, they do not adjust for height and ignore studies which have demonstrated that lung size is not a good predictor for sport performance. The differences are due to respiratory muscles enhancement, not lung size (Degens et al., 2019; Hopkins et al., 2018). These findings are misrepresented in the table with the conclusion that “Respiratory function, pulmonary ventilation (maximal)” are significant, when they are not. Specifically, “MBC is not likely to be an adequate physiological measure of the competence of the respiratory system in strenuous work and should be regarded rather as the	

						biomechanical limit of the possibilities of the ventilatory apparatus" (Breslav, Segizbaeva, & Isaev, 2000). Or that it is not a limiter for exercise, "After differences in lung volume are accounted for there is no intrinsic sex difference in the DLco, Vc, or Dm response to exercise" and "together, these data suggest that the pulmonary capillary blood volume response is proportional to lung size and is adequate to meet individual oxygen demand during exercise" (Bouwsema, Tedjasaputra & Stickland, 2017). The limiting factor in endurance sport however is oxygen carrying capacity of blood (red blood cell count which is affected by hormones dramatically) and heart muscle (Fomin et al., 2012; Åstrand et al., 1964). 8. Hemoglobin (red blood cell count) is drastically affected by HRT, falling in cis women's range after 6 months (SoRelle et al., 2019). This is largely ignored by the authors. 9. Table 4 reports absolute values for Wiik et al (2020) instead of the published height adjusted levels. 10. Hilton & Lundberg exclude the female reference values from Figuera et al (2018) presumably as the latter's conclusion was that appendicular lean mass was similar among trans and reference women, and lower in trans women when compared to cis men, a point that contradicts Hilton & Lundberg's argument.	
Harper, J., O'Donnell, E., et al.	2021	How does hormone transition in transgender women change body composition, muscle strength and haemoglobin? Systematic review with a focus on the implication for sport participation	Systematic review	Yes - lead author	Transwomen experience rapid reductions to hemoglobin as comparable with cis women. Decreases in strength, LBM, and muscle area are also observed but are still higher than cis women even after 36 months. Paper extensively reviews multiple areas that may impact performance such as body fat, hemoglobin, HCT, etc.	Authors use reference studies which largely are not height adjusted and are not comparing athletic sample groups. As a result, comparisons for LBM, muscle area, etc., may be overstated due to lack of appropriate comparison groups. Additionally, a statistical significance in higher LBM does not translate into a practical significance or performance advantage which is currently unmeasured. Authors also heavily rely on studies which use handgrip strength to measure overall strength. There are numerous issues with using this as a reliable test. However, grip strength is largely correlated with hand size due to gripping testing device easier. (i.e., height) Alahmari, K. A., Kakaraparthi, V. N., Reddy, R. S., Silvian, P. S., Ahmad, I., & Rengaramanujam, K. (2019). Percentage difference of hand dimensions and their correlation with handgrip and pinch strength	

						among schoolchildren in Saudi Arabia. Nigerian journal of clinical practice.	
Hamilton, B. R., et al.	2021	Integrating Transwomen and Female Athletes with Differences of Sex Development (DSD) into Elite Competition: The FIMS 2021 Consensus Statement.	Literature review of key leaders in field.	Unknown	There is a lack of data quantifying performance before, during, and after testosterone suppressing interventions. Other biomarkers are important including testosterone sensitivity and responsiveness. Longitudinal studies are required to generate data for biological and sports performance for different sports or athletic events. Authors agree that sport-specific policies are needed based on peer-reviewed scientific evidence. Trans women and women with DSD may still retain some advantage, however this may not be an unfair advantage compared to other genetic or environmental advantages. It may be considered part of that athlete's individual makeup. Recommendation of lowering the testosterone limit to 5nmol/l. Argument made against moving "goalpost" of advantage. Author argues that advantage can never be eliminated in sport but is rather a part of people's unique makeup. Authors suggest unfair advantage needs to be categorized and agreed to.	Study for testosterone limit is based on a limited sample size study (24 women) who were not elite athletes who received testosterone supplement and had moderate performance increases. This highlights a large divide in the literature between elite-level athletes, "active individuals" and untrained individuals. Testosterone likely plays a different moderating level for ceiling muscle mass (i.e., maximum results achieved for elite athletes) and the baseline sedentary levels. These two may not be impacted equally. Testosterone is argued as the only available biomarker that is widely available for eligibility purposes. However, I would argue that the "athletic gender" that is presented is widely flawed and can only be seen as "best available metric that is economical in its application." Paper does not include non-biological results including population differences based on access, nutrition/body composition or other determinants of health that can negatively impact these groups.	Highly influential paper. Large section describing consensus statements and dissenting opinions. There is no thought or reference to potential genetic or developmental advantages that men may have that confer "unfair advantage." While the prevalence of women with DSD and trans women in sports is higher than men with advantage, it seems selective to only be talking about women's protection and not men's as well.
Harper, J.	2015	Race Times for Transgender Athletes	Analysis of 200 race times (self-monitored and self-reported times) from 8 trans women runners.	Yes	Self-reported times were 10% slower after transition.	Not elite athletes	This study is widely considered foundational to the field, despite methodological concerns and criticisms.
Bermon, S. et al.	2017	Serum Androgen Levels in Elite Female Athletes	849 elite female track and field athletes were measured for serum testosterone (T) levels to determine if this population group has an elevated level of T compared to sedentary cis women. 99 th percentile of elite athletes (after removing DSD and doping violations) was 3.08 nmol/l below the 10nmol/l limit set currently for hyperandrogenic	No	Study established baseline values for serum androgen values for elite track and field cisgender female athletes. Individuals who were confirmed or suspected of being hyperandrogenic (DSD) or doping individuals were excluded. Study admits however that not all individuals who are DSD or doping would necessarily be filtered out. Individuals were asked about their menstrual status and oral contraceptive use. Additionally, confounding variables such as athletic event, age and ethnicity were also all evaluated. Authors suggest that baseline hormonal profile information can be used to develop an Athlete Biological Passport (ABP) for evidence-based, fair policies and recommendations around anti-	Population sample included track and field athletes, as a result these results are not generalizable to other sports or events where high T is an advantage (evidence for cardio-based activities minimizes T advantage compared with strength-based events). All but free testosterone (fT) differed significantly between types of events (age for sprinters was significant, while long distance runners had below average serum T levels). DSD is noted as 140x more prevalent than in normal population, this evidence should be examined for selection bias or under-representation of population sampling (i.e., we test athletes but not all individuals).	Why this advantage and not others (i.e., Michael Phelps arm span, oxidization)? Interesting crossover between doping concerns and baseline testosterone levels for women's sports. Historical bias (i.e., 1972 Olympics & soviet fears of forced doping.) Must evaluate not just effect of T but also DHEAS, SHBG or other receptor base which makes testosterone levels actually impact muscle mass (i.e., strength/athletic impact).

			women with androgen sensitivity.		doping regulation. However, it is important to note that, - “There is no clear scientific evidence proving that a high level of (sic, naturally produced) T is a significant determinant of performance in female sports.” Authors do not mention that DSD is overrepresented in elite athlete population group as an indicator that DSD and high levels of testosterone are indicative of high performance (i.e., selection bias of competition) and should check for social factors as well (i.e., physical appearance may socially select individuals to participate in sport).	ABP has been shown to be a more effective deterrent on doping in sports (5) and may be encouraged from a player safety and fairness perspective. Large distribution P0-P100 and P25-P75 suggests 99th percentile may not be as significant towards athletic effect. Serum T levels were not compared to athletic success at these events. As such it may be disingenuous to say that any population-based cut-off is appropriate. Elite athletes represent the top 99th percentile in athletic results (including speed, strength etc.) and therefore mean population distribution has little meaning as all elite athlete individuals are edge-case scenarios. Measurement for T is highly varied by time of day, this makes baseline testing very difficult unless T is measured repeatedly over several time intervals.	
Roberts, T. A., Smalley, J., & Ahrendt, D.	2021	Effect of HRT on certain physical abilities of trans men and women	(PICO where relevant: Population, Intervention, Comparator, Outcome) Population: 29 trans men and 46 trans women in the U.S. military, between the ages of 19 and 46 (78% were under 30). Intervention: Comparison of performance before and during the first 30 months of HRT. - Number of push-ups in 1 min, - Number of sit-ups in 1 min, - Time taken to run 1.5 miles (2,400 m). Comparator: cis men and cis women, no information given on the number, the average height/weight of the cis men is provided = 178 cm/83 kg as is the average	No	Background: The authors postulate that testosterone gives athletes a physical advantage when competing. The major changes occur during the first year of HRT. Methods: <i>Study population</i> - 29 trans men and 46 trans women under the age of 30 who are in the US Army, between 2004 and 2014. <i>Outcome measures</i> - fitness testing before HRT, during and after the first year on HRT, and for 30 months after starting treatment. Results: <i>Effect of gender affirming hormones on body composition and athletics performance</i> - The age at which the athlete begins HRT is shown to have no impact on the results. For trans women, estrogen intake is associated with weight gain and decreased physical ability. For trans men, testosterone is shown to have little impact on weight, but it increased their physical abilities. <i>Athletic performance among transgender service members</i> - Before HRT, trans women had a lower push-up score per minute than cis men, but higher than cis women. This difference was no longer present after two years of hormone treatment. The same is true when it comes to the number of push-ups completed. Their running times after HRT were lower than for cis men but not as low as for cis women. The trans men in the study did more push-ups than cis women before HRT but less than cis men. After one year of HRT, the difference between the trans men and cis men had disappeared.	This research suggests that it is possible to evaluate the physical abilities of trans athletes before and after starting hormonal treatment. However, the number of variables analyzed is limited. Drawing conclusions about athletic performance based on the number of push-ups and sit-ups a person can complete and how fast they can run 2,400 meters seems like a flawed exercise. Indeed, succeeding in these exercises cannot be correlated with an expectation of a high or very high level of performance in many sports. For example, the number of kick-ups that a person can do in soccer cannot be correlated with their level of performance in a game. Another interesting finding that has not been widely discussed is that trans men, who were trans before they started taking testosterone, performed better than cis women in push-ups and sit-ups. More importantly, they performed a similar number of sit-ups to cis men. The level of testosterone in the blood can therefore hardly be the only indicator of performance in sports. Intra-group differences are not analyzed.	Terminology: Transmen/ transwomen or transgender “cis gender women”

			height/weight of the cis women = 164 cm /65 kg. Outcome: Trans women: increased weight, decreased performance. Push-ups and sit-ups per minute comparable to cis women after HRT. Running time performance lower than cis men but better than cis women after HRT. Trans men: no significant change in weight, increased physical capacity. Number of push-ups per minute comparable to cis men after HRT. Number of sit-ups was comparable to cis men before HRT, increase in this performance after HRT. Running time similar to cis men after 1 year of HRT.		Discussion: They suggest waiting more than a year before allowing trans women to compete in the female category. <i>Study findings and prior research:</i> Trans men's physical abilities increase while trans women's physical abilities decrease. A difference is seen between strength and endurance events. Dysphoria and its impact on athletic performance must be taken into account. This would explain the higher physical abilities of trans men compared to cis women in push-ups and the opposite for trans women.		
Wiik, A., Lundberg, T. R., Rullman, E., Andersson, D. P., Holmberg, M., Mandić, M., ... & Gustafsson, T.	2019	n= 23 of which n= 11 trans men (TM) n= 12 trans women (TW)	(PICO where relevant: Population, Intervention, Comparator, Outcome) Population: trans men (n=11) with an average age of 25 years and trans women (n=12) with an average age of 27 years, all non-athletes Intervention: biomechanical measurements (radiodensity, muscle size)	No	Biomedical study of trans men (n=11) and non-athletic trans women (n=12) during their first year of hormone treatment. Knee extension and flexibility, muscle size, and radiodensity measurements were taken. The results show that the trans men showed a 15% increase in muscle mass in their thighs and quadriceps and a 6% increase in radiodensity. The trans women lost 5% of their muscle volume. No change was observed in radiodensity. The trans men experienced an increase in muscle strength while the trans women did not experience any change in this area.	Population: We do not know how many cis men and cis women participated in the study. We don't know what is going on with cis people: is there an increase or a decrease? No intra-group comparisons. This paper has several notable weaknesses which must be considered. These weaknesses do not justify the broad implications that are asserted within the paper or by its proponents. These weaknesses are: Very small sample size (n = 11 TW, n = 12 TM). Further: No indication of how participants were recruited or selected; Were all patients offered opportunity to be in study, and was everyone offered to be in the study included; Unknown bias by recruiters, i.e., use of a script? Study conducted	Terminology: Transgender men, transgender women, gender identity

			Comparator: cis men and cis women. Number not reported. Outcome: Increased muscularity in trans men, slight decrease of muscularity in trans women after 12 months of HRT			at a single center, represents a specific sub-population in Sweden; Non-athletes were used as a proxy; Issues relating to measuring and reporting of data collected such as: Baseline measurements done after 4 weeks gonad suppression; States some strength, size parameters greater in TW than TW or cis women (CW). However, does not show range of data and overlap, does not state if TW were outside normal range for TM or cis men (CM). CW measurements were obtained separately and prior to TW and TM; Few strength-based attributes measured, other measurements may be relevant; Other non-strength-based measurements may be relevant (e.g., muscular endurance, repetition, V02 max); Persons recording strength measurements were not blinded; No measurements beyond 12 months gonad suppression, only 11 months after cross-hormones added and with 11-month testing in multi-month interval. Unknown where changes peak, cannot predict ongoing effects muscle strength, size; No discussion of inter-group differences vs intra-group differences. Strength, size, radiography density used as proxies for athletic performance. This is problematic: Significant differences in muscle strength, size, density may not correlate to a significant difference in athletic performance; Even if athletic performance were maintained in TW, this would not necessarily correlate to a safety issue	
Bermon, S. & Garnier, P.-Y.	2017	2127 observations in male and female elite track and field athletes	2127 observations of competition best performances and mass spectrometry-measured serum androgen concentrations, obtained during the 2011 and 2013 International Association of Athletics Federations World Championships, were analysed. To test the influence of serum androgen levels on performance, male and female athletes were classified in	No	The type of athletic event did not influence fT concentration among elite women, whereas male sprinters showed higher values for fT than male athletes in other events. Men involved in all throwing events showed significantly ($p<0.05$) lower testosterone and sex hormone binding globulin than men in other events. When compared with the lowest female fT tertile, women with the highest fT tertile performed significantly ($p<0.05$) better in 400 m, 400 m hurdles, 800 m, hammer throw, and pole vault with margins of 2.73%, 2.78%, 1.78%, 4.53%, and 2.94%, respectively. Such a pattern was not found in any of the male athletic events.		

			tertiles according to their free testosterone (fT) concentration and the best competition results achieved in the highest and lowest fT tertiles were then compared.				
Karkazis, K., & Jordan-Young, R. M.	2018	Theoretical article, Discourse analysis	Analysis of the speech given at the IAAF by Stéphane Bremon, one of the members of the IAAF medical commission, during a presentation made in 2012 on the regulations that apply to hyperandrogenic athletes	Unknown	In this article, the authors show that the IAAF's regulations on hyperandrogenism and the arguments that surround and construct them are based on sexist, racist, and colonial assumptions. <u>"T talk,"</u> i.e., the dialogue surrounding the use of testosterone. This dialogue perpetuates the myth and misrepresentation of this hormone as being a "masculine hormone" by attributing all social behaviors of masculinity to it. Attributing gendered social behaviors to hormones in this way is central to the hierarchical positioning and normalizing of a rigid dichotomy of the sexes. This dialogue is so socially anchored that it can exist without a concrete scientific/biological basis. Indeed, the authors explain that if there is a group-level correlation between testosterone and strength, speed, and muscle mass, such a correlation has not been proven at the individual level. In other words, these abilities cannot be directly correlated to testosterone levels alone. The strength and pervasiveness of this dialogue allows the differences in access to sport between the Global North and the Global South to be hidden. So-called "<u>regimes of care,</u>" provide an explanation for the IAAF's justification of the implementation of these rules. These "regimes of care" perpetuate gender and race inequalities because under the pretext of care, athletes from the Global South are sent to the Global North, in this case, to France (a country that has a repressive migration policy) for the purpose of "treating"/ "saving" said athletes, whose countries' medical frameworks would not be able to effectively treat hormonal "pathologies," as they are defined in western medicine, even though such hormonal "pathologies" present no danger whatsoever to the individuals who are affected by them.	The article is interesting in that it shows the racial and geographical constructs of athletes who are accused of not fitting into the expected body standards of femininity. However, the article does not directly address trans athletes, since it is about cis intersex women. We can take away the following key points (or at least draw some parallels) from the article: that the regulations that trans women are subjected to form part of the history of the frameworks used to exercise control over women's bodies which are imposed by the medical profession. Such frameworks are based on gender and racial stereotypes that have important ramifications when it comes to athletes' health and well-being. And above all, that no consideration is given to the real lived experiences of the athletes who are subjected to the regulations, and who come from marginalized and oppressed populations in terms of gender and race. Furthermore, the dialogue surrounding testosterone is not based on any tangible medical evidence. This is demonstrated by the examples that are mobilized by the member of the IAAF medical commission, which were analyzed by Karkazis and Jordan Young. The painting of <i>La maja desnuda</i>, by Goya, (1797-1800) is used to represent the ideal woman: a white woman, non-athletic, naked, and lying down. The ideal man is represented by a black bodybuilder who is known to have doped for more than 20 years.	29: Hormone-based regulations put all athletes at risk "T talk" deflects attention from social structures and institutions, attributing the result of competitions completely to individual bodies, as though these bodies have developed, trained, and ultimately competed in some socially-neutral vacuum."

					The IAAF links doping to naturally high testosterone levels.		
Richardson, A., & Chen, M.	2020	Response to the literature review by Jones et al. (2017)	None	No	This article is a short response to the literature review by Jones et al. (2017). The authors wish to challenge two points: the fact that trans women would not have a physical advantage over cisgender women and, the failure to consider the usage of "inclusion policies" (their term) when it comes to sports requiring specific physical qualities such as size and strength. Transgender female advantage: To support their hypothesis that trans women have a physical advantage over cis women, the authors take the case of Laurel Hubbard (weightlifting), comparing her "pre-transition" (their term) and "post-transition" (their term) performance, noting that the difference is only 7%. They also highlight the fact that she would benefit from her years of training in the men's category. This point is accompanied by a paragraph citing various trans women who have appeared in the media. Transgender sporting policies: The authors claim that Jones et al. (2017) did not consider strength sports such as weightlifting, bodybuilding, MMA, wrestling, judo, rugby, or rock climbing (among others cited). The next paragraph cites the USA Powerlifting (USAPL) rulebook that would have provided evidence of the physical advantage of trans women. They end by citing Harper's (2015) study, saying that it proves nothing since it is not about sports (5k to 42k) that require physical abilities such as strength or speed.	This article relays a lot of false information without scientific precautions. For example, it is highly problematic that a number of trans women have been subjected to media enquiries (cissexist, sensationalist, and resulting in media abuse (Espiniera, 2015)) and that these enquiries have been used to prove that trans women have a physical advantage and pose a problem in certain sports. The authors contradict themselves by saying that running is not a strength sport to counter Harper's (2015) study, while they cite Terry Miller and Andraya Yearwood (track and field, sprinting) as evidence of physical advantages in sports that rely on strength, speed, and size. To cover their backs, they explain that for a marathon or a 5k race, you only need endurance (and no other physical ability). It is quite contradictory to isolate physical abilities in this way, especially in sports, which generally require a combination of many different physical and mental abilities. The surveys cited to attempt to prove that trans women have a physical advantage are not based on the performance of trans athletes but on the performance of cis men and women. They compare trans women to cis women on the basis of cis men and cis women.	
Jones, B.A., Arcelus, J., Bouman, W.P., & Haycraft, E.	2020	Response to a critique of their literature review, which was published in 2017		No	Jones et al. address the points put forward in the critique of their first article to show how biased the interpretation of it has been. They offer up some possible avenues to address the cissexist argument (this term is not used in the text) that has been put forward. Transgender female advantage: They highlight that at no point in their article do they state that trans women do not have a physical advantage, but rather that there are currently no scientific studies that prove a physical advantage. Jones et al (2020) point out that Chen and Richardson use sensationalist media articles to support their argument without reference to scientific literature as supporting material. The third point of response revolves around the fact that some physiological changes that produce physical benefits are accepted, while others (unproven), are not, such as Michael Phelps' physiological characteristics and the advantages that these characteristics bring.	This article highlights that the points of criticism in response to their article (on the systemic barriers experienced by trans athletes) are not based on consistent scientific evidence. Looking to news articles or scientific studies of cis people to make the argument about the supposed physical advantage of trans women cannot be considered as valid forms of evidence. The example of Michael Phelps is an interesting one. This example is often used in feminist literature (in the field of the social sciences of sport) to demonstrate the differences in consideration with regard to what is used to demonstrate an ethical physical advantage and what isn't. In particular, this example is often used to counter the dialogue about what level of testosterone is supposedly too high for sportswomen like Caster Semenya, Dutee Chand, Annet Negesa, etc.	

					Transgender sport policy: Jones et al. raise the fact that "outdated" (p.1862) studies on the differences between cis men and cis women are used in Richardson and Chen's (2020) response to prove that trans women have a physical advantage. Jones et al. also point out that there are already competitions whose categories are not based on sex/gender but rather on athletic ability, such as the <i>Limitless Strength Competition</i> in the UK. In response to Richardson and Chen's (2020) proposal to create sport categories specifically for trans people to compete in, Jones et al. conclude by explaining that there is no scientific evidence of this approach being useful and importantly, that trans people do not want to compete in a separate category.		
Ljungqvist, A.	2018	Document which chronologically surveys the implementation of the different IOC regulations		No. Details: IOC member from 1994 to 2012, + IAAF and World Anti-Doping Agency (WADA) member	In this article, the author looks back chronologically at the evolution of IOC regulations regarding intersex and trans athletes. He situates the regulations for trans athletes in the history of the femininity testing in sports competitions. He posits that the key to athletic performance is the difference in testosterone levels between women and men. He refers to testosterone as the male hormone. He argues that the existence of these systematic regulations since the 1960s is due to the need to protect the female category from intruders (= men who would come to compete in this category in order to win medals). He explains that the 2003 IOC rule emerged following a request from a national Olympic federation regarding the "case" of a trans athlete. He mentions that opponents complained to this federation. Following Caster Semenya's victory in 2009, the IOC brought together biomedical researchers to establish a regulation on her presence. These discussions lead the IOC to stipulate that the gender bi-categorization of competitions must absolutely be respected to "protect" all sportswomen. In 2011, the IOC publishes the regulation on hyperandrogenic athletes. The author refers to the ruling initiated by Dutee Chand at the Court of Arbitration for Sport (CAS) in which the IAAF was given 2 years to prove that athletes with a higher-than-average testosterone level than other women have a physical advantage. The author does not seem to doubt (article published online in Oct 2017) that the IAAF will have evidence to put forward. The last paragraph seems alarmist in that the author calls on the sports world to establish and impose regulations to protect the female category, even in	This article puts forward different points: testosterone is the key to performance in sports, it is necessary to protect the female category from intruders (men), that hyperandrogenic athletes have a physical advantage, that there is supporting evidence. However, there are no articles supporting these arguments in the bibliography. This article demonstrates the trans misogynous preconceptions (Serano, 2007) that sports federations rely on. The idea that a trans woman would actually be a man (paragraph 1), the idea that trans women could use their femininity to infiltrate (cis) women's spaces. As well as on sexist presuppositions that (cis) women would need to be protected and therefore that the "women's" category must remain inferior to the "men's" category (last paragraph). Thus, the regulations are established not only on the basis of biological data (which are, moreover, not exempt from biases and power relationships) but are also based on discriminatory preconceptions.	

					countries that allow people to transition medically and legally.		
Sánchez, F. J., Martínez-Patiño, M. J., & Vilain, E	2013	Theoretical article	Critical analysis of the IAAF and IOC regulations in 2011	No	In this article, the authors present a critique of the 2011 IAAF and IOC regulations and the responses that have come through social science research. In the first paragraphs, the authors review the story of Maria José Martinez-Patino, who was excluded from athletic competitions after a chromosomal test. In this context, the athlete was examined under the microscope by doctors and was the object of an important media enquiry that questioned her belonging to the female category. This situation had negative repercussions on her sporting career and on her life. The new policy is not about proving sex: The new policy is not about who is a man and who is a woman, but about medically defining the boundaries of the female category. The regulations were based on the idea of sexual dimorphism. However, the data show that the female and male categories are not biologically mutually exclusive. Chromosomal testing is not effective, since women can have an XY karyotype. The authors use the case of Ratjen at the 1936 Olympics to show that men do not necessarily perform better than women. The new policy does not aim to disqualify athletes with intersex conditions: DSD do not necessarily give rise to a physical advantage. E.g., those experiencing androgen insensitivity. Such women will not be excluded from competitions even if they have a higher-than-average testosterone level. The problem with grouping: The authors are opposed to the creation of a third sport class. Doing so would be even more detrimental to the athletes involved. Stereotypes influence athletes' performance. It is expected that female athletes will perform less well, so everything is done to ensure that this is the case. To break this rule is to risk being excluded from competitions. Conclusion: Athletes affected by the rules must be given a voice in this debate.	The main point of this article is that the authors highlight the negative repercussions of such regulations on the living conditions of the sportswomen who are targeted by them. On page 113, the case of Ratjen at the 1936 Olympics is presented but without putting it in perspective with the socio-historical context or analytical precautions as Bohuon (2012) does. On page 114, the authors put forward a link made between homosexuality and congenital adrenal hyperplasia in women. In an article, Michal Raz (2016) offers a proposed response to this result: "As for the results published on the sexual orientation of these individuals, no conclusion seems to be definitive, with rates of heterosexuality or homosexuality varying widely across the board, likely reflecting differences in the methodologies of these studies. In any case, some publications continue to refer to homosexuality as a "sexual orientation disorder" (Bouvattier, 2007), perpetuating a pathologizing viewpoint." Raz, M. (2016).. Finally, the conclusion that can be drawn from this type of article is that studies could be carried out on other body differences (e.g.: short vs. tall). However, in a patriarchal and racist society, certain data are put forward for comparison between groups that are considered homogeneous and natural by the dominant group while in fact, this stems from a social relationship of domination.	112: The violence with which medical tests/interventions are conducted and the whirlwind of media coverage on sportswomen = these have a negative impact on their living conditions "Even though she identified as female throughout her life, her sense of self was called into question because of the results of a cytogenetic test. After being subjected to intense medical and media scrutiny, it was determined her condition rendered her incapable of benefiting from the presence of the Y chromosome and she was once again reinstated in athletics. Nevertheless, her life and her athletic career were forever scarred by the incident (see Martinez-Patino, 2005)."
Pitsiladis, Y., Harper, J., Betancurt, J. O., Martinez-Patino, M. J., Parisi, A., Wang, G., & Pigozzi, F.	2016	Theoretical article / discussion		Yes – a trans woman and an intersex woman.	The authors explain that there is a lack of scientific knowledge about the supposed advantage of trans women in sports competitions. Among the studies mentioned, the authors start with Gooren and Bunck (2004) who demonstrate that during the first year of HRT, trans women have testosterone levels that fall in the middle of the levels seen in cis women. Then, referring to T'Sjoen et al. (2009), trans women observe a loss of muscle mass and bone density	This article points out the limitations and data that still need to be collected in order to gather more information about trans athletes.	Terminology: transgender women, MTF, male and female biology, female athletes, FTM, MTF transition

					as early as 6 months into their HRT. These studies therefore support the IOC regulations that allow trans women to compete in the women's category provided they are on hormone therapy. However, the authors also point out the lack of data on high-level trans sportspeople. The only biology study conducted to date with trans athletes was conducted with trans women at the amateur level (Harper, 2015). The authors therefore call for more research on the physical and physiological conditions of trans athletes compared to cis women.		
Sutherland, M. A., Wassersug, R. J., & Rosenberg, K. R.	2017	Does not use their own data	Discussion of published studies to draw their own conclusions about trans women	No	Intro: IOC regulations in 2004 and in 2016. Olympic history: Traces the history of the femininity test in sports competitions by fixing Ratjen's participation in the 1936 Olympic Games as a starting point and then highlighting the chromosomal test (Barr body and PCR-SRY), in use since 1968. Then, the problem of chromosomal testing for Complete Androgen Insensitivity Syndrome (CAIS) athletes is discussed. Transsexuals in sports: Starting with the 2004 regulations. The authors postulate that trans women have a biological advantage over cis women even after HRT due to their skeletal/bone structure. The osteological advantage: The authors state that the human skeleton cannot be modified by transitioning, which means that trans women have a physical advantage. The physical advantage that men have would be due to testosterone giving them a more imposing skeleton. Specific osteology and biomechanical advantage: the case of the knee: The authors postulate that one of the key differences between (cis) men and (cis) women is the q-angle ("the angle at which the quadriceps muscle meets the patella compared to the line formed by the ligament connecting the patella to the tibia" physicaltech.com). This difference in angle would have influence in sports such as football/soccer or cycling. The case of the elbow: In this part, the authors are interested in the carrying angle (the physiological valgus of the elbow = the same type of calculation but for the elbow). The authors postulate that this angle is a dimorphic feature even though they admit that this hypothesis has not been empirically verified and even though no studies have been carried out on the correlation between the accuracy of a shot and this angle.	Page 174: the authors postulate that the sporting federations' fear of seeing a man compete in the female category dates back to the Olympic Games of 1936, which saw Ratjen compete: False, if you refer to A. Bohuon and C. Louveau on the "process of virilization," which sportswomen were required to undergo even before 1936. In particular, the case of Violette Morris can be quoted. Violette was excluded from the FSFSF (Fédération des sociétés féminines sportives de France) with a lawsuit in 1930 for wearing "masculine clothes." Page 175: The authors point to a study that shows that women with CAIS have an average height of 1.70m, while women without CAIS have an average height of 1.65m (stating that the women with CAIS would not have a physical advantage). However, in Danilovic's (2007) study, for example, women with CAIS range in height from 1.54m to 1.80m, so creating an average over such a small number of women seems like a flawed approach, especially without looking at the standard deviation. The study cited by Sutherland et al. (2017) does not specify the number of women with CAIS who were counted. (Danilovic, D. L. S., Correa, P. H. S., Costa, E. M. F., Melo, K. F. S., Mendonca, B. B., & Arnhold, I. J. P. (2007)). Height and bone mineral density in androgen insensitivity syndrome with mutations in the androgen receptor gene. Osteoporosis International, 18(3), 369-374). In the article, the authors put forward the variable of height as one of the physical advantages that trans women possess, especially in volleyball. However, in a total contradiction, on page 177, it is stated that if you take the average height of all the volleyball teams in the Olympic Games, (with one exception since 1968) it has never been the tallest team that has won.	Terminology: Transsexual, biological males, genotypically male, MtF transsexuals, osteological males, human female, Correlation "transsexual" and "transhumanist" Deadname Renée Richards.

					The pelvis: The authors postulate that this feature is also dimorphic even though they admit that studies have failed to show a correlation between better motor performance and pelvic size. It is suggested that the advantage for men would be that their average pelvic shape would be correlated with fewer injuries. Fairness in the field: The authors propose to implement osteological and biomechanical tests to classify athletes according to this data in order to ensure fairness in sport. Transsexuals as pioneer transhumanists: The authors compare gender transition to transhumanism and call for vigilance regarding the various physical modifications that could be made by athletes to improve their performance.	Page 179: The authors argue that the high frequency of knee injuries in women is linked to the q-angle. However, they do not take into account the differences between men and women with regard to the way in which they compete in sports (the condition of the playing surface, the quality and number of training sessions completed, shortages of medical staff and follow-ups, lack of access to weight rooms, etc.). The problem is that gender is the variable that is being studied when looking at health. Living conditions are not taken into account. Page 186: The authors propose that athletes should compete in categories according to their bone/skeletal structure, but they don't take into account the fact that athletes adapt their physical abilities according to their morphology. Furthermore, this suggestion stands in contradiction to their postulate that bones/skeletons are dimorphic in nature. If this were the case, why suggest separating competitors into categories in accordance with their bone structure? This proves that the aim of the study is just to hide the authors' real agenda, which is a desire to force trans women to compete in the male category (without explicitly saying that this is the motive and without tangible medical evidence, since the studies cited were not carried out with trans athletes). In addition, this study: Men and women have similar Q angles: a clinical and trigonometric evaluation (Grelsamer, R. P., Dubey, A., & Weinstein, C. H. (2005)) is not cited in the paper; however, it shows that when comparing men and women of the same height, a similar q-angle is obtained .q-. Thus, the difference is to do with the person's height rather than their sex. It Is also worth noting that the example of the Olympic shooting event, which was originally mixed, was separated into non-comparable categories by sex (not the same distances) following the victory of women in this event. This calls into question the physical advantage argument Another overlooked fact is that bone data are the result of both biological and sociological factors as Anne Fausto-Sterling shows: ""Fausto-Sterlin's (2005) account of bone density provides a clear	

						ex- ample of how this plays out in scientific discourse and practice. Although sex is widely understood to be an important factor in bone fragility, few studies go beyond a male/female comparison to “examine the relationships among childbirth, lactation, and bone development” (2005, 1492), among other sex/gender-related factors that may influence bone strength, thereby re-informing the dominant tendency to treat sex as a singular, simple, binary variable. Fausto-Sterling offers a systems approach to thinking through these issues, which is able to “[embed] the proposed subsystems within the dimensions of gender, socioeconomic position, and culture” (1515). (In Ritz, 201 7: 321).	
Tannenbaum , C., & Bekker, S	2019	Commentary on the 2018 IAAF Regulations		No	This article offers a commentary on the 2018 IAAF regulations and the medical supervision of the women's category. New eligibility criteria: The maximum testosterone level is arbitrarily set at 5nmol/L. The author reminds the reader that hormonal levels are not mutually exclusive between women and men. There are no studies that prove a causal link between testosterone levels and sports performance (medaling) because there is no data available on this. This would require the systematic testing of all athletes. The survey conducted by the IAAF on the influence of testosterone on athletic performance shows a greater effect in the hammer throw and pole vault (4.53% and 2.94% respectively), even though these disciplines are not governed by IAAF regulations. Moreover, this study is marred by the "data errors" that the researchers have admitted. Far reaching implications: These studies are conducted for the purposes of the federations that commission them. They have an important impact on the lived experiences and athletic careers of the athletes.	The article does not mention trans athletes. It is more a general commentary explaining the IAAF 2018 regulations. The authors point out the limitations of such regulations: errors made in the initial investigation, no proven evidence, consequences for the athletes. Page 1-2: It is stated that the highest percentage correlation between testosterone levels and performance is seen in the hammer throw and pole vault events. However, the authors do not explicitly state that these disciplines are not covered by the IAAF regulations.	Terminology: This article does not refer to trans people.
Klein, A., Krane, V., & Paule-Koba, A. L.	2018	Qualitative analysis. N= 1 (trans man)	Methodology: The researchers followed the first year of a trans man’s hormonal transition. The trans man in the study was playing sports at university at the D1 collegiate level (running). The data in the wider project were collected through interviews and video diaries. This article	No	This article focuses on the first year of a trans athlete’s transition. The athlete was studying and competing at a university in the USA. The article alternates between long transcribed excerpts from the athlete's video diary followed by comments written by the author. The main takeaways are the effects of his hormonal treatment and the constraints he faces with regard to wishing to compete in a different category. The participant reports the body changes that he noticed during his first year of hormonal treatment (he was taking testosterone): genital	The authors fail to take into account both the social effects of taking testosterone and the psychological effect of taking hormones, nor do they consider how these two factors may also be interdependent. Thus, when the participant mentions being able to <i>pass</i> and that he is beginning to feel better mentally, we should consider this not only in terms of biology but also in terms of social factors. This article shows that even in a space where coaches and other athletes are not directly rejecting his transition, the athlete, Bryan, faces	555: Definition of transgender "Transgender can be an umbrella term for any individual whose gender identity and/or gender expression is incongruent with their physical sex (Krane and Symons 2014). Some transgender, or trans, people will identify and desire to be recognized as a different sex than they were assigned at birth. Others may identify as genderqueer, non-binary or gender fluid in which their gender expression is a combination of or shifting among traditionally masculine and feminine traits." 556: Definition of transition

			focuses on the results extracted from the video diary. Participant: 20 years old, trans man, pronouns he/him, track and field - cross country, D1 student athlete (USA collegiate). From the beginning of his hormonal treatment, he is no longer allowed to compete as part of the women's team (as per NCAA rules), but he was not immediately integrated to the men's team either.		growth, cessation of bleeding, facial hair growth, hair growth changes, a small increase in muscle mass, and lower fat distribution. In addition, the participant announces that he will stop playing collegiate level sports at university because of the obstacles he encountered during his transition. The authors propose the implementation of a <i>redshirt</i> year that would allow athletes to keep their scholarship and transition without losing a year of eligibility.	many obstacles which eventually lead him to stop competing in sport at university. Bryan outlines and explains the difficulties he faces when trying to continue competing in sports during his transition. For example, not being able to access a mastectomy is a hindrance which limits his motivation and involvement in sport. As a result, he makes the decision to stop competing. He explains that giving up his sport (running) will allow him to do more weight training and focus on his transition. He talks about the sacrifice he has to make, saying that he feels the need to choose between his two identities: being trans and being an athlete.	Transitioning is the process during which a transgender person alters their gender expression to be consistent with their gender identity. This may include changing the type of clothes they wear, restyling their hair, and/or changing their name and preferred pronouns. Some transgender people may choose to alter their bodies through hormone therapy during their transition and some may have surgical interventions. There is not a single way to transition; instead, there are multiple possibilities to transition and various ways to be and become one's gender. Transitioning athletes will develop the path most suited for them and that which best portrays and leads to comfortable sex and gender presentation.
Pape, M.	2017	Discourse analysis	Document 161, a report on the CAS ruling of the Dutee Chand vs IAAF case	No	In this article, Madeleine Pape demonstrates that sports institutions operate in line with the following principle: biological sex precedes social gender. She describes sports governing bodies as <i>gender-determining institutions</i>. That is, spaces where the notions of sex/gender are contested, debated, and defined in ways that reinforce the gender system, the differential valence of the sexes (not in these terms), and heteronormativity. Thus, the author analyzes how the categories of sex/gender/sexuality were destabilized by the athlete and then reified by the institutions during the trial (Dutee Chand vs the IAAF). The IAAF's regulations form part of a history of exercising control over women's bodies and over women's performance. Indeed, in the gender system, women must be inferior to men in order for men to maintain their dominant position in the hierarchy. For this reason, not only have rules been and continue to be put in place, but various tools for maintaining the hierarchy exist, such as the sexualization of women's bodies and the promotion of heterosexuality, or the lack of remuneration and financial means granted to women. There is a hierarchy when it comes to the consideration and valuation of scientific knowledge. Studies conducted by life scientists are deemed more valid than studies conducted in the social sciences. The results of such life	Two key takeaways can be drawn from this article: the fact that (at all costs) the sports institutions try to maintain the essentialist postulate that sex precedes gender and that their ability to maintain their domination on the basis of the rules is dependent on the organization of hierarchical scientific knowledge. Theorists in the social sciences, in particular within the fields of gender studies and within feminist criticism of the sciences, have demonstrated that it is in fact gender which precedes sex. In other words, the values attributed to men or to women do not come about organically but rather they are a product of a social hierarchy whereby men dominate women (i.e., concepts including: the differential valence of the sexes, gender, the social relations of the sexes, straight thought). This knowledge regarding gender is not taken into account by sports governing bodies because it belongs to the field of the social sciences. The hierarchical organization of knowledge is a product of a history of delegitimizing of knowledge, which, particularly in the social sciences came about due to the oppression of the researchers within these fields. Faced with leading governing bodies, those who carry this knowledge experience epistemic injustices and an enterprise of delegitimization.	Terminology: transgender 180: Difference in consideration between the sciences (social and biological) "I find that Chand's victory does not actually amount to a liberal shift in the sex/gender/sexuality system and the institutions that maintain it. The "non-scientific" claims of Chand's witnesses were ultimately marginalized within the courtroom space in favour of certain scientific criteria for gender determination, allowing hegemonic notions of the nature of sex and gender, and the relationship between them, to prevail."

				science studies are given more weight. The gender system is thus perpetuated, since men dominate in the life sciences while many social scientists are women. Dutee Chand was asked to not only prove that the IAAF studies were wrong but also to scientifically prove that testosterone is not a direct indicator of athletic performance. Dutee Chand's team brought up the argument of the complexity of gender difference and the causality of sports performance. Meanwhile, the IAAF came up with their own investigations. The arguments put forward by Dutee Chand's team were considered by the CAS panel to be nothing but unproven assumptions, speculation, and hasty conclusions. The social science researchers involved were discredited as merely over-interpreting medical data which do not fall within their field of expertise. All this took place despite the fact that a member of the IAAF team was found to have published data and an analysis on testosterone and sports performance that turned out to be false (admitted by the researcher). K. Karkazis' articles on bioethics were considered to be "sociological opinions" not resulting from real clinical knowledge. The IAAF arrived at the trial with a material advantage (and therefore a scientific advantage) because of its ability to finance research on its own terms. Compared to Dutee Chand, the IAAF also has incomparable human resources as a result of the sheer amount of data that they hold on their competitions (especially through the World Anti-Doping Agency) and which they have access to. The IAAF's strategy was to say that they do not seek to find out who is a man and who is a woman but rather that they seek to make a distinction between women in terms of access to sport. However, the author highlights the fact that the IAAF has never sought to medically supervise the male category. This strategy allowed the IAAF to transform the debate and the framework, making it seem purely medical. Additionally, an IAAF witness defended the regulation by stating that it would keep men out of the women's category. This suggests the real motives behind the regulation. Overemphasizing the medical/health aspect of a supposed pathology is simply a strategy. Dutee Chand has been		

					subjected to a lot of violence from the medical institutions within the framework of this regulation. This shows that the well-being of the women who are subjected to this regulation is not taken into account. Drawing upon regulation as thought has the effect of reinforcing the idea that "normal" women would be weaker, more vulnerable and more in need of protection than women who fall outside of this framework. Pape insists upon looking at regulations not only from a biological perspective but also from political and social perspectives. This framework of analysis allows us to highlight the way in which the same dialogues and myths about a social fact are reconfigured with new biological data to replace the old ones that have been proven to be obsolete.		
Ritz, S. A	2017	Theoretical discussion, sex variable and biomedical research		No	In this article, the author explores the limitations of biomedical research that attempts to take into account the variable of sex without questioning it or worrying about the consequences of such hasty generalizations. The definitions given in biomedical sciences of the notions of sex/gender are limited to an understanding of sex as being based on biological data and of gender as being based on social data. However, research in gender studies, in particular the feminist critique of science by Anne Fausto-Sterling, quoted here, has shown that sex is dependent on gender and that the gender system modifies so-called biological sex. The significant social aspect presents itself as one of the major limitations associated with trying to draw conclusions about sex/gender based on the observation of cells. The conditions under which cells develop within the laboratory environment differ quite considerably from the conditions of development that are actually present in a sexually differentiated and social body. 1) Obtaining cells from human tissue is complicated. The number of cells extracted tends to be reliable. Beyond the sex variable, there are also many other characteristics that come into play and these also need to be taken into account. 2) It would be better to talk about what type of sex we are talking about (i.e., whether we are talking about sex in terms of gonads, genitals, chromosomes) rather than drawing conclusions about an entire category from weak and incomplete data. 3) The	This article highlights the limitations of taking the sex variable into account in medical research. It is clear here that some research allows itself to make generalizations about differences between men and women based on a single variable that is often incomplete and erroneous. There is value in developing a broader understanding of sex/gender in biomedical research to avoid these pitfalls.	Terminology: does not refer to trans people but refers to the "cis-normative gender binary" 320: Limitations of the designation of the categories "male" and "female" "We make use of the labels "male" or "female" as though we are stating a singular biological reality, but really we are invoking an entire constellation of characteristics that, at best, have a reasonably strong correlation with one another. In doing so, we are engaging in "interested instances of power ... with real material consequences" (Barad 1996, 182) for how we understand the impact of sex on health." 320-321: Impact of gender stereotypes on research "The upshot is that in treating sex as a unitary dichotomous variable and comparing females and males, we are allowing stereotyped thinking about sex and gender to substitute for the mechanistic understanding that is presumably the goal of experimental research, doing a disservice to people of all genders with respect to our understanding of biology and health."

					production of hormones within the endocrine system can be dependent on the social context, on physiological and reproductive functions, or even on age. The levels of hormone production thus vary according to the internal and external context. In the laboratory, cells are isolated from this social, hormonal, nervous, etc. context. The reactions we see in the lab are therefore distinct depending on whether we are looking at an <i>in vitro</i> situation or an <i>in vivo</i> situation. When men and women are separated under experimental conditions, the variable of sex is taken as a whole without taking into account its complexity and the different dynamics that constitute it. A problem also arises in that when we look at one component of sex, we assume that all the others are aligned. Moreover, the biological categories attributed to men and women are not dimorphic. The conclusions drawn cannot be generalized; they are, at best, trends of observed correlations that do not take into account every factor. The impact of social factors is very frequently neglected. We must recognize that all knowledge is situated, constructed, and biased. Even if the cells that are taken come from donors whose sex is known, this fact does not constitute a functional variable in the research. For example, some research examines the effect of estrogen on cells as a female variable, even though all bodies produce estrogen. It is not possible to isolate the biological and the social when one influences the other and vice versa.		
Sullivan, C. F	2011	Theoretical discussion of rules and regulations, supervision of the bodies of sportswomen		No	In this article, the author reviews the main regulations that have marked the history of the medical supervision of women's bodies (cis, trans and/or intersex) by sports governing bodies. The concept is based on the preconceived myth that all men have a physical advantage over all women (hegemonic masculinity). To maintain this system, women must remain inferior to men at all costs. Different markers have been used throughout history to identify the sex of sportswomen (genitals, chromosomes, hormones). Each test has been built on the assumption of unproven sexual dimorphism. Systematic gender testing is a product of the Cold War; the first test of this kind was administered in	The author examines the regulations governing trans people's participation in sports (with a focus on trans women in particular). She situates this within the framework of the history of the femininity test. She highlights the limitations of these tests and the disastrous consequences that such tests have had on sportswomen. Page 409: The author highlights the lack of consideration in the literature of the increased risk of injury that trans people and particularly trans women may experience: "Trans athletes who carry "male" skeletal structure and height on "female" musculature have been found to be more prone to injury (Carlson, 2005)." This is one element from a response to the Sutherland (2017) article.	Terminology: Transsexual or transgender

					1966 at the European Athletics Championships. All participating athletes were required to undergo a genital examination that was humiliating and degrading. This was followed by genetic tests that proved to be non-functional; the sports world learned of the existence of intersex conditions. Maria Jose Martinez Patino, who had obtained a certificate of femininity during the first phase of testing, was outed as being intersex following a chromosomal test. Her certificate of femininity was subsequently revoked as a result. The fact that she finally presented as having an insensitivity to androgens despite her karyotype led the federation to readmit her 3 years later and to permit her to compete. However, she was never able to regain her sporting level due to the violence she experienced at the hands of the sporting and medical institutions which forced her to stay away from the field. The 1990 recommendations to stop femininity testing were not accepted. A second phase of chromosomal testing was introduced. As of the year 2000, these femininity tests are no longer systematic. They are carried out on the basis of doubts about someone's sex based on visual examination; therefore, their usage is based on external criteria of cis-heterosexist femininity. The author takes the 2003 Stockholm consensus as a starting point and shows that factors such as whether or not a given country's legal system permits a person to change their civil status, how easy/difficult it is to access hormones, and how easy/difficult it is to access surgery all depend on the social and geographical position of the athletes. The 2-year transition period is arbitrary. Far from having a physical advantage, trans people may suffer injuries as a result of their transition and may experience health problems related to medical interventions. The Gay Games applied very discriminatory rules (until 2018). The 2004 World Out Games in Montreal used the 2003 IOC rules. Most federations use rules similar to the IOC rules. The regulations in force now focus on hormonal levels under the impetus of the IAAF, which calls testosterone a "male" hormone, even though all bodies produce it.		

Pape, M.	2019	Theoretical discourse analysis	CAS ruling, Dutee Chand vs IAAF, discourse analysis	No	Exclusion of certain knowledge by sports governing bodies as a result of scientists' restricted definition. This makes it impossible to see the power dynamics at stake in the creation, maintenance, and legitimization of the regulations. Instead of considering non-dimorphic findings as being part of the diversity of human bodies, these findings, when they manifest in women, are pathologized and excluded from the studies. When scientific investigations are proposed by both sides (e.g., Chand vs. IAAF) only peer-reviewed studies that provide a narrow definition of testosterone and its impact on the body are considered by the CAS panel; namely, studies conducted by life scientists. The production of knowledge is dependent on the material and symbolic resources that are allocated to it. Moreover, the CAS asked the IAAF to provide new evidence, siding with the IAAF despite having no evidence, and basing this ruling solely on a hunch that they would be able to provide supporting evidence. Conversely, Dutee Chand was not given the opportunity to come back with new evidence.	This article demonstrates the hierarchy of knowledge at work in the legitimization/delegitimization of certain knowledge produced on testosterone. It's worth noting that the IAAF regulations stand in line with the pathologization of women's bodies. Indeed, the author demonstrates that when women's bodies fall outside of the norm, such women are considered to be unwell. However, when men's bodies fall outside of the norm, they are just considered as being out of the ordinary. The material and symbolic resources of knowledge production are to be taken into account in the evaluation and consideration of different knowledge that is published on the subject.	Terminology: transgender women
Travers, A.	2017	Introduction to their book <i>Transgender athletes in competitive sport</i>	/	/	In this introduction, the authors develop the idea that trans athletes highlight the flaws of the sport categorization system by refusing to accept the categories determined by the sex/gender system.	Caitlin Jenner is misgendered from the first paragraph. Santhi Soundarajan is referred to as a trans woman when at the time of the book's publication it seems quite clear that she is a cis woman who has been excluded from competition because of her intersex condition.	
Teetzel, S.	2017	Semi-structured interviews: n= 10 (5 trans and 5 cis)	(PICO where relevant: Population, Intervention, Comparator, Outcome) Population: 10 respondents: 5 cis women, 3 trans men, and 2 trans women. Intervention: Semi-structured interviews about regulations governing the participation of trans athletes in sports.	No	In this article, the author interviews trans and cis athletes about the rules and regulations that govern trans athletes' participation in sports. Uncertainty regarding where the science is at Participants struggle with delineating what would count as a physical advantage. The cis participants have almost no knowledge of the endocrine system. Unlike the trans participants, the cis participants had not previously thought about or been confronted with (and therefore not been forced to think about) the issues surrounding such regulations. The trans participants pointed to the lack of available data and the quasi-systematic exclusion of trans women. The notion of passing seems to be paramount in understanding the differences in access to sport.	There is little socio-demographic data on the participants, which limits the analysis. It may be difficult for active trans athletes to criticize the rules because of their position in the sport space.	

			Comparator: None		A commitment to some sort of fairness None of the participants agreed with the myth that some people would transition just to change their gender category in competitive sports. It is important to take into account class differences and the economic capital needed to take part in certain sports. This in itself is an advantage. Connecting inclusion and respect One way for trans athletes to protect themselves from transphobic and trans misogynous attacks is to seek refuge in the very rules that place medical limitations on their participation. In line with the results obtained, the author proposes moving away from the concept of fairness and toward the concept of respect. Thus, operating from a place of morality rather than basing decisions on regulations which imply a state of equality that doesn't even exist.		
Vilain, E., Ospina Betancurt, J., Bueno-Guerra, N., & Martinez-Patino, M-J.	2017	Theoretical article	/	No	The article provides a discussion/ contextualization of some of the regulations that trans athletes are subjected to. There is a long history of men and their institutions banning women from taking part in sports competitions. E.g.: Marathon – women were banned from taking part in Marathon events at the Olympic Games for 84 years. The division between women and men in sport is a product of this history. The authors review the different phases of the femininity tests used in sports competitions. These tests are currently based on external criteria of femininity. For example, Caster Semenya was forced to undergo a femininity test based on doubts about her sex based on her “questionable visual appearance.” A look at the IAAF and IOC regulations.		
Heggie, V.	2010	Theoretical article	/	No	The desire to maintain a framework for the female category predates the systematic implementation of gender tests/femininity tests and dates back to the beginning of the 20th century. During the 20th century, it was mainly FTM transitions (or the possibility of them) that worried sports organizations. This was the case for Zdenek Koubkova, Mark Weston, and Willy de Bruyn. There was a particular panic about the masculinization/virilization of women and the impact that sport would have on women. This		

					argument was also used to justify limiting or even prohibiting women's access to sport. Review of the different tests and their failures.		
Buhon, A.	2012	Theoretical Paper	Historical summary – review of historical literature on perceptions of femininity in female athletes and/or female sports.	No	Policing of women's bodies is significantly linked to cultural values of femininity. Racism and expectations around the cultural roles of women are a significant predictor of public concern around "fairness of sport" (i.e., athletes presenting more feminine or hiding "masculine" traits). Many of these controls were put in place and established for geo-political reasons (i.e., 1960's cold war fears "Russian women superiority"). Author suggests that authorities rely on these subjective evaluations of aesthetic and visual assessments and no longer test systematically. Bias exists between North/South (white/black) and is used to control not only gender but the "non-hegemonic" femininity of eastern sportswomen.	Potential avenue to evaluate perceptions of feminine aesthetic as a predictor for testing/criticism. Well documented history of discriminating against women who do not appear culturally feminine (from a European/American point of view).	Caster Semanya's results were not world record breaking, and yet still of significant concern due to public perception. Interesting how comparative advantage is perceived based on the skill and/or ability of the competition. Are women's sports only fair if competition is "less" than men's sports?
Devine, J.	2019	Gender, Steroids, and Fairness in Sport	Review	No	Author concludes that there is a valid parallel between trans women participation in sport and that of individuals caught with doping violations returning to the sport prematurely or at all. Author does note that binary gender norms should be abandoned. - Author presents idea of tolerable unfairness which is an interesting avenue to consider. - Author examines values of fairness in respect to inclusivity. And has reasoned arguments against "trans" category in sport as well as forcing athletes to compete with birth gender. Author admits that his thesis is speculative but qualified i.e., that even if the flawed basis is proven true it only establishes pro-tanto reasoning. (Reviewer disagrees that even partial "only to extent" pro-tanto reasoning exists.)	Advantages conferred are not equivalent nor did the author present any evidence to suggest as such. Author relies on logically flawed conclusions by establishing "facts" which are not supported by evidence. Suggest that the conclusions of this article be ignored, however some information within the article could prove to be useful. Author ignores, for example, trans women skeletal changes during puberty which result in a total body mass increase which may act differently to a reduction in T (especially in terms of athletic performance). Author assumes trans women exhibit same physical traits as cis men, this is incorrect due to socio and medical reasons (higher rates of mental health issues, eating disorders, etc.).	There is a biologic basis for structural brain differences between trans women and cis men (i.e., trans women's brain activity matches more closely with cis women). It would be interesting to see if any research has been done to categorize these biologic differences in terms of differences in core functionality (or population evaluation of body mass, etc., of trans women, if any exist).
Foddy, B., & Savulescu, J.	2011	Time to re-evaluate gender segregation in athletics?	Selective review of literature, no new empirical evidence was presented. (Recommend rejection)	No	Author contests that female athletes are justified in arguing for exclusion of other women based on a false premise that intersex or trans athletes are still "partially male." Author suggests this could be overridden by relaxing restrictions on doping without addressing any of the potentially negative health consequences to athletes. Author (without proper citations) indicates that men perform at much higher levels of sport despite having access to same levels of equipment, training methods and both work equally hard at training. This point is reoccurring	Article mentions that Caster Semanya's victory was still not a world record (yet still unacceptable because she is "partially male apparently.") This is analogous to an argument that elite athletes should not be allowed to play recreational sports because they would dominate. 1. The differences between sexes is not based purely on gender, it is because height- and weight-adjusted men still outperform women (almost entirely because women carry higher body fat % and therefore less lean muscle mass). 2. Training and equipment is optimized for male performance; recent study suggests that women	Paper describes two different frameworks for evaluating sport. 1) to identify natural potential of individuals, therefor genetic variation is desired. And 2) reward the hardest worker (which is currently obviously untrue).

					throughout literature, so it needs to be addressed (points 1-4 in next column). 57% of serum testosterone between individuals is caused by genetic factors (Ring et al., 2005). (Suggestion that this suggests a strong environmental factor to serum testosterone levels as well, and should be examined). Michael Phelps example of Marfan syndrome, arm span (does not include oxidization advantage however) “naturally occurring” seems to only impact women’s sports and men are not regulated as such. The authors (Foddy and Savulesco) are wrong about Phelps. He does not have Marfan syndrome.	should train on different interval sets (higher rep) for optimal strength gains. 3. “Working just as hard” ignores social realities which disadvantage women from being able to dedicate time towards their sport. 4. Confirmation bias towards lack of permutation tests (see women Chess player rankings).	
Genel, M.	2017	Transgender Athletes: How Can They Be Accommodated ?	Select review of existing literature	No	The author does not present their own conclusions; however they do mention some interesting details. 1) Many of these limit requirements face difficulty when assessing intersex individuals. 2) Likely there will be more trans athletes being included in interscholastic sport.	The 10nmo/L threshold is arbitrary and is not set on any population-level data by cis women. Further, it is not clear that individual variation within testosterone limits is a clear indication of performance advantage, let alone an “unfair” advantage in all sport (some evidence is present re: intersex sprinters).	
Gill-Peterson, J.	2014	The Technical Capacities of the Body: Assembling Race, Technology and Transgender	N/A	No	The author presents no valid qualitative or quantitative evidence nor draws any useful information on which to draft this report. Paper discusses competing ideologies of race/technology/ecological impacts and gender.	Recommend removal from list.	
Handelsman m, D., Hirschberg, A., & Bermon, S.	2018	Circulating Testosterone as the Hormonal Basis of Sex Differences in Athletic Performance		Unknown	Author argues that circulating testosterone is the most important marker for athletic advantage because of increasing muscle mass, strength, bone size, density, and hemoglobin. Androgen sensitivity for men with testes removed may play a significant moderating role.	Author uses terminology like “bone size” as if this is different from height or frame size, neither of which are an established basis for discrimination. Rates are used from cancer patients, and likely are not representative for elite athletes. Paper makes inaccurate conclusions on the initial performance advantages of men vs women.	Literature is very dense and requires an additional reviewer to provide some more specific background and verification of points.
Hargreaves, J.	2012	Gender Equality in Olympic Sport	A review of women’s participation in sports, no new evidence presented.	No	Sport has been an integral part of modernization in Gulf Cooperation Council (GCC) countries and in particular Arab women have been able to leverage this to become agents of change. Author argues that sport reflects and influences cultural values.	This may form a basis for inclusion of trans women and DSD women in sport irrespective of advantage. Representation matters not only to individual health but also to societal value changes as sport has an ability to change societal perceptions of equality.	Limited scope “story”
Harper, J. et al.	2018	The Fluidity of Gender and Implications for the Biology of Inclusion for Transgender	Survey analysis	Yes – Lead author	Paper examines survey data from three different events 1) the 12 th International Congress of the Sports Medicine Association of Greece; 2) public lecture at the University of Brighton; and 3) the 2018 spring conference of the British Association of Sport and Exercise Medicine (BASEM). The	Paper provides interesting insight into the thought process of academics, but I do not believe it has relevance for this study.	Can illustrate some of the epistemological challenges of the subject.

		and Intersex Athletes			author shows that there exists a wide spectrum of opinion when it comes to testosterone regulation for both athletes with DSD and transwomen. This range includes individuals who are concerned with doping, and innate biological advantages, among others.		
Henne, K.	2014	The “Science” of Fair Play in Sport: Gender and the Politics of Testing	Social and historical analysis of the issue.		Women’s sport has a lengthy history of being categorized for cultural and political reasons. Author argues that gender verification is not only degrading to women, but it upholds myths around gender that form the basis for fair play. While testing has found results in gendered differences when it comes to sport, they are based on an idea that biological sex should align with culturally constructed myths of gender. These are used “under the guise of leveling the playing field for female athletes.” The author argues that DSD regulation seeks to preserve the idea that “woman is inherently distinct from and less able than man.” Fair play is rooted in values of amateurism which are no longer practically relevant for most sport. Similar arguments were put forth in questioning the validity of using prosthetics in sport (Pistorius).	Author has solid arguments on the basis for what sports should strive to become, i.e., independent of cultural myths around gender. However, when discussing trans participation in sport there exists some evidence of performance-related data which suggest potential issues around safety and fairness in sport for identification-only policies. This very may well be socially constructed artifacts, however given that we are informing policies for where society is at now, within Canada, reasonable restrictions should not be rejected out of hand out because of a contradictory ideological stance.	Many authors reject gender verification on the grounds that it is degrading to women (Skirstad, 2000).
Ingram, T.	2019	Transgender Policy in Sport, A Review of Current Policy and Commentary of the Challenges of Policy Creation	Review	No	Author looks at the history of trans participation of sport from high school to professional levels. There exists limited scientific data as it relates to performance advantages held by transwomen in sport, further women’s sport is poorly defined (other than being separate from men’s). Author suggests it is difficult to make inclusive policy that is fair but accessible. Author concludes that ongoing study and input is required by the medical and scientific community in the topic.	Paper references (table 3) strength gains and losses which are inaccurate. In particular, the decrease to muscle mass and strength is largely unknown and the interval stated should not be used to inform policy.	This article leads to an entire section which should relate to how policy should be constructed to enable it to be more equitably accessed, i.e., not having sport federations monitor their athletes, but rather have policies that are behind a physician’s recommendation. This raises issues of compliance.
Karkazis, K., & Jordan-Young, R.	2015	Debating a testosterone “sex gap”	Article, not peer reviewed.	No	The author states that DSD women and women with naturally occurring high levels of T must be included when considering what is fair in sport. And that a conclusion drawn decades ago was those “who were raised as girls and classify themselves as female should not be excluded from competition as women.” The basis for these arguments is social and ethical around how we classify human diversity.	The arguments made are logical, however as it relates to transgender individuals, we have no evidence to suggest that pre-treatment trans women have similar performance and strength profiles of DSD women or women with high T levels. As a result, there may be a basis for requiring some form of HRT, however this is still largely unresearched.	In the article <i>The testosterone rule—constructing fairness in professional sport</i> , Sudai (2017) refers to a study, commissioned by the IAAF and conducted at the 2011 IAAF Track and Field World Championships in Daegu, South Korea (referred to as the Daegu study) where the authors found that: “there is no clear scientific evidence proving that a high level of T is a significant determinant of performance in female sports.” (Bermon, S. et al., 2014).
Pike, J.	2021	Theoretical paper	A philosophical discussion of the relationship between concerns about safety, fairness, and inclusion in policy making about	No	The researcher argues for an approach based on lexical priority rather than simple ‘balancing,’ considering the different values in a specific order. A justificatory framework for the World Rugby (WR) Guidelines that exclude trans women		

			the inclusion of trans women athletes into women's sport.		from the women's game in WR competitions is provided. An account of a maximally safe, maximally fair and maximally inclusive form of sex categorisation in sport is offered.		

*None of the literature talks about performance advantages of men vs women in terms of either resourcing (men’s teams receive more resources for training, and training is optimized for male bodies (kin study available)). They also do not include any basis for permutation (instance rate and variation among edge scenarios – look at chess participation rates and its impact on performance rates (<https://en.chessbase.com/post/what-gender-gap-in-chess>) for elite athletes).

Grey Literature

Table 12 Detailed review table of grey literature.

Author(s)	Year	Kind of Study and/or Sample	Self-identified trans researcher(s) lead and/or trans research team members?	Key Conclusions	Key Reviewer Criticisms	Other notes
World Anti-Doping Agency (WADA)	2019	/	/	Regulations for obtaining a Therapeutic Use Exemption (TUE). Provides a detailed medical file and the rules of the sports federation.		3: Composition of the medical file "All TUE applications must include a report from a healthcare professional who treats transgender individuals. This report must provide details of the athlete's medical history, including whether the athlete has undergone any partially or fully reversible physical therapy. This document should be accompanied by an endocrinology report from the endocrinologist who initiated the hormone therapy as well as a surgical report, if applicable. A full medical evaluation is required prior to the initiation of any treatment to determine the level of individual risk associated with the various treatment options."
World Health Organization (WHO)	2019	/	/	The WHO takes a stand against the 2019 IAAF regulation that requires women to medically reduce their natural testosterone levels.		World Medical Association (WMA) President Statement: WMA President Dr. Leonid Eidelman said: "We have strong reservations about the ethical validity of these regulations. They are based on weak evidence from a single study, which is currently being widely debated by the scientific community. They are also contrary to a number of key WMA ethical statements and declarations, and as such we are calling for their immediate withdrawal."
Canadian Centre for Ethics in Sport (CCES)	2016	/	/	Best practices (respect for the privacy of players, right to freedom choice of first name/pronoun/gender, providing information, the inclusiveness of rules, being attentive to the needs of trans athletes, training/prevention, access to toilets and lockers for all, proposing uniforms in accordance with gender expression). There is no tangible evidence about the effect of hormones. Recommendation: gender identity regulation. If other criteria apply, then it is up to the federation to prove legitimacy.		20: About hormone levels in regulations "Unfortunately, neither the 2015 IOC consensus meeting nor the NCAA [National Collegiate Athletic Association] policy are grounded in direct scientific evidence of hormone levels having a significant long-term impact on athletes' performance. No research has been done in this regard." 20: Elite recommendation "Based on this context and the evidence that is available, the Expert Working Group has reached the conclusion that transgender athletes should be able to participate according to the gender with which they identify, regardless of whether they have undergone hormonal treatment. If a sport organization can prove that hormonal treatment would be a reasonable and bona fide condition (meaning a required response to a genuine need) in order to create a level playing field in high performance sport, exceptions may apply."
Longman, J.	2016	Journalistic article, opinion piece	No	Argument: The discriminatory treatment of Caster Semenya.	Statement from the IAAF (P. Weiss) vs Semenya Statement by K. Karkazis on bias and stereotyping	

				Many champions have different physical advantages that are not subject to as much regulation, violence, and exclusion.	Example: Kenyan high-altitude training Example: The body size comparison between K. Durant and B. Griner Example: E. Mantyranta (who had a genetic mutation causing him to produce a higher-than-average amount of hemoglobin)	
Lenskyj, H. J. (Only chapter 4)	2018	Theoretical article	No	In countries such as Canada and Australia there have been political debates about making sport exempt from having to comply with anti-discrimination laws. The media's treatment of Laurel Hubbard makes it seem as if she made the decision to transition suddenly in a bid to win competitions. This demonstrates an ignorance of the lived experiences of trans people. "Objective science"? Biases that may appear in research: - Considering sport as a space that is reserved for men and masculinity, - Not taking into account biological and social constructs, - Assuming that testosterone gives athletes a physical advantage. Confusing causality with association.		
Pieper, L.P.	2016	History book of the femininity test in sports competitions (Introduction)	No	Introduction The IOC often uses the concepts of gender and sex interchangeably, especially between the years 1968 and 2000. The discursive change between "sex testing" (1968 to 1976/80) and "femininity testing" (1976 to 2000) (« contrôle de sexe » and « contrôle de féminité » in French) shows that biological data are not the only things that are being evaluated. Cold War: sport and gender control = confrontation surrounding sex (even if this did not systematically exist prior to the Cold War). The new "other" since 1990 = racialized women from the continents of Africa or Asia. Problem with the dialogue around <i>fair competition</i> = this is a goal that is not achievable anyway, but it is mobilized for the purpose of excluding certain populations.		
Westbrook, L.	2016	Theoretical article	Non-binary (they)	An article that attempts to trace the history of the terminology used to refer to trans people. Also attempts to think about trans people in relation to categories of sexuality.	Trans people are thought of almost exclusively through the prism of gender subversion. This approach is flawed; it obscures the social relation of the sexes and the consequences of this on the lived experiences of trans people.	

					The article highlights, without any real source or justification, both the beginning of the use of the term <i>transsexual</i>, pinpointing the first case of its usage in 1952, as well as the case of Christine Jorgensen. The conclusions drawn not only seem precarious, they also underline the cis centrism of the article. What is presented is a cis interpretation of the terms that are used by cis people to refer to trans people (but without making this point of view explicit, of course). The article takes an essentialist view of sex and gender by making a distinction between the term <i>transsexual</i> (defined as the act of changing one's biological sex) and <i>transgender</i> (defined as the act of changing one's gender). However, if the sex of an individual is determined by their gender, we can just as easily say that a person has changed their sex (or gender) regardless of the type of transition (whether it be social, medical, institutional) that has taken place. The author discusses the fact that the only word currently used to describe being attracted to trans people would be the slur <i>tranny chaser</i>. She goes on to propose potentially less offensive terms without taking into consideration the power dynamics that come into play in the fetishization of trans people by cis people. She even goes so far as to propose a new meaning for the word <i>transsexual</i>, suggesting that this term could be used to refer to individuals who are attracted to trans people. In proposing a new meaning for this term, the author is furthering the cis appropriation of terms relating to the trans experience. A portion of the trans population has already reclaimed this word.	
Pape, M.	2020	Qualitative semi-structured interviews n=62, with athletes, coaches, staff members, managers, officials, and federation representatives, media professionals, academics and activists between 2009 and 2016 = inclusion criterion: involved to any	No	Men at the elite level in athletics have hormone levels that are equivalent to the average hormone levels seen in women. Ignorance = an active process whereby it would have been possible to find out about a particular topic but where this knowledge has not been sought out or obtained. The 3 types of ignorance: 1. Disinformation Most athletes were in favour of the IAAF rules. But most of them did not really know much about what the stipulations laid out in the rules consisted of. The majority think that this is an ethical issue and not a scientific debate. Many did not know the history of the femininity test (one person proposed - without knowing that one had	This article allows us to examine the process of ignorance observed in members of the sports movement in cases that involve athletes with an endogenous testosterone level that is higher than the average level for women. The failure to inform oneself, to avoid confronting certain information, to question the actions of the federation, and to train/educate people about the discrimination experienced by these athletes is socially situated. Although the author accurately shows the three types of ignorance at play, the social positions of the different surveys could have been better taken into consideration, in particular, it would have been helpful to look at how the different power dynamics have an impact (notably where race, gender, class and nationality are concerned).	

		extent in the implementation of the testosterone regulations in the female category.		been done and without knowing the problems posed - to carry out a chromosomal test). There was a lot of confusion about the terms used in the debate such as the term "hermaphrodite." Some athletes were referred to as men. Pathologizing intersex athletes. 2. Ideology The formulation of the regulations = an enclosed and private space for the construction of knowledge. Preconceived ideas about the issue being discussed affect how the regulations are established in the first place. Most respondents strongly believe that testosterone levels have an impact on the differences in athletic performance. Many were incredulous and were surprised that the CAS suspended the regulation in 2015 due to a lack of scientific evidence. Confusion between endogenous and exogenous testosterone. Some chose to ignore the glaring lack of scientific evidence and were instead guided by their beliefs/stereotypes. This was particularly true for those in charge of formulating the regulations. 3. Avoidance Some federation workers who were contacted for an interview said that this was not their area of expertise and referred the interviewer to the federation's physicians. An official who tried to get more information and came up with evidence that the rules were not working at the IAAF was removed. No questioning of the rules; coaches placed their trust in the IAAF. Fear of backlash if the rules are challenged. Silence also forms part of the social position; some people have benefitted from the fact that the regulations remain in place, even though their underpinning is not scientifically correct. The federations were involved in maintaining the silence of the athletes. Some advised the athletes just to answer that the 800m did not concern them.	Even though cases involving trans athletes are not mentioned, it can be observed that these mechanisms are also at work in such cases.	

Appendix B: Scoping Review Yield

Figure 2 Summary of scoping review yield from June 2021.

#	Editor	Database	Types	Results
1.	Elsevier	Embase	Biomedical Sciences	96
2.	OVID	Medline	Biomedical Sciences	263
3.	ProQuest	PAIS International	Public Affairs	16
4.	OVID	PsycINFO	Psychology	193
5.	ProQuest	Sociological Abstracts & Social Services Abstracts	Social Sciences	121
6.	Proquest	Sport Medicine & Education Index	Sport Science	169
7.	EBSCO	SportDiscus	Sport Science	328
8.	CLARIVATE	Web of Science, Core Collection	Multidisciplinary	342
9.	EBSCO	Women's Studies International	Women	49
10	ProQuest	Worldwide Political Science Abstracts	Political Science	19
			TOTAL	1697
			Duplicates	703
			Primary	994

Appendix C: List of Some Canadian Organizations Who Have Trans Inclusion Policies at Competitive/Elite Levels

These Canadian sport organizations' policies take different approaches to including trans women, some choosing to focus on accepting all athletes' embodied strengths to be celebrated, including trans women's, without restrictions, and others taking a narrower approach to defining what kinds of embodiments are permissible.

- Archery Canada
- Biathlon Canada
- Bowling Federation of Canada
- Bowls Canada
- Canada Basketball
- Canadian Powerlifting Union
- Canoe Kayak Canada
- Climbing Canada
- Cycling Canada
- Field Hockey Canada
- Lacrosse Canada
- Quidditch Canada
- Ringette Canada
- Rowing Canada
- Rugby Canada
- Skate Canada
- Softball Canada
- Ultimate Canada
- Volleyball Canada
- Water Polo Canada
- Wheelchair Basketball Canada
- Wheelchair Rugby Canada

Joint position statement of the International Federation of Sports Medicine (FIMS) and European Federation of Sports Medicine Associations (EFSMA) on the IOC framework on fairness, inclusion and non-discrimination based on gender identity and sex variations

Fabio Pigozzi ^{1,2,3} Xavier Bigard^{1,4,5} Juergen Steinacker ^{1,6}
 Bernd Wolfarth ^{1,7} Victoriya Badtieva ^{1,8,9} Christian Schneider ^{1,10}
 Jeroen Swart ^{1,11} James Lee John Bilzon ^{1,12} Demitri Constantinou ^{1,13}
 Michiko Dohi ^{1,14} Luigi Di Luigi^{1,15} Chiara Fossati ^{1,2,3} Norbert Bachl^{1,16,17}
 Guoping Li^{1,18} Theodora Papadopoulou^{1,4,19} Maurizio Casasco^{1,4,20}
 Dina Christina (Christa) Janse van Rensburg ^{1,21,22} Jean-François Kaux^{1,23}
 Sandra Rozenstoka^{1,24} Jose-Antonio Casajus ^{1,25} Irina Zelenkova^{1,25}
 Emre Ak^{1,26} Bulent Ulkar^{1,27} Francisco Arroyo ^{1,28} Anca Ionescu^{4,29}
 André Pedrinelli ^{1,30} Mike Miller³¹ Patrick Singleton³¹ Malav Shroff³¹
 Nick Webbhorn^{32,33} James Barrett³⁴ Blair Hamilton ^{32,35} Michael Geistlinger³⁶
 Gianfranco Beltrami^{37,38} Sergio Migliorini³⁹ Lenka Dienstbach-Wech⁴⁰
 Stéphane Bermon ^{41,42} Yannis P Pitsiladis ^{1,4,32,35} on behalf of the
 International Federation of Sports Medicine (FIMS) and the European Federation of
 Sports Medicine Associations (EFSMA)

To cite: Pigozzi F, Bigard X, Steinacker J, *et al.* Joint position statement of the International Federation of Sports Medicine (FIMS) and European Federation of Sports Medicine Associations (EFSMA) on the IOC framework on fairness, inclusion and non-discrimination based on gender identity and sex variations. *BMJ Open Sport & Exercise Medicine* 2022;**8**:e001273. doi:10.1136/bmjsem-2021-001273



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to

Dr Yannis P Pitsiladis;
Y.Pitsiladis@Brighton.ac.uk

ABSTRACT

The IOC recently published its framework on fairness, inclusion and non-discrimination based on gender identity and sex variations. This framework is drafted mainly from a human rights perspective, with less consideration for medical/scientific issues. The framework places the onus for gender eligibility and classification entirely on the International Federations (IFs), even though most will not have the capacity to implement the framework. The position of no presumption of advantage is contrary to the 2015 IOC consensus. Implementation of the 2021 framework will be a major challenge for IFs that have already recognised the inclusion of trans and women athletes with differences of sexual development (DSD) using a scientific/medical solution. The potential consequences for sports that need to prioritise fairness or safety could be one of two extremes (1) exclusion of all transgender or DSD athletes on the grounds of advantage or (2) self-identification that essentially equates to no eligibility rules. Exclusion of all transgender or DSD athletes is contrary to the Olympic charter and unlawful in many countries. While having no gender eligibility rules, sport loses its meaning and near-universal support.

Key messages

What is already known

- ▶ Athletes are currently excluded from the female category in sport based on transgender or differences of sexual development status.
- ▶ The IOC published its new framework on fairness, inclusion and non-discrimination based on gender identity and sex variations in November 2021.
- ▶ The publication of this framework has generated debate and discussion in sport and exercise medicine.

Athletes should not be under pressure to undergo medical procedures or treatment to meet eligibility criteria. However, if an athlete is fully informed and consents, then it is their free choice to undergo carefully considered or necessary interventions for gender classification for sport to compete fairly and safely in their chosen gender. Free choice is a fundamental human right, but so is the right to fair and safe competition.

Key messages

What are the new findings

- ▶ It aims to facilitate a necessary critical discussion leading to a potential revision of the IOC framework.
- ▶ It strongly supports the right of each athlete to make their own choice based on their own needs and situation.
- ▶ It seeks to ensure that all athletes remain entitled to fair competition consistent with the WADA code that protects an athlete's fundamental right to participate in sport where fellow athletes have not been modified to their advantage by doping or other means.
- ▶ It suggests that it is essential that multisport international organisations such as the IOC take the responsibility to set standards and expectations based on competitive fairness and the best available science that all International Federations (IFs) can follow.
- ▶ It encourages all stakeholders in sport including the IOC, the IFs, the sponsors of sport, the WADA and research organisations including medical/biomedical research councils to dedicate the necessary funding to conduct essential research to support more evidence-based scientific solutions that are consistent with a rounded view of human rights and fairness.

The IOC published its new framework on fairness, inclusion and non-discrimination based on gender identity and sex variations¹ on 16 November 2021. This framework drafted mainly from a particular human rights perspective with little consideration of medical/scientific issues supersedes the 2015 IOC consensus on sex reassignment and hyperandrogenism that was concluded following a rigorous in-person IOC consensus meeting that focused on scientific and medical aspects of sex, gender and performance.² The 2015 consensus was drafted with the overriding sporting objective 'the guarantee of fair competition' and the realisation that 'restrictions on participation are appropriate to the extent that they are necessary and proportionate to the achievement of that objective'.² The 2021 IOC framework's position of 'no presumption of [performance] advantage' that states 'until evidence determines otherwise, athletes should not be deemed to have an unfair or disproportionate competitive advantage due to their sex variations, physical appearance or transgender status' is in stark contrast with the outcome of the 2015 IOC consensus, the scientific evidence,^{3,4} and the subsequent assessment of numerous sports medicine associations/commissions.^{5–11} For instance, the Sports Medicine Commission of World Rowing, also known as the World Rowing Federation (previously Fédération Internationale des Sociétés d'Aviron (FISA)), concluded that 'the FISA Sports Medicine Commission, in acknowledgement of the scientific and medical literature, see an important role of testosterone for performance, training, and regeneration in rowing and therefore supports the listing of testosterone in the World Anti-doping Agency (WADA) prohibited list (International Standard)',¹²

Given the above, this joint position statement aims to present an evidence-based critique that is consistent with a more rounded view of human rights and promote

discussion of this new framework, especially among those responsible for the care of athletes. This joint position statement of the International Federation of Sports Medicine (FIMS) and European Federation of Sports Medicine Associations (EFSMA) has been prepared by expert members of the respective Executive Committees and relevant Commissions, members and affiliates of the FIMS Collaborating Centres of Sports Medicine and other invited medical experts from the international sports and exercise medicine community, including Chief Medical Officers of numerous International Federations (IFs). A number of the authors of this joint position statement were also members of the 2015 IOC consensus on sex reassignment and hyperandrogenism.²

NOT SCIENTIFIC OR MEDICALLY-BASED

The new IOC framework mainly focuses on a particular human rights perspective, and the scientific, biological or medical aspects are not considered. This is highlighted specifically in point 5 of the framework, which states that there should be 'no presumption of advantage'¹ due to an athletes sex variations or transgender status. While not being named specifically in the framework but clarified in the presentation of the framework by the IOC,¹ it is clear that this point refers to the androgenic hormone testosterone and that there should be no presumption of advantage due to high concentrations of testosterone in the male range of 9.2–31.8 nmol/L¹³ for long periods. Testosterone is well established in the literature to promote the male secondary sex characteristics¹⁴ and is the primary driver for the increase in muscle mass,³ enhanced physique and performance for athletes.¹⁵ High concentrations of testosterone drive an increase in fat-free mass, which is responsible for much of the sex differences in sports performance between cisgender men and cisgender women.¹⁶ The performance-defining qualities of testosterone are also reflected in the fact that the WADA lists testosterone as an S1 anabolic agent and 'prohibits its use at all times'.¹⁷ Therefore, there is little doubt that high testosterone concentrations, either endogenous or exogenous, confer a baseline advantage for athletes in certain sports. Hence, it is clear to uphold the integrity and fairness of sport that these baseline advantages of testosterone must be recognised and mitigated, as has been called for previously.^{5 18 19}

Second, point 7.1 of the new framework mischaracterises the medical treatment of transgender athletes as a 'medically unnecessary procedure or treatment'.¹ Gender-affirming hormone treatment has been shown to have both positive physical and psychological effects, such as improved quality of life²⁰ and mood²¹ of the transitioning individual, with the administration of exogenous virilising hormones considered a mainstay treatment for many transgender patients²² and importantly, medically necessary for these patients.²³ The protocol for the treatment of trans women is to seek testosterone suppression and feminising exogenous oestradiol supplementation to the norms of cisgender women (testosterone 0.5–2.4 nmol/L;

oestradiol 15–350 pg/mL²⁴), while trans men seek the virilisation of exogenous testosterone into the norms of cisgender men (testosterone 9.2–31.8 nmol/L²⁴). This protocol for the treatment of trans women is consistent with the scientific consensus that trans women's testosterone should be suppressed to below 5 nmol/L to be eligible to compete in the female category of sport⁵ and therefore, conflicts with the statement that this treatment is 'medically unnecessary'.¹ The implementation of such eligibility criteria for trans women and the integration of trans men into the male category due to their now high concentrations of testosterone upholds the integrity of sport and upholds the protected category of women's sport. This implementation would also combat the concern about self-identification in the female category of sport due to the medically necessary treatment of transgender patients. Integrating cisgender women athletes with differences of sexual development (DSD) into the female category of sport is further complicated by differing levels of hyperandrogenism. Hence, the authors are sympathetic to the predicament that these cisgender women athletes with DSD face. However, as high testosterone concentrations can provide a baseline advantage for competitors in certain sports, high testosterone concentrations must be mitigated in the female category of these sports to maintain fairness and integrity.

Third, the Framework document states in item 7.2 that 'criteria to determine eligibility for a gender category should not include gynaecological examinations or similar forms of invasive examination, aimed at determining sex, sex variations or gender'. Although the need for such examinations to be carried out by an experienced practitioner must always be carefully considered, not being able to consider information that can be gleaned from a physical examination conflicts with current recommendations of endocrine and gynaecological scientific societies.²⁵ Indeed, a thorough evaluation should be considered if menarche has not occurred by 15 years of age or 3 years post thelarche. Moreover, some IFs set their rules for the eligibility of athletes with a DSD based on specific diagnoses and their level of androgen sensitivity (a clinical assessment so far). Not allowing so-called 'invasive tests' would sometimes result in the IF not being able to enforce its rules and the athlete not being able to comply with them.

IMPLEMENTATION

Implementation of this framework will create a dilemma for IFs that have already recognised the unique challenges raised by the inclusion of trans and women athletes with DSD. Recently proposed interventions for gender classification were based on the 2015 IOC Consensus and the respective IFs own comprehensive analyses with many stakeholders, including ethical, social, cultural and legal experts. For example, in 2020, World Rowing implemented a bylaw to rule 13 for men's and women's events as follows:

Eligibility by Gender 1) A rower is eligible to compete in a men's event or as a man in a mixed event if the gender of the rower is Male in the rower's passport or national identity card. 2) A rower is eligible to compete in a women's event, or as a woman in a mixed event, if: a) The gender of the rower is Female in the rower's passport or national identity card; and b) where applicable, the rower meets the requirements of paragraph 3 below 3) Where, either: a) the rower's gender has changed; or b) the rower has otherwise been required by the Executive Committee to establish eligibility to compete as a woman; the rower first satisfies the FISA Gender Advisory Panel that the rowers' serum testosterone concentration has been less than 5 nmol/L continuously for a period of at least the previous 12 months and secondly meets any other requirements reasonably set by the Executive Committee.²⁶

Similar solutions to those implemented by World Athletics^{6 7} have been adopted by other IFs such as Union Cycliste Internationale²⁷ and World Rowing²⁶ and now in conflict with the IOC framework (table 1). Such conflicting guidelines, rules and recommendations will only confuse the IFs and athletes and provide legal ambiguity for lawyers to exploit when pursuing a gender-related case at the Court of Arbitration for Sport.

In another departure from the 2015 IOC consensus, the 2021 IOC framework places the responsibility for gender classification entirely on the IFs, even though most IFs will not have the capacity, resources or necessary expertise to adopt the framework. For instance, the 2021 framework requires 'Any restrictions arising from eligibility criteria should be based on robust and peer-reviewed research that demonstrates a consistent, unfair, disproportionate competitive advantage in performance or unpreventable risk to the physical safety of other athletes'.¹ The burden of proof is now on the IFs to provide 'evidence-based' eligibility criteria within the very narrow constraints imposed by the framework that requires 'athletes should be allowed to compete in the category that best aligns with their self-determined gender identity' and 'athletes should never be pressured by an International Federation, sports organisation, or any other part (either by way of the eligibility criteria or otherwise) to undergo medically unnecessary procedures or treatment to meet eligibility criteria'.¹

CONSEQUENCES

The potential consequences of these imposed constraints could be one of two unwanted extremes (1) exclusion of transgender or DSD athletes on the grounds of performance advantage or (2) self-identification that all but equates to no eligibility rules. By adopting the recent IOC framework without the possibility of necessary interventions for gender classification (the authors preferred use of the term rather than the unhelpful and emotionally charged concept of 'unnecessary medical intervention'),

Table 1 Selection of International Federations policies on integrating trans women and female athletes with differences of sexual development (DSD) into the female category of sport

International Federation (eligibility criteria)	Rule
World Athletics (trans women) ⁷	The athlete must demonstrate that the concentration of testosterone in serum has been less than 5 nmol/L continuously for at least 12 months, and keep serum testosterone concentration below 5 nmol/L to maintain her eligibility.
World Athletics (female athletes with DSD) ⁶	The athlete, if deemed relevant, must reduce her blood testosterone level to below five (5) nmol/L for a continuous period of at least 6 months to be eligible for restricted events, and henceforth must maintain her blood testosterone level below five (5) nmol/L continuously.
USA Hockey (trans women) ²⁹	A trans woman desiring to play girls competitive hockey must confirm by a medical professional that the athlete has undergone at least 1 year of testosterone suppression therapy. The athlete must additionally provide a personal statement, confirming the athlete's gender identity, and written confirmation of gender identity from a healthcare provider.
World Rugby (trans women) ⁸	Transgender women may not currently play women's rugby.
Scottish Women's Football Association (trans women) ¹¹	May compete in female or mixed-sex domestic competition by providing evidence that her hormone therapy has brought her blood measured testosterone levels within the range of her affirmed gender.
International Tennis Federation (trans women) ¹⁰	The Athlete must provide a written and signed declaration, that her gender identity is female; and must demonstrate that the concentration of testosterone in her serum has been less than 5 nmol/L1 continuously for at least 12 months and that she is ready, willing, and able to continue to keep it below that level for so long as she continues to compete in the female category of competition.
USA Gymnastics (trans women) ⁹	USAG believes that transgender and non-binary gymnasts should not be restricted from taking part in gymnastics competitions based on their gender identity. Athletes wishing to compete at the international track level must comply with the IOC guidelines for transgender athletes.
Union Cycliste Internationale (trans women) ²⁷	A signed declaration that her gender identity is female, demonstrate that the concentration of testosterone in her serum has been less than 5 nmol/L2 continuously for at least 12 months and she must keep her serum testosterone concentration below 5 nmol/L to maintain eligibility.
World Rowing (trans women) ²⁶	A rower is eligible to compete in a women's event, or as a woman in a mixed event, if: - The gender of the rower is Female in the rower's passport or national identity card and - where applicable, the rower meets the requirements of paragraph three below. 3. Where, either: - the rower's gender has changed; or - the rower has otherwise been required by the Executive Committee to establish eligibility to compete as a woman; the rower first satisfies the World Rowing Gender Advisory Panel that the rowers' serum testosterone concentration has been less than 5 nmol/L continuously for a period of at least the previous 12 months and second meets any other requirements reasonably set by the Executive Committee.
World Rowing (female athletes with DSD) ²⁶	The Executive Committee will appoint and maintain from time to time a panel of experts in the specialist areas of Gender Identification, Sex-reassignment, Hyperandrogenism, Transgender and Differences of Sexual Development (DSD) to be known as the Gender Advisory Panel. The purpose of that panel is to evaluate cases seeking a determination of gender eligibility and to provide expert advice to the Executive Director, the Executive Committee, or the Council (as the case may require) on those specialist areas.

exclusion of all transgender or DSD athletes on the grounds of performance is likely in sports where safety and fairness are prioritised (eg, Athletics, Rugby, Boxing, Judo); at least during the time it will take for confirmatory research to be conducted. A recent viewpoint provided a potential roadmap for integrating trans women into the elite female category of sport.¹⁹ Some sports may be impacted by higher testosterone concentrations, while others may not. Safety is not an issue for sports that do not include contact with an opponent but have a physical challenge (eg, archery) and could be considered a

testosterone impacted sport. Therefore, eligibility regulations would then be drawn up by the sports IF based on fair competition. Conversely, some sports do not include contact with the opponent or a physical challenge (ie, shooting) which could be considered a non-testosterone impacted sport. Therefore, the IF would then prioritise inclusion by maintaining baseline eligibility regulations necessary to uphold sporting integrity and prevent the premise of self-ID in the female category. However, we believe that these decision-making principles could be

used for all IFs when considering the integration of trans women into the elite female competition.

The development of the 2021 IOC framework would in many countries be unlawful and against the Olympic charter that states:

“The enjoyment of the rights and freedoms set forth in this Olympic Charter shall be secured without discrimination of any kind, such as race, colour, sex, sexual orientation, language, religion, political or other opinion, national or social origin, property, birth or other status”.²⁸

In the other extreme case of an equally undesirable consequence of having no gender eligibility rules, that is, self-identification that amounts to a free choice to compete in any gender classification, sport would lose its integrity and near-universal support. As we have seen during the COVID-19 crisis, sport is much poorer without supporters. Without rules that are perceived as fair, sport will not engage the younger generation and likely negatively impact future participation rates in the female category. As stated in the 2021 framework, athletes should never be pressured by an IF, sports organisation, or any other party to undergo any medical procedures or treatment to meet eligibility criteria. However, if an athlete is fully informed and consents, then it is their free choice to undergo ‘necessary interventions for gender classification’ to compete in the gender classification of their choice and return to the main theme of the new IOC framework, free choice is a fundamental human right.

CONCLUSIONS

The new IOC framework leaves all responsibilities to the IFs, whereas the authors believe the IOC should provide direction to the IFs. The IOC framework only deals with this important issue from a particular human rights perspective, yet this must be seen in a more rounded human rights perspective and is also a medical and scientific matter. The authors would like to see further discussion and consultation with all stakeholders leading to a balanced framework that protects the rights of all athletes and gives IFs the tools they need to ensure inclusion and fairness.

Author affiliations

¹International Federation of Sports Medicine (FIMS), Lausanne, Switzerland

²Department of Movement, Human and Health Sciences, University of Rome “Foro Italico”, Rome, Italy

³Villa Stuart Sport Clinic, FIFA Medical Center of Excellence, Rome, Italy

⁴European Federation of Sports Medicine Associations (EFSMA), Lausanne, Switzerland

⁵Union Cycliste Internationale (UCI), Aigle, Switzerland

⁶Division of Sports and Rehabilitation Medicine, Department of Internal Medicine, Ulm University Hospital, Ulm, Germany

⁷Department of Sports Medicine, Humboldt University and Charité University School of Medicine, Berlin, Germany

⁸Moscow Research and Practical Center for Medical Rehabilitation, Restorative and Sports Medicine, Moscow Healthcare Department, Moscow, Russian Federation

⁹I.M. Sechenov First Moscow State Medical University (Sechenov University), Ministry of Health of Russia, Moscow, Russian Federation

¹⁰Orthopaedic Center Theresie, Munich, Germany

¹¹Health through Physical Activity, Lifestyle and Sport Research Centre (HPALS), Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

¹²Department for Health, University of Bath, Bath, UK

¹³Centre for Exercise Science and Sports Medicine, University of the Witwatersrand, Johannesburg, South Africa

¹⁴Sports Medical Center, Japan Institute of Sport Sciences, Tokyo, Japan

¹⁵Unit of Endocrinology, Department of Movement, Human and Health Sciences, University of Rome “Foro Italico”, Rome, Italy

¹⁶Institute of Sports Science, University of Vienna, Vienna, Austria

¹⁷Austrian Institute of Sports Medicine, Vienna, Austria

¹⁸National Institute of Sports Medicine, Beijing, China

¹⁹Defence Medical Rehabilitation Centre, Stanford Hall, Loughborough, UK

²⁰FIMS Collaborating Center of Sports Medicine, Institute of Sports Medicine in Milan (Istituto di Medicina dello Sport di Milano), Milano, Italy

²¹Section Sports Medicine, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa

²²Medical Board Member, World Netball, Manchester, UK

²³Sports2, Liège University and University Hospital of Liège, Liège, Belgium

²⁴FIMS Collaboration Centre of Sports Medicine, Sports laboratory, Riga, Latvia

²⁵GENUD research group, FIMS Collaborating Center of Sports Medicine, Department of Physiatry and Nursing, University of Zaragoza, Zaragoza, Spain

²⁶FIMS Collaborating Center of Sports Medicine, Gloria Sports Arena Belek, Antalya, Turkey

²⁷Sports Medicine Department, Faculty of Medicine, Ankara University, Ankara, Turkey

²⁸FIMS Collaborating Center of Sports Medicine, Guadalajara, Mexico

²⁹Sports Medicine, Carol Davila University of Medicine and Pharmacy, Bucuresti, Romania

³⁰Department of Orthopaedics, University of São Paulo Medical School, São Paulo, Brazil

³¹World Olympians Association (WOA), Lausanne, Switzerland

³²School of Sport and Health Sciences, University of Brighton, Eastbourne, UK

³³Medical Committee, International Paralympic Committee (IPC), Bonn, Germany

³⁴The Gender Identity Clinic Tavistock and Portman NHS Foundation Trust, London, UK

³⁵Centre for Stress and Age-related Disease, University of Brighton, Brighton, UK

³⁶Department of Public, International and European Law, Unit International Law, University of Salzburg, Salzburg, Austria

³⁷Medical Commission, World Baseball Softball Confederation, Pully, Switzerland

³⁸Faculty of Sport Sciences, University of Parma, Parma, Italy

³⁹World Triathlon Medical, World Triathlon, Lausanne, Switzerland

⁴⁰Department of Orthopaedics, Spine and Trauma Surgery, Hospital zum Heiligen Geist Frankfurt, Frankfurt, Germany

⁴¹World Athletics, Health and Science Department, Monaco

⁴²LAMHESS, Université Côte d’Azur, Nice, France

Twitter Blair Hamilton @BlairH_PhD

Contributors All authors have contributed significantly to the preparation of this viewpoint and fully share its contents.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Fabio Pigozzi <http://orcid.org/0000-0001-5808-9405>

Juergen Steinacker <http://orcid.org/0000-0001-8901-9450>

Bernd Wolfarth <http://orcid.org/0000-0001-6501-3003>

Victoriya Badtieva <http://orcid.org/0000-0003-4291-679X>

Christian Schneider <http://orcid.org/0000-0003-4834-4382>
 Jeroen Swart <http://orcid.org/0000-0001-7098-0313>
 James Lee John Bilzon <http://orcid.org/0000-0002-6701-7603>
 Demetri Constantinou <http://orcid.org/0000-0002-3363-7695>
 Michiko Dohi <http://orcid.org/0000-0002-1126-7849>
 Chiara Fossati <http://orcid.org/0000-0002-2870-7185>
 Dina Christina (Christa) Janse van Rensburg <http://orcid.org/0000-0003-1058-6992>
 Jose-Antonio Casajus <http://orcid.org/0000-0002-7215-6931>
 Francisco Arroyo <http://orcid.org/0000-0001-5072-1189>
 André Pedrinelli <http://orcid.org/0000-0002-8449-7493>
 Blair Hamilton <http://orcid.org/0000-0001-7412-1188>
 Stéphane Bermon <http://orcid.org/0000-0002-9529-2901>
 Yannis P Pitsiladis <http://orcid.org/0000-0001-6210-2449>

REFERENCES

- 1 International Olympic Committee. Framework on fairness, inclusion and non-discrimination on the basis of gender identity and sex variations, 2021. Available: <https://stillmed.olympics.com/media/Documents/News/2021/11/IOC-Framework-Fairness-Inclusion-Non-discrimination-2021.pdf>
- 2 International Olympic Committee. Consensus meeting on sex reassignment and hyperandrogenism November 2015, 2015. Available: https://stillmed.olympic.org/Documents/Commissions_PDFfiles/Medical_commission/2015-11_ioc_consensus_meeting_on_sex_reassignment_and_hyperandrogenism-en.pdf
- 3 Handelsman DJ, Hirschberg AL, Bermon S. Circulating testosterone as the hormonal basis of sex differences in athletic performance. *Endocr Rev* 2018;39:803–29.
- 4 Handelsman DJ, Bermon S. Detection of testosterone doping in female athletes. *Drug Test Anal* 2019;11:1566–71.
- 5 Hamilton BR, Lima G, Barrett J. Integrating Transwomen and female athletes with differences of sex development (DSD) into elite competition: the FIMS 2021 consensus statement. *Sports Med* 2021;51.
- 6 World Athletics. Eligibility regulations for the female classification (athletes with differences of sex development), 2019. Available: <https://www.worldathletics.org/about-iaaf/documents/book-of-rules>
- 7 World Athletics. Eligibility regulations transgender athletes, 2019. Available: <https://www.worldathletics.org/about-iaaf/documents/book-of-rules>
- 8 World Rugby. World rugby transgender guideline, 2020. Available: <https://playerwelfare.worldrugby.org/?documentid=231>
- 9 USA Gymnastics. USA gymnastic policy for transgender inclusion, 2020. Available: https://usagym.org/PDFs/About%20USA%20Gymnastics/transgender_policy.pdf
- 10 International Tennis Federation. Transgender policy, 2018. Available: <https://www.itftennis.com/media/2163/itf-transgender-policy.pdf>
- 11 Scottish Womens Football Association. Transgender and transsexual policy, 2019. Available: <https://scotwomensfootball.com/wp-content/uploads/2019/03/SWF-Policy-Transgender-People-Playing-in-SWF-FINAL.pdf>
- 12 Steinacker JM, Koubaa D, Nielsen HB, et al. Statement of FISA sports medicine Commission: biological effects of testosterone. *Dtsch Z Sportmed* 2019;2019:83–4.
- 13 NHS. Testosterone, 2020. Available: <https://www.gloshospitals.nhs.uk/our-services/services-we-offer/pathology/tests-and-investigations/testosterone/>
- 14 Mooradian AD, Morley JE, Korenman SG. Biological actions of androgens. *Endocr Rev* 1987;8:1–28.
- 15 Institute of Medicine, Board on Health Sciences Policy, Committee on Assessing the Need for Clinical Trials of Testosterone Replacement Therapy. *Testosterone and aging: clinical research directions*. National Academies Press, 2004.
- 16 Nickerson BS, McLester CN, McLester JR, et al. Relative accuracy of anthropometric-based body fat equations in males and females with varying BMI classifications. *Clin Nutr ESPEN* 2020;35:136–40.
- 17 World Anti-Doping Agency. What is prohibited: anabolic agents, 2021. Available: <https://www.wada-ama.org/en/content/what-is-prohibited/prohibited-at-all-times/anabolic-agents>
- 18 Hamilton BR, Martinez-Patiño MJ, Barrett J, et al. Response to the United nations human rights Council's report on race and gender discrimination in sport: an expression of concern and a call to Prioritise research. *Sports Med* 2021;51:839–42.
- 19 Hamilton BR, Guppy FM, Barrett J, et al. Integrating transwomen athletes into elite competition: the case of elite archery and shooting. *Eur J Sport Sci* 2021;21:1500–9.
- 20 Gorin-Lazard A, Baumstarck K, Boyer L, et al. Is hormonal therapy associated with better quality of life in transsexuals? A cross-sectional study. *J Sex Med* 2012;9:531–41.
- 21 Wierckx K, Mueller S, Weyers S, et al. Long-term evaluation of cross-sex hormone treatment in transsexual persons. *J Sex Med* 2012;9:2641–51.
- 22 Unger CA. Hormone therapy for transgender patients. *Transl Androl Urol* 2016;5:877–84.
- 23 Coleman E. Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People: An Introduction. In: *Principles of gender-specific medicine*. Elsevier, 2017: 69–75.
- 24 Safer JD, Tangpricha V. Care of transgender persons. *N Engl J Med Overseas Ed* 2019;381:2451–60.
- 25 Klein DA, Paradise SL, Reeder RM. Amenorrhea: a systematic approach to diagnosis and management. *Am Fam Physician* 2019;100:39–48.
- 26 World Rowing Federation. Rule 15 and Bye law to rule 15—Men's and Women's Events, 2020. Available: www.worldrowing.com
- 27 Union Cycliste Internationale. Part 13 medical rules: chapter V eligibility regulations for transgender athletes, 2020. Available: <https://archive.uci.org/docs/default-source/rules-and-regulations/part-xiii-medical-rules-01.03.2020.pdf>
- 28 International Olympic Committee. Olympic charter, 2020. Available: www.olympic.org/documents/olympic-charter
- 29 USA Hockey. Transgender athlete eligibility policy, 2019. Available: https://cdn3.sportngin.com/attachments/document/8a0b-1766565/USA_Hockey_Transgender_Athlete_Eligibility_Policy.pdf



The current knowledge on the effects of gender-affirming treatment on markers of performance in transgender female cyclists.

Pr. Xavier Bigard
Update June 2022

It is now commonly accepted that biology does not neatly divide humans into two separate sexes. There are two main groups of people (i.e., intersex and transgender) who fall outside of the binary division that most people take for granted. This is the origin of the different concepts of sex and gender. Sex is defined by the human genotype and pertains to biologic differences between males and females (Bassett et al., 2020). Gender is a fluid concept shaped by men's and women's self-perceptions, social constructs, and culturally charged attitudes and expectations. The gender identity is one of the manifestations of biological sex and its inclusion as one of the biological components of sex is not without controversy.

In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), people whose gender at birth is contrary to the one they identify with are diagnosed with gender dysphoria (Cohen-Kettenis and Pfafflin, 2010). Male-to-female gender dysphoric persons, referred to as TransWomen, are commonly treated with “gender-affirming treatments” comprising estradiol preparations in combination with testosterone blockade drugs, with or without surgical sex reassignment.

Some Transgender athletes would like to participate in competitive sport, which requires determining the conditions under which these individuals can compete in their new gender category. The current debate over including Transgender athletes in sports competitions is centered on biological differences between genders, and especially between TransWomen and CisWomen. It would be reasonable to allow transgender athletes to

compete with other female athletes if, and only if the inclusion of these athletes does not unduly alter the health and safety of participants and guarantee fair and meaningful competitions.

I. Sporting performance advantages in males

Performance disparities between male and female athletes vary across sports (Figure 1). These differences in athletic performance don't appear until after puberty and are thought to be most likely due to increased circulating testosterone levels in "male" athletes whose sex was assigned at birth (CisMen), compared to "female" athletes whose sex was assigned at birth (CisWomen).

With puberty, testosterone induces changes in muscle mass, strength, anthropometric variables and hemoglobin levels in males (Handelsman et al., 2018). Physiologic sex-based differences lead to a gap in sports performance between males and females, mainly explained by the biological effects of elevated pubertal testosterone (Bassett et al., 2020; Handelsman et al., 2018). Different sports require different physiological qualities and an advantage in one discipline may be neutral or even a disadvantage in another. But there are only a few sports where men do not have a performance advantage over women because of the physiological determinants of performance affected by testosterone.

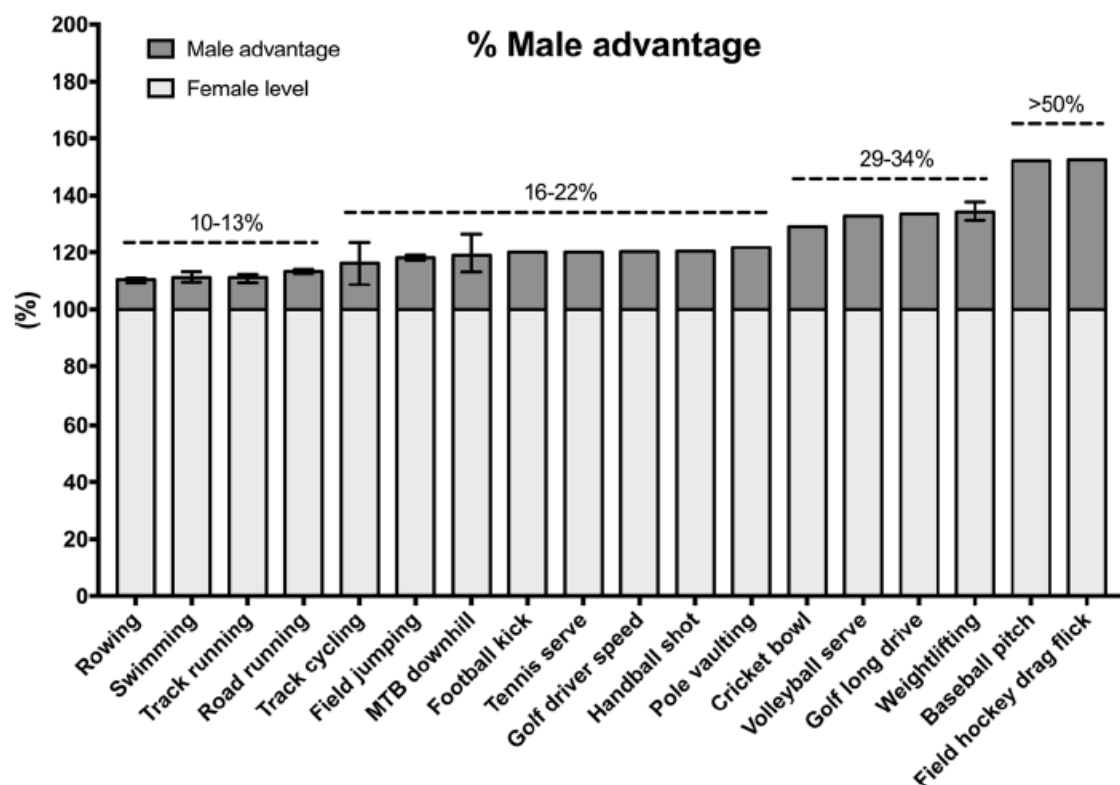


Figure 1. Male performance advantage over females across various sporting events. The female level is set to 100%. The metrics were compiled from publicly available databases (from Hilton and Lundberg, 2021).

A longitudinal analysis of 82 Olympic events found that the performance disparity between males and females has remained relatively stable since 1983 (Thibault et al., 2010). Only one cycling discipline is comparable over time in terms of performance, i.e. track sprint. The gender gap has been stable since 1993 and estimated at approximately 8.7%. In another

study, performance measures were compiled from publicly available sports federation databases and/or tournament/competition records (Hilton and Lundberg, 2021). The performance gap was estimated to an average of 16% in track cycling (Figure 1), with high variation across disciplines (from 9% in the 4000 m team pursuit to 24% in the flying 500 m time trial).

By analogy, we can look at cycling performance differences during triathlon. An analysis of long-distance triathlon performance estimated to 12.7% the sex-based difference in cycling time (Lepers 2008). A separate investigation measuring short-distance triathlon performance found an even greater performance gap between males and females for cycling, i.e. 13.4% (Etter et al., 2013). The idea that women can excel in endurance events has been supported by studies showing that the performance gap between males and females decreases in longer events (Bassett et al., 2020). However, it is not known whether this also applies to long-duration cycling events.

In summary, a performance gap exists on the basis of gender, with men performing better than women, which can be estimated to approximately 9-16% in track cycling and 13-14% in road cycling. Despite an increase in female participation in sport competitions, this performance gap has remained stable since the 1980s and is rooted in underlying physiologic and hormonal sex-based differences. Males have longer greater muscle mass and strength, and greater aerobic capacity, while females exhibit less muscle fatigability and faster recovery after endurance exercise. These physiologic differences are at the center of contentious discussions regarding the eligibility of TransWomen athletes for competing in the female category.

II. Limiting factors of performance in Cycling.

An overview of the physiological and metabolic factors associated with cycling performance is necessary to support eligibility rules for Transgender cyclists. A better understanding of the mechanisms underlying performance in cycling competitions will allow evidence based regulations for the inclusion of TransWomen in the female category.

In most endurance cycling events, performance is mainly determined by the maximal sustained power production for a given race distance, and the energy cost of maintaining a given racing speed (Mujika et al., 2016). For other cycling disciplines (e.g. sprints in track and road cycling, BMX, etc.), muscle power is a major determinant of performance.

1- The maximal oxygen uptake.

There is substantial evidence demonstrating that successful professional road cyclists possess high values of the absolute maximal oxygen uptake ($\dot{V}O_{2max}$) (~ 74 mL/kg/min) and a lactate threshold (LT2) that is $\sim 90\%$ of $\dot{V}O_{2max}$ (Faria et al., 2005).

Estimated absolute maximal oxygen uptake values ($\dot{V}O_{2max}$) are significantly higher in flat terrain riders (FT, 5.67 ± 0.44 l $\cdot$ min $^{-1}$) and time trial riders (TT, 5.65 ± 0.53 l $\cdot$ min $^{-1}$) than in uphill riders (UH, 5.05 ± 0.39 l $\cdot$ min $^{-1}$). On the other hand, $\dot{V}O_{2max}$ relative to body mass was significantly lower in FT (74.4 ± 3.0 mL $\cdot$ kg $^{-1}\cdot$ min $^{-1}$) than in TT, AT, and UH (79.2 ± 1.1 , 78.9 ± 1.9 and 80.9 ± 3.9 mL $\cdot$ kg $^{-1}\cdot$ min $^{-1}$, respectively) (Padilla et al., 1999).

$\dot{V}O_{2max}$ is not only a limiting factor for road cycling, but also for all endurance disciplines, MTB cross-country, track pursuit, track peloton races, cyclo-cross, etc. However, $\dot{V}O_{2max}$ alone is not a good predictor of endurance performance when athletes of similar endurance ability are compared. The mechanisms that underlie why lactate parameters

provide a better predictor of endurance performance than $\dot{V}O_2\text{max}$ continue to be examined. The argument has been presented that $\dot{V}O_2\text{max}$ is mainly limited by the oxygen supply to the close muscle mitochondria. However, lactate levels are related to the capacity to transport lactate and proton (H^+) out of the myofibres, and the capacity of skeletal muscle to take up lactate.

Central factors are likely to limit $\dot{V}O_2\text{max}$, while the lactate response to exercise is primarily related to peripheral factors in the trained skeletal muscles. These peripheral factors include the skeletal muscle capillarity, percentage of slow-twitch fibres, activities of key oxidative enzymes and mitochondrial respiratory capacity.

Lactate Threshold-2 (LT2) has been reported as the highest possible steady-state work intensity that can be sustained for a prolonged period of time. It has been shown that the LT2- $\dot{V}O_2$ is a strong predictor ($r = 0.96$) of endurance performance among trained cyclists with similar $\dot{V}O_2\text{max}$ (Coyle et al., 1991). A close relationship exists between LT2- $\dot{V}O_2$ and future performance potential in cycling. Therefore, this parameter is also an excellent endurance index (Faria et al., 2005).

2- Maximal power output.

There is substantial evidence demonstrating that absolute maximal power output values (W_{max}) obtained during a maximal incremental cycling test can be used as predictor of cycling performance in endurance disciplines. Changes in W_{max} contribute to explain 82% of the variability in performance during a 20 km cycling time trial. This is why W_{max} is a valid predictor of the performance during this cycling exercise (Hawley and Noakes, 1992). In addition, power output at lactate threshold (LT) has also been shown to be a reliable predictor of cycling potential ($r = 0.88$) (Faria et al., 2005).

The highest W_{max} values are commonly measured in Flat Terrain riders (FT, 461 ± 39 W), this value being higher than that of All Terrain (AT, 432 ± 27 W) and Uphill (UH, 404 ± 34 W, $P < 0.05$) (Figure 2) (Padilla et al., 1999). Time Trial specialists also showed significantly higher W_{max} values (457 ± 46 W) than UH (Figure 2).

When expressed relative to body mass, UH presented the highest W_{max} values (6.47 ± 0.33 W·kg⁻¹), followed by TT, AT, and FT (6.41 ± 0.12 , 6.35 ± 0.18 and 6.04 ± 0.29 W·kg⁻¹, respectively). These values were significantly different between UH and FT (Figure 2). A W_{max} /body weight ratio higher than 5.5 W·kg⁻¹ has been considered a necessary prerequisite for top-level competitive cyclists. However, this criterion must be used with caution as the protocol used during testing can affect the outcome of power output. Moreover, this suggested value seems to be slightly low for professional cycling; previous studies reported W_{max} /body weight ratio values varying between mean values of 6.34 W·kg⁻¹ (with a lowest value of 5.58 W·kg⁻¹) (Padilla et al., 1999) and 6.79 W·kg⁻¹ (Ice et al., 1988).

The importance of muscle mass for endurance cycling performance has been highlighted, especially in Women, with a significant correlation between the changes in mean power output during a 40-min all-out test, mean $\dot{V}O_2$ during the test, and changes in a marker of the quadriceps femoris muscle mass ($r = 0.73$, and $r = 0.59$, respectively) (Vikmoen et al., 2016). The relationship between lower body muscle mass and mean W_{max} measured during cycling exercises of different durations ranging from 1 second to 10 min has been examined (Haakonssen et al., 2013). Competitive female cyclists with high lower body muscle mass have high W_{max} values, (1 kg lower body lean mass = ~4% increase in mean W_{max} during the 10-min test).

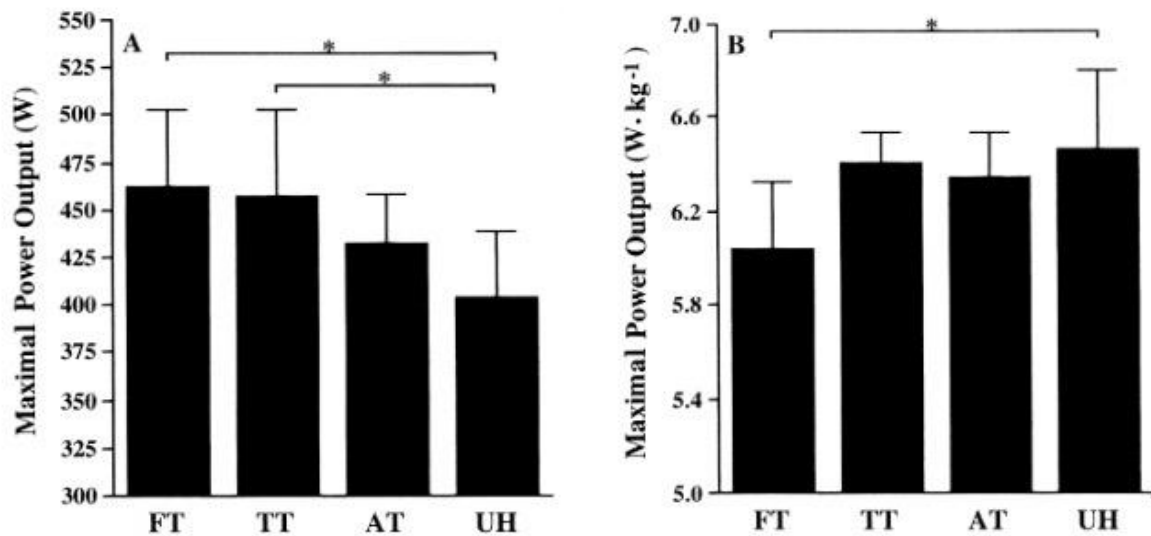


Figure 2. Maximal power output (W_{max}) values 1 (Mean $\pm$ SD) for flat terrain (FT, $N = 5$), time trial (TT, $N = 4$), all terrain (AT, $N = 6$), and uphill (UH, $N = 9$) specialists. A: absolute values; B: relative to body mass. * denotes a significant difference ($P < 0.05$) between groups. (from Padilla et al., 1999).

3- Efficiency

Efficiency is a measure of the percentage of total energy expended that produces external work. It has been shown that in professional cyclists the rate of the rise in $\dot{V}O_2$ during graded exercise decreases from moderate to high workloads, to the maximal attainable power output (Lucia et al., 2002). This finding is mainly related to an increase in mechanical efficiency with rising exercise loads intensity, and then, extremely high workloads can be sustained for extended periods of time, representative of high cycling efficiency. This cycling efficiency during heavy exercise appears to be positively related to the percentage of type I myofibres in the vastus lateralis and a lower oxygen cost during submaximal exercise.

4. Anaerobic power.

During accelerations and sprints, anaerobic capacity and maximal speed contribute to cycling performance. Therefore, the ability to generate high power in a short period of time is undoubtedly an important factor in cycling performance, regardless of the cycling discipline. This ability is essential when a cyclist needs to close a gap, break away from the peloton, or win an intermediate or a final sprint in road cycling. But this ability is also essential in track cycling, BMX, cross-country MTB.

One of the key determinants of anaerobic capacity and maximal speed is muscle mass. Competitive female cyclists with greater lower body muscle mass have $\sim 9\%$ higher W_{max} per kg muscle mass over 1 sec and 6 sec, measured during all-out cycling exercises in comparison with other female cyclists (Haakonssen et al., 2013). During a 30-sec maximum sprint, regression analysis indicated that 1 kg of muscle mass was associated with an additional 35 W maximal power output. During sprint of short duration, female riders were able to produce approximately 50-80 $W.kg^{-1}$ muscle mass, based on DXA assessment of lean mass and the highest 1 sec power produced during an all-out 6 sec sprint (Haakonssen et al., 2013).

The SRM system allows to calculate W_{max} from the torque and the angular velocity, and may be used during both laboratory and field-based studies. This system is able to record power, speed, distance covered, cadence and heart rate.

In summary, these data show that in addition to aerobic capacity, muscle strength / power contributes to improved performance in endurance cycling, by improving economy of movement. In addition, strength and power abilities, anaerobic capacity and then maximal speed remain essential for sprinting disciplines. Therefore, for all cycling disciplines, performance is based on both endurance and strength / power abilities, with different weighting factors for long duration (road races, track pursuits, mountain biking, etc.) and short duration disciplines (sprint track, BMX racing, etc.).

III. Is the male performance advantage lost when blood Testosterone is significantly reduced in TransWomen?

Whether TransWomen should be allowed to compete against CisWomen, and if so, under what conditions, is extremely controversial. In addition to their well-known anabolic consequences on lean body mass, androgens also stimulate erythropoiesis mental drive and aggressiveness. They improve physical performance in both strength/power sports and aerobic sport (Handelsman 2018).

Therefore, the female sport needs to be a protected category in order to preserve the safety, fairness and integrity of cycling. There are many quantifiable performance-related differences between male and female athletes (see paragraph I of the present report). In contrast, the performance-related differences between TransWomen who have received transition treatment (i.e. gender affirming hormone treatment and eventually surgical sex reassignment) and CisWomen are less clear, mainly due to a lack of available experimental data. The world of sport is now facing the challenge of how to include Transgender people in sporting competitions, especially TransWomen in the female category. Questions then arise as to which category Transgender athletes and especially TransWomen should compete in.

Despite only very few experimental data, the general consensus is that differences in testosterone levels is currently the single most important factor contributing to the performance differences between male and female athletes (Handelsman, 2018). This view is supported by the results several studies that demonstrated a significant advantage for women with higher testosterone levels in selected athletic performance (Bermon et Garnier 2017 ; Bermon et al., 2018). When compared with the lowest free testosterone tertile, women athletes with the highest free testosterone tertile demonstrated significantly better performances in running races, with calculated differences of 2.73%, 2.78%, and 1.78% in 400 m, 400 m hurdles, and 800 m, respectively. Moreover, hyperandrogenic athletes (i.e., with either 5α -reductase deficiency or with partial androgen insensitivity) were overrepresented by a factor of 140 during the 2011 IAAF world championships (Bermon et al. 2014). In another study, it was demonstrated significant correlations between endogenous androgen profile, lean body mass and physical performance in CisWomen athletes members of a national Olympic team, involved in either power, endurance or technical sport categories (Eklund et al., 2017). Taken together, these data underline the importance of testosterone for sports performance, here in athletics.

Biological research studies on transgender athletes are rare. To date, there have been no prospective studies investigating the changes in athletic performance in transgender athletes after hormonal transition. Studies in non-athletic TransWomen report changes in lean body mass, muscle cross-sectional area, muscular strength, haemoglobin and/or haematocrit, during the transition treatment, all of which are of relevance for cycling

performance. The important question is the timing of responses of these important parameters for performance under gender affirming hormone treatment.

1- Muscle mass

Muscle mass and muscle strength/power are key parameters underpinning male performance advantages. Unfortunately, studies on the effects of testosterone suppression on muscle mass and strength in transgender athletes are rather scarce.

Studies in non-athletes TransWomen showed a decrease in lean body mass during the first year of transition treatment. The collective evidence from 12 longitudinal studies suggests that 12 months of testosterone suppression to female reference blood levels result in a modest (between -3 to -5.4%) loss of lean body mass or muscle size (Hilton and Lundberg, 2021; Harper et al., 2021). No study has been able to show a decrease in muscle mass greater than -12% after 3 years of testosterone suppression (Gooren and Bunck, 2004) and -17% after a mean of 8 years of treatment (from 4 to 20 years; Lapauw et al., 2008).

After 1 year of androgen deprivation in TransWomen, the mean cross-sectional muscle area, a marker of muscle mass, had decreased significantly but remained significantly higher than in CisWomen. After 1 year of gender affirming treatment, thigh muscle area decreased by -9.5%, quadriceps muscle by -4.2%, calf muscle by 8.9%, and forearm muscle by -4 to -8.6% (Harper et al., 2021). The decrease in thigh muscle area reached -11.7% after 3 years of gender affirming treatment (Elbers et al., 1999), and -24% in forearm muscle after an average of 8 years of treatment (Lapauw et al., 2008).

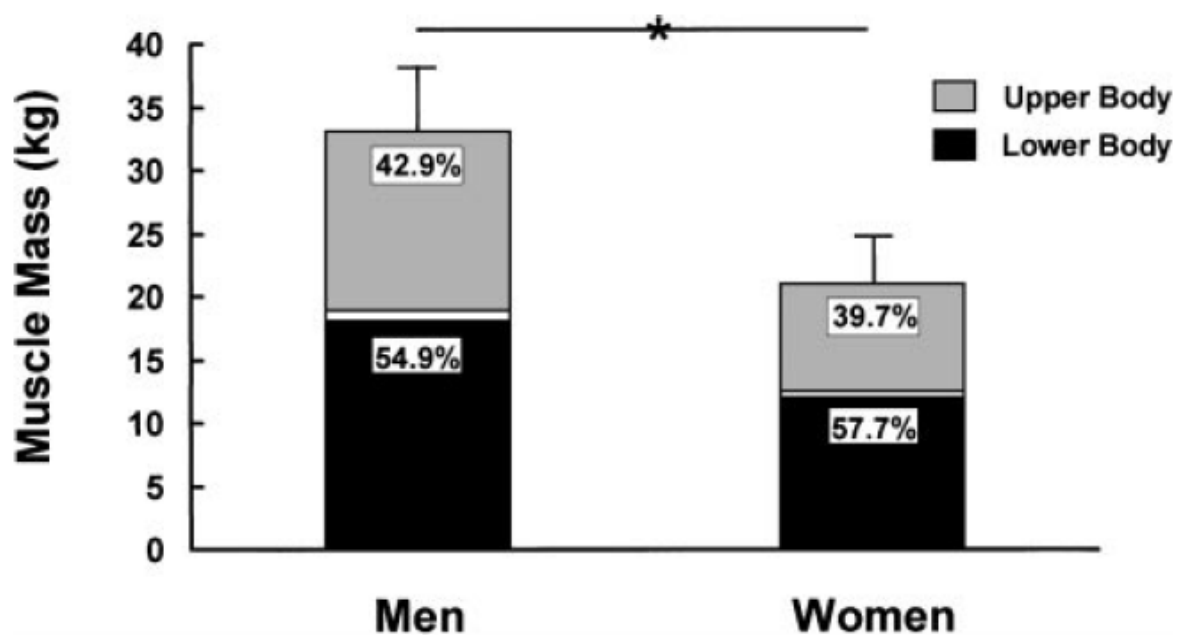


Figure 3. Skeletal muscle mass and distribution in CisMen and CisWomen. Values are means $\pm$ SE. (from Janssen et al., 2000).

In 11 untrained TransWomen, after 12 months of testosterone suppression, the thigh muscle volume decreased slightly by only 4%, quadriceps cross-sectional area by 4%, while radiological density, a marker of the density of contractile proteins, remained unaltered (Wiik et al., 2020). In a recent meta-analysis it was shown that during the first year of transition

treatment, total lean body mass decreased, ranging from -2.4 to -3.1 kg (4 to 5.5% of initial lean body mass) in TransWomen (Klaver et al., 2016).

One cross-sectional study measured body composition and muscle mass in non-athletes TransWomen. Twenty three TransWomen were recruited at least 3 years after sex reassignment surgery and a mean duration of 8 years with cross-hormone treatment, and were compared with healthy age and height-matched control males (Lapauw et al., 2008). The results showed that TransWomen had 17% less lean body mass than the control males. However, the typical gap in lean mass between CisMen and CisWomen exceeds the reductions reported in this study. The final average lean body mass of the TransWomen puts them in the 90th percentile for CisWomen (Lapauw et al., 2008). However, it should be considered that analyzing cross-sectional data in the absence of a baseline assessment should be very cautious, longitudinal studies quantifying changes within subjects having a greater power.

In conclusion, there are large baseline differences in muscle mass between males and females (Figure 3), with differences of 54%, 48% and 64% in total skeletal muscle mass, lower body muscle mass and upper body muscle mass, respectively (Janssen et al., 2000). Given this finding, the reduction in muscle mass achieved by 12 months of testosterone suppression can reasonably be assessed as small, with only slightly greater reductions in the arm compared with the leg region (Hilton and Lundberg, 2021; Harper et al., 2021). A slight decrease in lean body mass of approximately -4 to -8% was observed after 1 year of gender affirming therapy, and no more than -17% after 8 years of treatment.

2. Muscle strength/power

The difference in muscle strength between males and females is often more pronounced than the difference in muscle mass. Unfortunately, only few studies have examined the effects of testosterone suppression on muscle strength in transgender individuals and no studies have involved regularly trained athletes.

The time course of changes in grip strength was examined in 171 non-athletes TransWomen after one year of transition treatment (Scharff et al., 2019). A mean decrease in grip strength with -1.8 kg occurred after 1 year of transition treatment (-4,75%). The largest decrease in grip strength (66% of the total decrease) took place during the last 3 months (Figure 4). After 1 year of testosterone suppression, the median grip strength of TransWomen falls into the 95th percentile for age-matched females. This means that the median of grip strength values measured in TransWomen remain well above the median values of the female reference population, and 95% of the female reference population have grip strength values below the median for Transgender women. Thus, TransWomen are still stronger than average females. Moreover, handgrip strength in TransWomen was in approximately the 25th percentile for males (i.e. this means that the median grip strength of TransWomen was higher than 25% of the male reference population). In this study, no association between change in grip strength and change in arm or leg lean body mass was seen (Scharff et al., 2019).

In another study, isometric strength levels were maintained after 1 year of transition treatment for both knee extension and knee flexion (Wiik et al., 2020). Isokinetic strength at 60°/s showed a main effect of time for both knee extension and flexion, whereas strength at 90°/s knee extension was maintained over the 12 months of treatment. After 1 year of transition treatment, the absolute and height-adjusted values of isometric and isokinetic strength as well as muscle volume remained about 50% higher in TransWomen than in CisWomen ($P<0.05$).

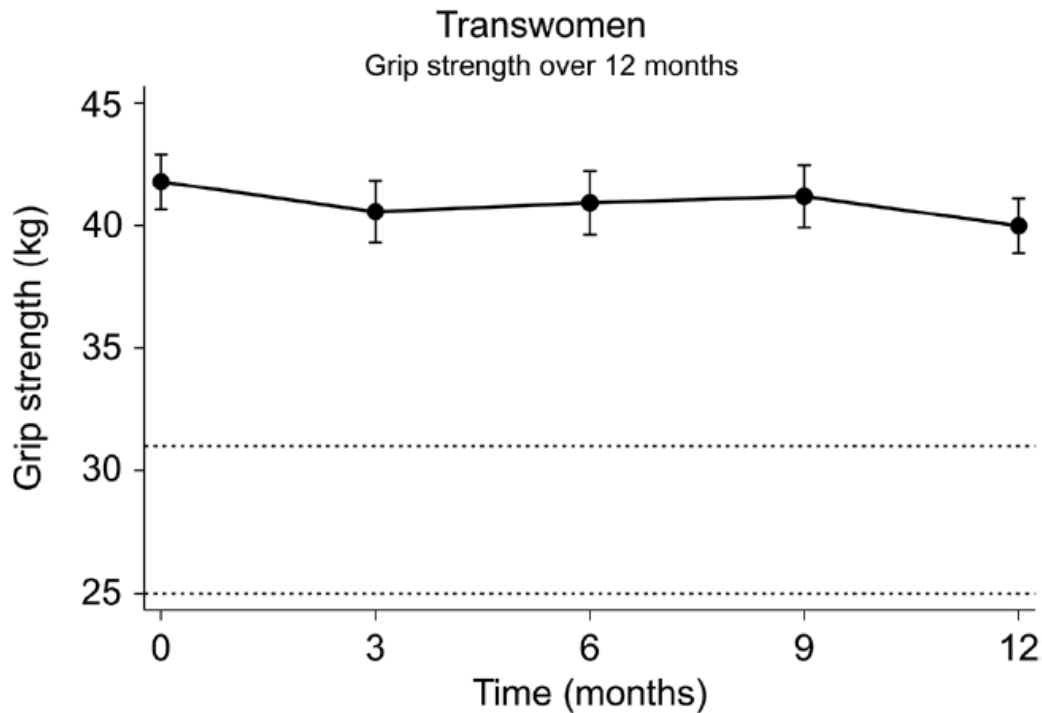


Figure 4. Change in grip strength during the first 12 months of gender-affirming hormonal treatment in TransWomen. Data are presented as means with 95% CI. The 25th and 75th percentiles of the reference populations are shown with dashed lines (25 kg and 31 kg, respectively) (From Scharff et al., 2019).

In a cross-sectional study muscle strength and torque values in non-athletes TransWomen were compared with healthy age and height-matched control males (Lapauw et al., 2008). The results showed that TransWomen had 25% lower peak quadriceps peak torque than the control CisMen after a mean of 8 years of cross-sex hormonal treatment. The median value of the maximum grip strength (50th percentile) in a female reference population aged 25 to 34 was estimated to be 27.8 kg (Wong, 2016). After a mean of 8 years of transitional treatment, the final mean grip strength was 41 kg in TransWomen, 47% higher than the female reference value. Despite the limits of cross-sectional studies, the results of this experiment suggest a retained physical advantage in TransWomen, even after 8 years of testosterone suppression.

3. Markers of endurance performance

Oxygen transport in blood. Hemoglobin (Hgb) is a protein present in red blood cells that is responsible for transporting oxygen from the lungs peripheral tissues, and especially to skeletal muscles. Low Hgb or low hematocrit (Hct) levels lead to a diminished supply of oxygen to the skeletal muscles, and therefore have a direct negative effect on endurance performance. There is a robust positive relationship between Hgb mass and $\dot{V}O_2\text{max}$ and the reduction in Hgb is generally associated with reduced aerobic capacity.

Basal values for Hgb differ between males and females, with values ranging between 13.1 to 17.9 g/dL for men and 11.7 to 15.5 g/L for women. Circulating hemoglobin levels are at least partly androgen-dependent and are typically reported as 12% higher in men compared with women. Hct values are also higher in men than women, 42% to 52%, versus 37% to 47%, respectively. Since Testosterone exerts erythropoietic effects that result in increases in both Hct and Hgb, it is interesting to examine the effects of transition treatment

in TransWomen. As for previous physiological parameters, only data in non-athletic TransWomen are currently available.

Nine studies were included in a recent systematic review, reporting the levels of Hgb or Hct in TransWomen before and after several forms of transition treatments, from a minimum of 3 to a maximum of 36 months post cross-sex hormonal treatment (Harper et al., 2021). In 8 of these studies, it was found that hormone therapy led to a significant decrease in the oxygen-carrying capacity expressed as the Hgb/Hct ratio (-4.6% to -14.0%; $P<0.01$). In 6 of these 8 studies, mean Testosterone after treatment was less than 2.0 nmol/L. Overall, these studies showed that by 3 to 4 months of transition treatment, the Hct and Hgb levels of TransWomen matched those of CisWomen. Moreover, the Hct and Hgb levels remained stable within the 'normal' female range for studies lasting up to 36 months. Given the rapid fall in the Hgb/Hct ratio to female reference values, it is possible that gender affirming hormone treatment impairs endurance performance, in comparison with CisMen, in part due to reduced oxygen transport from the lungs to the working muscles. The treatment-induced reduction in the oxygen-carrying capacity reported in TransWomen has very likely negative consequences on endurance performances, estimated at -2 to -5% for the female athletic population.

Body weight, body fat mass and endurance performance. In endurance sports such as cycling, the Wmax/body weight ratio is a very important marker of performance. Wmax expressed by a rider reflects the speed during a flat race or the ability to climb a greater slope at the same speed. On the other side, lower body weight of the athlete can be an advantageous factor considering that a lighter cyclist spends less energy to maintain the same speed and therefore should be faster during a climb.

Maximal aerobic power output relative to body weight (Wmax/body weight ratio) has been a popular measure of ability among competitive riders. Success in sustained cycling exercise has been predicted most commonly using this individual parameter. Maximizing the Wmax/body weight ratio can be achieved by a) specific training programs, b) body weight reduction, or c) a combination of both interventions.

Several studies examined the changes in body weight and body composition induced by gender affirming hormone treatment in non-athletes TransWomen. It was shown that during the 3-to-24 months period of transition treatment, both total body weight and total body fat increased, mean +1,8 kg and +3 kg, respectively (Klaver et al., 2016). More recently, a large prospective observational study in non-athletes transgender individuals examined the effects of transition treatment on changes in regional body composition using DXA measures (Klaver et al., 2018) (Figure 5). It was shown that after the first year of transition treatment body weight and total body fat increased in non-athletes TransWomen (+3% and +28%, respectively, $P<0.001$), whereas total lean body mass decreased by -3% ($P<0.001$). Regional changes in body fat ranged from +18% in the android region, to +42% in the leg region and +34% in the gynoid region (Figure 5). Regional changes in lean body mass ranged from 0% ($P=0.61$) in the android region to -6% ($P<0.001$) in the arm region (Figure 5). TransWomen persons with a BMI <20 underwent larger changes in all body fat measures.

Although these data have been reported in non-athletes, the typical increase in body fat commonly reported in TransWomen should be considered as a disadvantage in cycling, where body weight (and especially body fat mass and distribution) is one of the determinants of performance. But the effects of these body-composition changes on cycling endurance performance of TransWomen need to be confirmed and quantified.

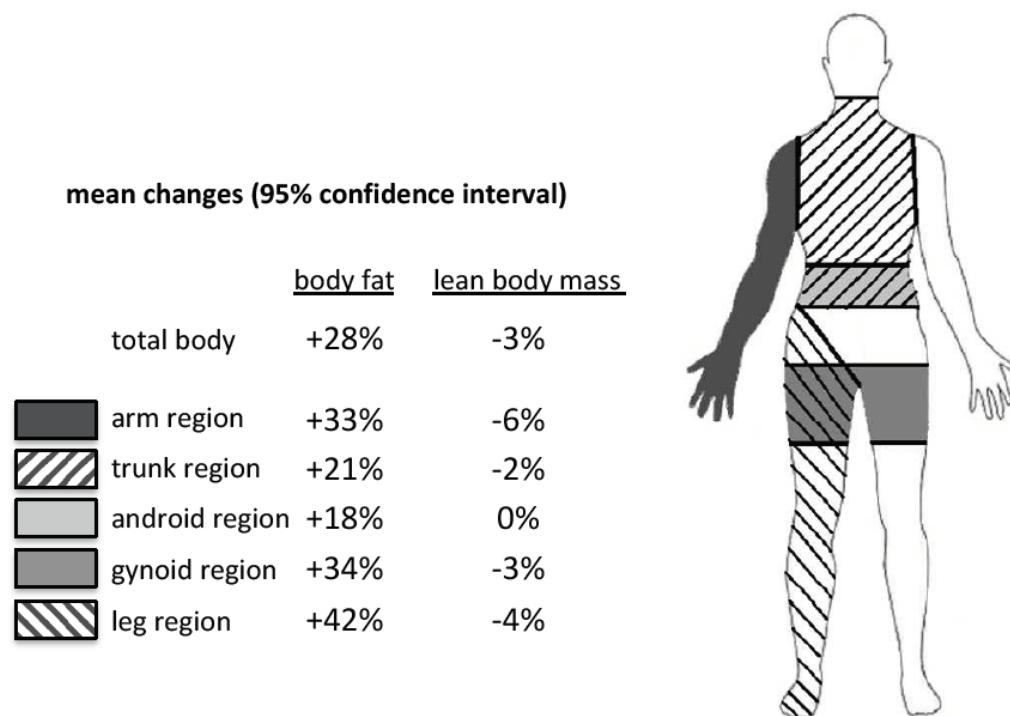


Figure 5. Percent changes in total and regional body fat and lean body mass in 179 non-athletes TransWomen (From Klaver et al., 2018).

However, it is unclear to what extent in athletes, the expected increase in body fat could be offset by nutritional and exercise countermeasures. In addition, there is variability in changes in body composition in response to transition treatments; for example, in one of previous studies, it has been shown that 3 out of the 11 TransWomen were completely resistant to the increase in total adipose tissue (Wiik et al. 2020). This inter-individual variability in the responses to gender affirming hormone treatments represents a challenge for sports governing bodies who publish rules based on average effect sizes.

In conclusion, the effects of testosterone suppression on endurance performance markers remain insufficiently explored. The responses of $\dot{V}O_{2\max}$, left ventricular size, stroke volume, cardiac output, lactate threshold, and exercise economy to testosterone reduction should be clarified in further studies. However, given the plausible disadvantages induced by gender affirming hormone treatments (i.e. decreased oxygen carrying capacity, increased body fat mass), the balance between inclusion and equity of endurance ability is likely close to equilibrium in weight-bearing endurance sports such as cycling (and much less balanced in strength/power sports where the male advantage is still substantial).

IV. Physical performance changes in Transgender people

In parallel with the changes in physiological capacities with gender affirming hormone treatments, it is also important to evaluate the effects of these treatments on sports or exercise performance. Very few data exist, none in cycling to our knowledge, and especially very few studies in athletes trained at high level during the transition period.

1- Gender affirming treatment and athletic performances.

Monitoring physical performances obtained from hyperandrogenic DSD female athletes before and after testosterone suppression is a valuable source of information to examine the effects of lowering blood testosterone levels within the normal female range on athletic performance. Reducing blood testosterone levels to the normal female range led to an average decrease of -3.8% and -5.7% of their best chronometric running performance over a 1-year and 2-year period, respectively (Bermon 2017).

In another study, running performances were obtained from eight TransWomen distance runners before and after transition (Harper, 2015). The run times were then compared using the age-graded methodology, and it was concluded that the eight runners had an overall decline in performance collected months to years before and after starting gender affirming hormone treatments. The eight runners were much slower competing in the female category; slow enough, so that their age-graded performances are nearly identical to their male age grades. However, in this study, no information on the duration of the transition treatments is available, which make it possible to achieve running performances similar to those of CisWomen age grades.

The effects of gender affirming hormones on body composition and athletic performance were examined among 46 TransWomen military personnel (US Air Force), before and after they started their transition treatment (Roberts 2020). In TransWomen, both gender affirming hormones (oestradiol valerate, cypionate, oral or transdermal) and testosterone blockade (spironolactone 80%, GnRH agonist 2.2%, and both 2.2%) were prescribed. Although these individuals are not athletes, they were trained regularly, and their continued service in the Air Force requires a certain level of physical ability. The physical fitness assessment was performed every 12 months, and included a 1.5 miles run performance. Run times among TransWomen were similar to times among CisMen and faster than running performance among CisWomen prior to gender affirming treatment. Run times worsened among TransWomen after starting oestrogen administration and testosterone blockade, and became slower than times in CisMen but remained faster than CisWomen at all time points (Figure 6).

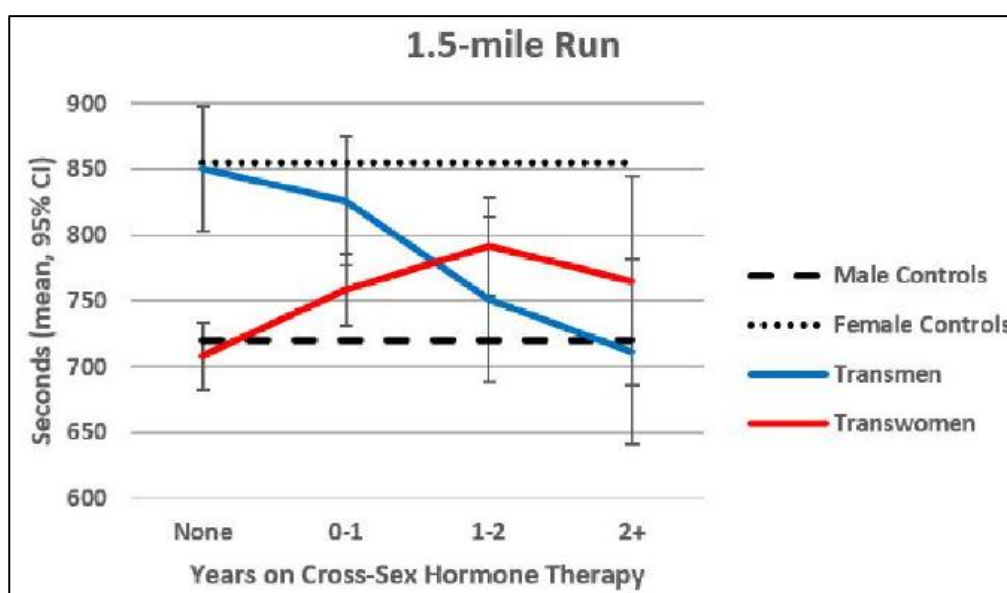


Figure 6. The effects of gender affirming treatment on the number of sit-ups performed in 1 min. Female controls = CisWomen. (From Roberts et al., 2020)

It is obvious that if these data give interesting information on the changes reported in physical performance under transition treatment, they are only relevant for long-distance running. The lack of similar data in cycling is a definite handicap in order to consider the eligibility of TransWomen to compete in the women's category of this sport.

2- Transition treatment and physical performance.

In the study referenced above, the effect of gender affirming hormones were examined on body composition and exercise performance (Roberts 2020). As previously reported, an increase in body weight occurred in TransWomen with transition treatment. The physical fitness of all transgender individuals was regularly assessed on the basis of push-up and sit-up exercises. Prior to the transition treatment, TransWomen performed more push-ups in 1 min than CisWomen but this difference disappeared after 2 years of treatment (Figure 7). Prior to the transition treatment, there was no difference in sit-ups among TransWomen compared with CisMen. After 2 years of gender affirming hormone treatment, TransWomen performed the same number of sit-ups in 1 min than CisWomen (Figure 8).

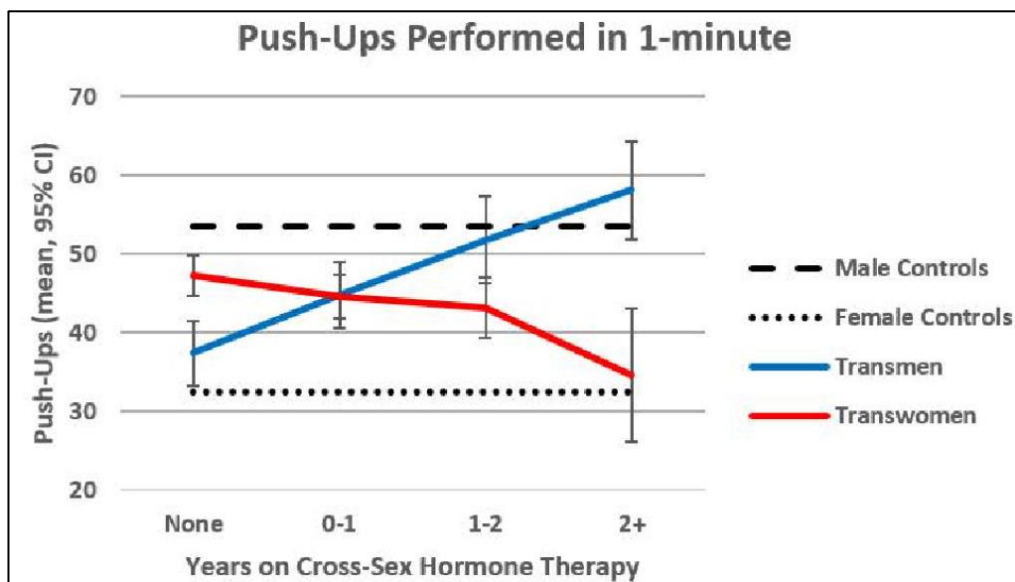


Figure 7. The effects of gender affirming treatment on the number of pus-ups performed in 1 min. Female controls = CisWomen. (From Roberts et al., 2020)

These results (on push-ups and sit-ups performed in 1 min), confirm the decrease in strength associated with the transition treatments in TransWomen. that was found in some studies. But in the present experiment, the effects of gender affirming hormones on muscular strength were examined using repeated submaximal efforts over a 1 min period as opposed to a single maximal effort. Such outcomes capture differences in both muscle endurance and strength rather than just strength and have more relevance to sports that require sustained effort over time, like cycling, rather than single explosive efforts like power lifting.

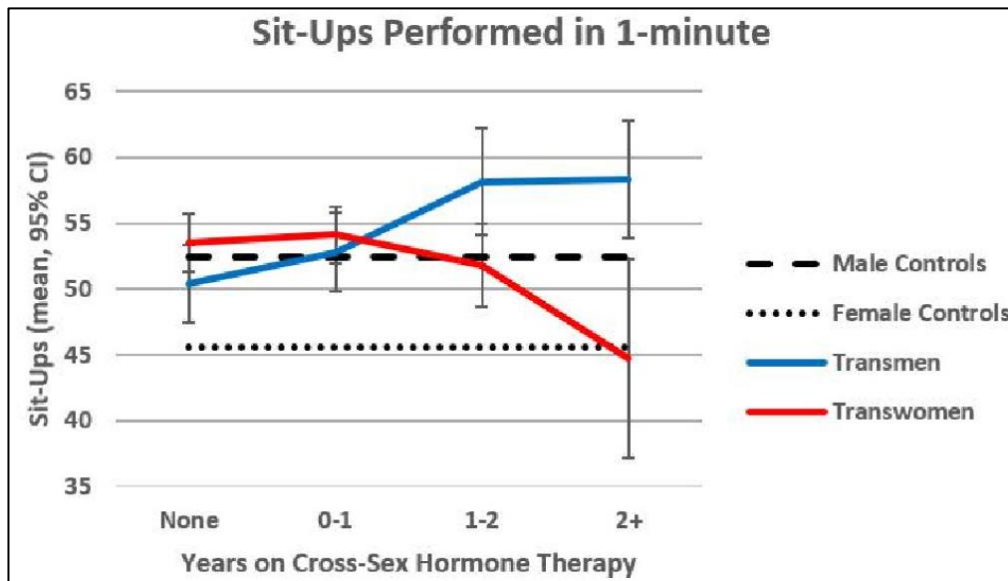


Figure 8. The effects of gender affirming treatment on the number of sit-ups performed in 1 min. Female controls = CisWomen. (From Roberts et al., 2020)

V. Main information for eligibility rules.

The intention for separating athletes into male and female categories is to provide women athletes with meaningful competition. It would be reasonable therefore to allow transgender to compete with other female athletes if their inclusion guarantees fair and meaningful competitions. It may not be necessary, or even possible, to eliminate all individual advantages held by a transgender. It is paramount, however, that all athletes competing have a chance to succeed, albeit not necessarily an equal chance and in line with the true essence of sport.

Gender affirming blockade of testosterone and administration of estrogen in Transwomen are at the origin of a decrease of muscle mass, but Transwomen retain an advantage in muscle mass, volume, and strength over CisWomen after 12 months of transition treatment (Hilton and Lundberg, 2021). The few existing experimental data confirm that gender-affirming hormones are associated with only slight changes in muscle performance, with pretreatment differences between TransWomen and CisWomen, especially in muscle strength /power persist beyond 12 months, time requirement imposed in the UCI rules. This suggests that for sports that require muscle mass, strength and power, including cycling, TransWomen will still have a physical advantage after 12 months of treatment, even if serum testosterone levels are maintained below the current officially requested threshold. Therefore, it can be hypothesized that prolonged testosterone suppression, well beyond the 12-month transition period mandated by the UCI, is necessary to substantially reduce muscle mass and strength in Transwomen (Lapauw et al., 2008; Roberts et al., 2020).

In addition to the known effects on muscle mass and erythropoiesis, exposure to testosterone during puberty results also in sex differences in height, pelvic architecture and leg bones in the lower limbs. These anatomical differences give TransWomen an athletic advantage after puberty for certain sports, and may not respond to low blood testosterone levels in post-pubertal adults. To what extent these morphological peculiarities, based in particular on the length of the long bones, constitute an advantage for performance in some cycling disciplines must be studied in the future. But it is possible that these differences could

be minimized in TransWomen who begin gender affirming hormone therapy shortly after the onset of puberty.

An important issue is that the current studies assessed the changes in lean body mass, muscular strength and Hgb/Hct in non-athletic TransWomen following treatment with gender affirming hormones. However, it is essential to keep in mind that there are no data on changes in cycling performance with transition therapy, especially in well-trained subjects or top athletes. Therefore, the effects of testosterone suppression on these parameters, or even on the athletic performance of TransWomen athletes who engage in physical training during the gender affirming treatment, remain unknown. Available data in non-athletic TransWomen and non-sports performance measures make it difficult to suggest when the athletic abilities of TransWomen undergoing transition treatment become comparable to those of CisWomen, especially given interindividual variability. While the existing studies give the opportunity to study the effects of transition treatment in non-athletes individuals, it is still uncertain how these findings would translate to Transgender athletes undergoing advanced training regimens during the gender-affirming intervention.

For further research, it would be interesting to evaluate the changes in muscle mass and strength/power in Transgender athletes, after a longer follow-up, in order to examine if the strength/power performances will reach the strength reference values for CisWomen, and to test the impact on cycling performance.

VI. Final conclusion

Given the current body of knowledge, the question of when it is fair to authorize TransWomen to compete in sports in line with their experienced gender identity is challenging. Despite an obvious lack of knowledge in well-trained athletes, and based on the most recent current literature (Harper et al., 2021; Hilton and Lundberg, 2021; Roberts et al., 2020), it can be hypothesized that more than 12 months of testosterone suppression may be necessary to ensure that TransWomen do not have an unfair competitive advantage when competing at an elite level. Very little data have been provided to clarify on the potential remaining physical advantage for TransWomen after medical interventions, but based on one of the only published studies to date, it can be assumed that this **potential advantage on muscle strength / power cannot be erased before a period of 24 months** (Roberts et al., 2020).

The maximum serum testosterone concentration required is a fairly easy question to answer. The 95% confidence interval for serum testosterone in CisWomen is 0.6 - 1.68 nmol/L (Handelsman et al., 2018). For a 99.99% confidence interval (which involves no more than 1 in 10,000 values outside the confidence interval), the highest value of serum testosterone is 2.44 nmol/L. Therefore **the maximum serum testosterone value can be defined as 2.5 nmol/L**.

References

- Bassett AJ, Ahlmen A, Rosendorf JM, Romeo AA, Erickson BJ, Bishop ME. The biology of sex and sport. *JBJS Rev.* 2020, 8(3):e0140.
- Bermon S. Androgens and athletic performance of elite female athletes. *Curr. Opin. Endocrinol. Diabetes Obes.* 2017, 24:246Y51.
- Bermon S, Garnier PY. Serum androgen levels and their relation to performance in track and field: mass spectrometry results from 2127 observations in male and female elite athletes. *Br J Sports Med.* 2017, 51(17):1309-1314.
- Bermon S, Hirschberg AL, Kowalski J, Eklund E. Serum androgen levels are positively correlated with athletic performance and competition results in elite female athletes. 2018, 52(23):1531-1532.
- Bermon S, Garnier PY, Hirschberg AL, Robinson N, Giraud S, Nicoli R, Baume N, Saugy M, Fénichel P, Bruce SJ, Henry H, Dollé G, Ritzen M. Serum androgen levels in elite female athletes. *J Clin Endocrinol Metab.* 2014, 99(11):4328-4335.
- Cohen-Kettenis PT, Pfafflin F. The DSM diagnostic criteria for gender identity disorder in adolescents and adults. *Archives of Sexual Behavior* 2010, 39:499–513.
- Coyle EF, Feltner ME, Kautz SA. Physiological and biomechanical factors associated with elite endurance cycling performance. *Med Sci Sports Exerc* 1991, 23:93-107.
- Eklund E, Berglund B, Labrie F, Carlström K, Ekström L, Hirschberg AL. Serum androgen profile and physical performance in women Olympic athletes. *Br J Sports Med.* 2017, 51(17):1301-1308.
- Elbers JM, Asscheman H, Seidell JC, Gooren LJG. Effects of sex steroid hormones on regional fat depots as assessed by magnetic resonance imaging in transsexuals. *Am J Physiol* 1999, 276:E317–E325.
- Etter F, Knechtle B, Bukowski A, Rüst CA, Rosemann T, Lepers R. Age and gender interactions in short distance triathlon performance. *J Sports Sci.* 2013, 31(9):996-1006.
- Faria EW, Parker DL, Faria IE. The science of cycling: physiology and training - part 1. *Sports Med.* 2005, 35(4):285-312.
- Gooren LJG, Bunck MCM. Transsexuals and competitive sports. *Eur J Endocrinol.* 2004, 151(4):425–429.
- Haakonssen EC, Martin DT, Martin JC, Burke LM, Jenkins DG. Muscle mass - cycling power relationships in female road cyclists. *Med Sci Sports Exerc.* 2013, 45(5S):129-138.
- Handelsman DJ, Hirschberg AL, Bermon S. Circulating testosterone as the hormonal basis of sex differences in athletic performance. *Endocr Rev.* 2018, 39(5):803–829.
- Harper J. Race times for transgender athletes. *J. Sporting Cultures Identities.* 2015, 6:1Y9.
- Harper J, O'Donnell E, Sorouri Khorashad B, McDermott H, Witcomb GL. How does hormone transition in transgender women change body composition, muscle strength and haemoglobin? Systematic review with a focus on the implications for sport participation. *Br J Sports Med.* 2021, 55(15):865-872.
- Hawley JA, Noakes TD. Peak power output predicts maximal oxygen uptake and performance time in trained cyclists. *Eur J Appl Physiol Occup Physiol.* 1992, 65(1):79-83.
- Hilton EN, Lundberg TR. Transgender Women in the female category of sport: perspectives on testosterone suppression and performance advantage. *Sports Med.* 2021, 51(2):199-214.
- Ice RG, Millman PL, Ice DC, Camp JC. A physiological profile of the 1984-1986 race across America winner. In: *Medical and Scientific Aspects of Cycling*, E. R. Burke and M. M. Newsom (Eds.). Champaign, IL: Human Kinetics, 1988, pp. 173-180.
- Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. *J Appl Physiol* 2000, 89(1):81-88.

- Klaver M, Dekker MJHJ, de Mutsert R, Twisk JWR & den Heijer M. Cross-sex hormone therapy in transgender persons affects total body weight, body fat and lean body mass: a meta-analysis. *Andrologia* 2016 1-11.
- Klaver M, de Blok CJM, Wiepjes CM, Nota NM, Dekker MJHJ, de Mutsert R, Schreiner T, Fisher AD, T'Sjoen G, den Heijer M. Changes in regional body fat, lean body mass and body shape in trans persons using cross-sex hormonal therapy: results from a multicenter prospective study. *Eur J Endocrinol*. 2018, 178(2):163-171.
- Lapauw B, Taes Y, Simoens S, et al. Body composition, volumetric and areal bone parameters in male-to-female transsexual persons. *Bone*. 2008, 43(6):1016–1021.
- Lepers R. Analysis of Hawaii ironman performances in elite triathletes from 1981 to 2007. *Med Sci Sports Exerc*. 2008, 40(10):1828-1834.
- Lucia A, Hoyos J, Perez M, et al. Inverse relationship between $\dot{V}O_2\text{max}$ and economy/efficiency in world-class cyclists. *Med Sci Sports Exerc* 2002, 34: 2079-2084.
- Mujika I, Rønnestad BR, Martin DT. Effects of increased muscle strength and muscle mass on endurance-cycling performance. *Int J Sports Physiol Perform*. 2016, 11(3):283-289.
- Padilla S, Mujika I, Cuesta G, Goiriena JJ. Level ground and uphill cycling ability in professional road cycling. *Med Sci Sports Exerc* 1999, 31(6):878-885.
- Roberts TA, Smalley J, Ahrendt D. Effect of gender affirming hormones on athletic performance in transwomen and transmen: implications for sporting organisations and legislators. *Br J Sports Med* 2020:bjsports-2020-102329.68
- Scharff M, Wiepjes CM, Klaver M, Schreiner T, T'Sjoen G, den Heijer M. Change in grip strength in trans people and its association with lean body mass and bone density. *Endocr Connect*. 2019, 8(7):1020-1028.
- Thibault V, Guillaume M, Berthelot G, et al. Women and men in sport performance: the gender gap has not evolved since 1983. *J Sport Sci Med*. 2010, 9(2):214–223.
- Vikmoen O, Ellefsen S, Trøen Ø, Hollan I, Hanestadhaugen M, Raastad T, Rønnestad BR. Strength training improves cycling performance, fractional utilization of $VO_2\text{max}$ and cycling economy in female cyclists. *Scand J Med Sci*. 2016, 26(4):384-396.
- Wiik A, Lundberg TR, Rullman E, Andersson DP, Holmberg M, Mandić M, Brismar TB, Dahlqvist Leinhard O, Chanpen S, Flanagan JN, Arver S, Gustafsson T. Muscle strength, size, and composition following 12 months of gender-affirming treatment in Transgender individuals. *J Clin Endocrinol Metab*. 2020, 105(3):dgz247.
- Wong SL. Grip strength reference values for Canadians aged 6 to 79: Canadian Health Measures Survey, 2007 to 2013. *Health Rep*. 2016, 27(10):3-10.



Review

Transwoman Elite Athletes: Their Extra Percentage Relative to Female Physiology

Alison K. Heather

Department of Physiology, School of Biomedical Sciences, University of Otago, Dunedin 9054, New Zealand; alison.heather@otago.ac.nz

Abstract: There is increasing debate as to whether transwoman athletes should be included in the elite female competition. Most elite sports are divided into male and female divisions because of the greater athletic performance displayed by males. Without the sex division, females would have little chance of winning because males are faster, stronger, and have greater endurance capacity. Male physiology underpins their better athletic performance including increased muscle mass and strength, stronger bones, different skeletal structure, better adapted cardiorespiratory systems, and early developmental effects on brain networks that wires males to be inherently more competitive and aggressive. Testosterone secreted before birth, postnatally, and then after puberty is the major factor that drives these physiological sex differences, and as adults, testosterone levels are ten to fifteen times higher in males than females. The non-overlapping ranges of testosterone between the sexes has led sports regulators, such as the International Olympic Committee, to use 10 nmol/L testosterone as a sole physiological parameter to divide the male and female sporting divisions. Using testosterone levels as a basis for separating female and male elite athletes is arguably flawed. Male physiology cannot be reformatted by estrogen therapy in transwoman athletes because testosterone has driven permanent effects through early life exposure. This descriptive critical review discusses the inherent male physiological advantages that lead to superior athletic performance and then addresses how estrogen therapy fails to create a female-like physiology in the male. Ultimately, the former male physiology of transwoman athletes provides them with a physiological advantage over the cis-female athlete.

Keywords: sex differences; exercise physiology; transgender; testosterone; hormone therapy



Citation: Heather, A.K. Transwoman Elite Athletes: Their Extra Percentage Relative to Female Physiology. *Int. J. Environ. Res. Public Health* **2022**, *19*, 9103. <https://doi.org/10.3390/ijerph19159103>

Academic Editors: Stacy T. Sims and Christopher T. Minson

Received: 8 March 2022

Accepted: 7 July 2022

Published: 26 July 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Sports have been a major part of human culture throughout history, with ancient Greeks and Romans showing mastery through competition. Indeed, few areas of culture have the power to influence people as strongly as sports. It is often the intense emotional bond fans develop with teams and players that underlies their passion for sport. Fans can live vicariously through their chosen elite athletes and sportsmen and women are often considered role models for society. Amateur athletes and young emerging hopefuls strive to reach the highest levels within their chosen sport by modeling their idols.

Given the passion associated with sports, any controversy surrounding a result can lead to strong debate, especially if there is a perception that fairness has been jeopardized. The concept of fairness is the justification for dividing most sports into male and female categories. Without such segregation, females would have little chance of winning. World records show that males consistently perform better in sports [1–5]; the most recent Olympic gold, silver, and bronze medal results show that females would not have medaled in an open competition for a wide variety of sports (same distance raced by male and female) (Table 1; <https://www.olympic.org/olympic-results> (accessed on 1 January 2019)). This remains despite increased female participation in sports [6] and female-centric technologies applied to training and equipment. Despite the recognition of the male dominance of

athletic performance, the male and female divisions are becoming blurred as transgender women (individuals that are born as male and identify as female) athletes enter the female division. The inclusion of transgender women athletes has raised concerns about the fairness of the female division for biological female athletes (ciswomen, where gender identity aligns with their biological sex).

Table 1. Gold medal distances or times for selected sporting events recorded for males and females at the RIO Olympics 2016.

Sport	Male	Male	Male	Female	Finishing Position for Female Gold in Male Event
Athletics	Gold	Silver	Bronze	Gold	
10,000 m run	27.05.17 s	27.05.64 s	27.05.26 s	29.17.45 s	32nd
100 m run	9.81 s	9.89 s	9.91 s	10.71 s	Would not have qualified for gold medal final
400 m run	43.03 s	43.76 s	43.85 s	49.44 s	Would not have qualified for the gold medal final
800 m run	1:42:15 min	1:42:61 min	1:42:93 min	1:55:28 min	Would not have qualified for the gold medal final
marathon	2.08.44 h	2.09.54 h	2.10.05 h	2.24.04 h	90th
long jump	8.38 m	8.37 m	8.29 m	7.17 m	<12th (cut off at 7.82 m)
Triathlon	1.45.01 h	1.45.07 h	1.45.43 h	1.56.16 h	50th
Swimming					
100 m freestyle	47.58 s	47.8 s	47.85 s	52.70 s	51st out of 57 in the heats
400 m individual medley	4.06.05 m	4.06.75 m	4.09.71 m	4.26.36 m	26th out of 27 in the heats
Canoe sprint					
K-1200 m (Kayak single)	35.197 s	35.362 s	35.662 s	39.864 s.	Would not have placed in the top 16 to make finals (cut off 38.061)

Distances are given as meters (m), and times are given as seconds (s), minutes (mins), or hours (h).

To compete in the female division as defined by current International Olympic Committee (IOC) regulations, a transgender woman athlete must agree to gender-affirming hormone therapy to lower, and then maintain, testosterone levels to below 10 nmol/L for one year (IOC Consensus Meeting on Sex Reassignment and Hyperandrogenism November 2015). Estradiol therapy is the common hormonal regime used to reduce testosterone levels in transwomen athletes [7,8].

The underlying question asked in this descriptive review is whether the IOC 2015 guidelines that allow transgender women to compete in the female division are fair. In order to address this question, the review aims to (A) explain the physiology behind why males perform better in sport and (B) document why male physiology cannot simply be reformatted into female physiology by estrogen therapy in transwomen athletes. In preparing this review, studies targeting (1) sex differences in athletic performance (2) testosterone administration to males or females and how this affects athletic performance and (3) transfemale or transmale physiology post-transitioning were included. The objective of this review is to increase awareness of male physiology and how it pertains to athletic performance so as to highlight issues facing the female sports division. Most importantly, the review aims to identify key physiological factors that need to be considered by sporting organizations and relevant authorities when interpreting fairness in sport.

2. Male Physiology Provides an Athletic Performance Advantage

Testosterone drives anatomical and physiological sex differences in the human body (Figure 1). These sex differences can be architectural and therefore permanent, or can be influenced by adult-level, circulating testosterone concentrations, and therefore modifiable. Permanent sex differences that affect athletic performance involve the (i) brain, (ii) skeletal structure, and (iii) cardiorespiratory system. Modifiable sex differences include testosterone effects on (i) muscle mass and strength and (ii) aerobic capacity.

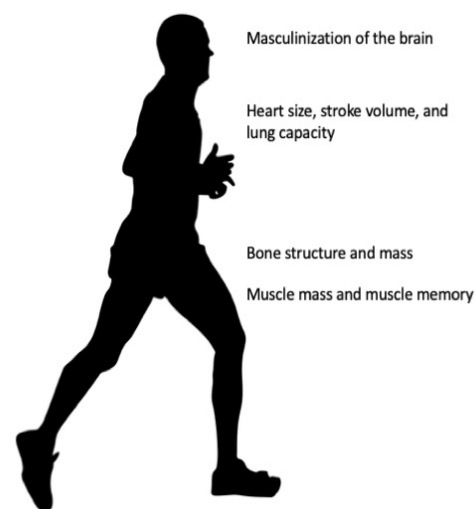


Figure 1. Irreversible changes to male physiology. Figure 1 shows the irreversible changes of testosterone conditioning throughout life. Testosterone masculinizes the brain in utero and during early life. Testosterone drives anatomical structure design specific to the male skeleton. Testosterone drives muscle mass, muscle fiber type, and muscle memory. Most of the effects driven by testosterone cannot be reversed with estradiol (or cross) hormone therapy.

2.1. Prenatal Testosterone and the Male-like Brain

Anatomical sex differences in the brain appear during early life when the in utero and postnatal surges of testosterone masculinize the male brain [9,10]. Ascribing specific behaviors to these anatomical sex differences has been challenging [11] and may involve differences in cell morphology as well as the connections between brain networks [12–16]. For example, diffusion magnetic resonance imaging (MRI) shows increased intraconnectivity in males for regions of the brain attributed to perception-action coordination, auditory/visual spatial awareness and processing, cognitive processes and complex reasoning and control [16]. Females, on the other hand, show more interconnectivity in those regions of the brain attributed to memory, social cognition, and non-verbal reasoning. The sex-specific connectivity of these subnetworks may underlie the ability of males to show consistently higher levels of motor and visual spatial skills in addition to elevated sensory input from vision and proprioception [17–20].

There is little debate that better motor skills, visual spatial skills, and proprioception will improve coordination and subsequent athletic performance. These differences in brain structure are evident in childhood, with 8–13 year olds showing behavior patterns that become further differentiated with the onset of puberty and aging into adulthood [16].

An aggressive, competitive nature also underpins better athletic performance [21]. Although it is difficult to attribute prenatal testosterone exposure directly to levels of aggression in the adult, indirect evidence suggests that such a relationship may exist. Development of the fourth digit (4D), but not the second digit (2D), is highly sensitive to testosterone, so that in utero androgen exposure results in lower 2D:4D ratios in males compared to females and is considered an index of prenatal testosterone exposure [22–25]. There is a clear association between 2D:4D ratios and male-typical behaviors [24,26] and, interestingly, professional male football players with low 2D:4D ratios receive more yellow or red card penalties [27]. Even with females, lower 2D:4D ratios in females are associated with the more aggressive form of sabre fencing [28]. Such examples suggest the possibility that in utero androgen exposure leads to later-life aggressiveness.

2.2. Testosterone and Muscle Mass

For many decades, it has been recognized that testosterone drives muscle mass and clear sex differences exist. For example, elite male athletes have, on average, more muscle mass than elite female athletes, for any given body weight [29]. Males have approximately twice the cross sectional area of upper body muscle, and 30% more cross sectional area of

lower body muscle relative to females [30]. The difference in muscle mass emerges during puberty as circulating testosterone levels increase in boys [31].

Circulating testosterone is the key physiological parameter driving muscle mass in both males and females [32–34]. For example, 19–40 year old males given supraphysiologic doses of testosterone for 10 weeks increased muscle mass, muscle size, and strength by up to 10%. If this treatment was combined with strength training, the increase in muscle mass was 27% [32]. A follow-up study by the same laboratory [33] showed that the testosterone effect on muscle mass was dose-dependent. Males, 18–35 years old, were treated with a gonadotropin-releasing hormone (GnRH) agonist to suppress endogenous testosterone production and then administered testosterone for 20 weeks at either 25, 50, 125, 300, or 600 mg, resulting in circulating concentrations of 8.8, 10.6, 18.8, 46.7, and 82.2 nmol/L, respectively, covering low physiological to supra-physiological levels. Supraphysiological concentrations (>40 nmol/L) increased leg muscle mass and strength, whereas mid-range testosterone level administration increased muscle mass with maintenance of leg strength. Interestingly, low testosterone levels (<10 nmol/L) maintained leg muscle mass and strength. This latter finding is in keeping with research in rodents that shows testosterone is not needed for muscle maintenance in adult male mice [35]. In this study, orchidectomised mice aged from young through to old were assessed for muscle mass after 28 days of testosterone depletion. Only the youngest mice showed reduced muscle mass, while the older, adult mice showed no effect on muscle mass. Therefore, it appears that testosterone may not be critical for maintenance of muscle mass in mature male mice [35]. In females, testosterone administration to raise circulating levels from 0.9 nmol/L to 4.3 nmol/L in young women (average 28 years) increased muscle mass and strength, as well as enhanced athletic performance as evidenced by time to exhaustion and Wingate testing [36].

2.3. Testosterone and Bone Structure

Bone structure and bone length changes in both sexes as children progress through puberty, with estradiol and testosterone having important roles in bone growth [37,38]. However, the effects of testosterone are stronger than those of estradiol, as exemplified by the 10% greater bone mass density and the larger and longer bones in post-pubertal males. These sex differences in bone structure provide males with increased fulcrum power, improving jumping, throwing, and other movements requiring explosive actions. The stronger bones also tolerate more trauma and thus males are more resistant to injury. Larger bones in males provide a greater articular surface that, in turn, allows placement of more skeletal muscle. For example, broader shoulders in males allows the build-up of more muscle, thereby increasing upper body strength [39].

Sex differences in bone shape driven by early life testosterone exposure can affect athletic performance. The most obvious structural difference between males and females is pelvis width, with estradiol driving the wider shape required for childbirth [40]. A narrower pelvis has a direct impact on the Q angle at the knee joint. The Q angle forms between the quadriceps muscles and the patellar tendon and is responsible for generating force during a knee extension. The smaller Q angle of males generates a greater force upon extension [41]. This has implications for sports that involve standing from a squatting position, kicking a ball, or a pedaling motion. There is also a sex difference in the angle formed between the humerus and ulna at the elbow, with the angle smaller in a male [42]. The smaller angle for males again allows a greater force upon extension, benefiting sports involving throwing and hitting with bats and rackets.

2.4. Testosterone and the Cardiorespiratory System

Early life testosterone exposure also drives sex differences in the cardiorespiratory system. Females have, on average, a 10–12% smaller lung volume than males, accounting for height, age, and within sex variation [43]. This smaller lung volume is established within the first few years of life in females due to a lower rate of alveolar multiplication [44,45]

and shorter diaphragm that reduces ribcage dimensions [46]. These anatomical differences therefore drive a lower oxygen uptake capacity in females [43,44]. Females also have a heart size that is about 85% that of males, relative to body size [47]. This anatomical difference decreases the volume of blood that can be pumped to the body with every contraction of the heart. The larger heart size of males translates to a larger left ventricle and therefore, stroke volume. On average, the stroke volume of females is just one-third that of males. As such, a female's heart rate must increase proportionally more to achieve a cardiac output necessary to supply active skeletal muscle with enough oxygen.

Active skeletal muscles require the efficient delivery of oxygen, and aerobic capacity is essential for athletic performance. Males have much higher arterial oxygen levels, primarily due to testosterone-regulated synthesis of hemoglobin [48]. The increased hemoglobin levels coupled with increased lung capacity provides males with a distinct respiratory and oxygen carrying advantage over females. It is consistently reported that hemoglobin concentrations are 12% higher in males than females, and this sex difference in hemoglobin emerges during puberty driven by testosterone [48]. Administration studies show that testosterone increases hemoglobin levels in a dose-dependent fashion [49], and medical castration to lower circulating testosterone levels in prostate cancer patients decreases hemoglobin levels [50].

These effects of testosterone on oxygen carrying capacity, together with the anatomical advantages of male anatomy, help explain the superiority of the male cardiovascular system as it relates to athletic performance. The $\text{VO}_{2\text{max}}$ of an elite male is in the order of 70–85 mL/kg/min, while that of females is 60–75 mL/kg/min; a difference of 15–30% [51].

3. Male Physiology Cannot Be Reformatted into Female Physiology by Estrogen Therapy

As noted above, the combined effect of testosterone-driven male physiology culminates in greater athletic performance, as evidenced by the dominance of males with respect to World Records and Olympic Gold medals [1–5]. In strength-related sports, world records can differ by 10–30% between males and females [1–5]. As such, to ensure a fair playing field in the female division, a transgender woman athlete should not retain any advantage from her prior testosterone-driven physiology. The evidence below indicates that male physiology cannot be reformatted to female physiology simply by gender-affirming estradiol therapy in a transgender woman training at a high-performance level.

3.1. Difficulties in Achieving Female Levels of Circulating Testosterone in Estrogen-Treated Transwomen

The estrogen treatment regimens used in transgender women aim to lower testosterone levels to within the female range (<1 nmol/L) [52]. However, hormone therapy alone has met limited success in suppressing testosterone levels, with many transgender women failing to achieve the desired level. In recent studies of transgender women, one quartile failed to achieve any significant suppression [53] and one-third failed to suppress testosterone levels despite achieving desired estradiol levels [54]. Another study reported that only 49% of transgender women showed suppressed testosterone concentrations after 6 months or more of estrogen with the addition of antiandrogen therapy [55]. Notably, Jarin and colleagues show that testosterone levels in transgender women decreased significantly from former male levels, however nearly all participants maintained their testosterone levels above the female range [56]. Whether elite transwoman athletes experience the same difficulties in suppressing testosterone levels with estrogen therapy has not been reported.

3.2. Estrogen Therapy Does Not Reformat Male-Like Brain Networks

At present, there is little understanding about changes in brain structure and function in transgender individuals. Almost all research in this area has focused on trying to delineate neurobiological pathways that underpin transgenderism, rather on specific areas of the brain related to athletic performance. Overall, current evidence indicates that

transgender hormone therapy either has no effect or generates structural and functional changes in the brain that are intermediate between biological males and females [57–59].

For transgender women, gender-affirming surgery and estrogen therapy have typically, but not always [57], been shown to reduce brain size and increase ventricular volume towards the parameters measured for biological females [60–64]. While MRI has shown consistent sex differences in functional connectivity within the brain, any alterations following hormonal treatment in transgender individuals remain unclear with studies typically showing no change or the appearance of an intermediate male–female state [63–67]. Notably, the biological male dominance in spatial ability, visual memory tasks, and perception [65–67] shows no decrease in transwomen after 12 months of estrogen therapy [68]. A meta-analysis of transgender individuals receiving gender affirming hormone therapy for 3–12 months shows transgender men had a significant enhancement in visuospatial ability (ref. [69]), with no significant changes for either transgender men or women in verbal memory, verbal reasoning, verbal working memory, computation, or motor coordination. There is an estrogen therapy-related change in transgender women if treated for longer than 12 months with a decreased proneness towards anger and aggressiveness [70].

While more research is required for definitive answers, the current data demonstrates that estrogen therapy in transwomen can drive some brain structures towards that of the biological female [71–73] but does not do so quickly and appears to not reformat the sex-typical male brain responses into a female-like brain. This is compatible with the concept that both the in utero and perinatal surges of testosterone secretion occurring in males drive permanent sex differences in brain structure and function which are apparent in young boys before puberty [74]. Human spatial ability, for example, appears beneficially affected by prenatal androgens [75,76], with second trimester testosterone levels correlated positively in biological females and negatively in biological males at age 7 [77].

3.3. Estrogen Therapy Does Not Reformat Male Skeletal Architecture but Does Decrease Muscle Mass

As there is a dose-dependent relationship between testosterone and muscle mass [32–34], lowering circulating testosterone levels from an average male level to <10 nmol/L should decrease muscle mass in a transwoman. Indeed, studies report muscle mass loss, with a 5% loss for lower limb mass or a 9.4% for total muscle mass loss after 12 months of estrogen therapy [78,79]. The loss of muscle mass did not, however, associate with loss of strength or muscle fiber density or performance [79]. For example, prior to transitioning, transwoman airforce personnel recorded a 12% faster time for a 1.5 mile run than their biological female peers that declined to a 9% difference after 2–2.5 years on estrogen therapy [80]. This decline in performance is similar to a self-reported study of running times in transwomen in the 12 months after transitioning [81]. While such results represent a marked decrease in performance, the running times of the transwomen group remain significantly higher than those of the biological women [80], despite prolonged estrogen therapy. The performance benefit of prior testosterone exposure for the running test is likely attributable to not only muscle mass but male skeletal architecture that, as discussed earlier includes longer limbs, a narrower pelvic structure and a greater cardiorespiratory size—all of which will not respond to changes in circulating testosterone levels in adulthood. Further to this, studies show that there is no bone mass loss in transwomen after 28–63 months of estrogen therapy [82].

As discussed earlier, sex differences in muscle mass in elite athletes can be 50–75% [30] in favor of males, thus the decrease of 5–10% reported in studies of transwomen after 1–2 years of estrogen therapy will most likely provide, at most, a modest reformatting of male muscle strength in the transwoman athlete. Further evidence to support maintenance of muscle mass in the face of lowered testosterone levels is observed in prostate cancer patients. Such patients are on androgen-deprivation therapy for extended periods to lower testosterone levels to very low levels (i.e., within the female range) but only report a small loss (2–4%) in muscle mass over 12 months [83]. Notably, this effect can be mitigated with an exercise training program [79,84,85]. Therefore, it follows that a transwoman

athlete following a high-performance training program enabling competitiveness at an elite level throughout the 12-month estrogen therapy transition period could similarly mitigate muscle mass loss.

The difficulty of reformatting muscle physiology to female levels in transwomen likely results from their life-long exposure to testosterone prior to transitioning and prior levels of exercise as a male. Increased muscle mass arises from hypertrophy of individual muscle fibers in response to enhanced protein synthesis within the cells. Muscle cells recruit nuclei from nearby helper satellite cells to increase protein synthesis and allow muscle cell hypertrophy [86–89]. The most important stimulus for muscle hypertrophy is exercise and thus, muscles subjected to overload exercise recruit nuclei. If the muscle then undergoes a period of rest, the muscle cell will atrophy back to its baseline size but will retain the nuclei acquired during the hypertrophic phase. In humans, nuclei numbers are very stable and may even be permanent [90]. When these cells with higher numbers of nuclei are again subjected to overload exercise, the cells can quickly ramp up protein synthesis and hypertrophy. Thus, muscle cell nuclei number represents a form of “muscle memory” that is a functionally important indicator of prior strength and explains how previous exercise improves the ability to regain muscle mass later in life, even after long sedentary periods [91,92].

Mouse studies have shown that testosterone administration for 2 weeks significantly increased muscle cell hypertrophy and generated an increase in muscle cell nuclei number that was maintained for the next 8 weeks. Mice were then subjected to overload training and those animals that had been treated with testosterone showed a 3-fold increase in muscle hypertrophy compared to controls [88].

Muscle memory is, therefore, a critical factor when considering the physiology of transwoman athletes. Prior to transitioning, the post-pubertal exposure to high androgen levels, relative to a biological female, would increase muscle cell nuclei number [93], a long-term benefit that is not quickly, if ever, reversed. This androgen-induced muscle memory effect has been used to argue that a two-year sanction from elite competition is not sufficient for those athletes found to have consumed exogenous androgens because of the potential on-going athletic performance advantage [94,95].

3.4. Estrogen Therapy and Effects on the Cardiorespiratory System

The physiological parameter that will be affected most by estrogen therapy is $\text{VO}_{2\text{ max}}$ or maximum aerobic performance. Due to the dependence of $\text{VO}_{2\text{ max}}$ on hemoglobin levels, and the relationship between testosterone and hemoglobin, reduced testosterone will decrease $\text{VO}_{2\text{ max}}$. Importantly, hemoglobin is sensitive to testosterone even at low concentrations [96], with dose-dependent increases measured in females within the 0–4 nmol/L range [96]. Males on androgen-deprivation therapy show a significant 9% drop in hemoglobin levels after 12 months, with a further variable decline by 12.8–29% after 24 months [97]. This decrease in hemoglobin will likely decrease maximal aerobic performance. The hemoglobin response to testosterone concentrations, whether increasing or decreasing, occurs within weeks [98], thus, if the hemoglobin levels are to remain lowered in transfemale athletes, circulating testosterone levels must remain consistently reduced. As discussed above, achieving testosterone suppression to very low levels in transwomen can be difficult [53–56], where nearly all transwomen involved in reported studies failed to achieve or maintain testosterone levels in the biological female range, which was consummate with a higher hemoglobin level than that of biological females [56].

While hemoglobin levels respond closely to circulating testosterone levels, other cardiorespiratory system parameters are unlikely to be impacted significantly by estrogen therapy. For example, sex differences in lung size and alveolar numbers, total heart size, left ventricular size, stroke volume, and subsequent cardiac output will not be changed significantly. All of these parameters are defined by anatomical structures that were programmed by early life and early pubertal exposure to testosterone.

4. Conclusions

Testosterone drives much of the enhanced athletic performance of males through in utero, early life, and adult exposure. Many anatomical sex differences driven by testosterone are not reversible. Hemoglobin levels and muscle mass are sensitive to adult life testosterone levels, with hemoglobin being the most responsive. Studies in transgender women, and androgen-deprivation treated cancer patients, show muscle mass is retained for many months, even years, and that co-mittant exercise mitigates muscle loss. Given that sports are currently segregated into male and female divisions because of superior male athletic performance, and that estrogen therapy will not reverse most athletic performance parameters, it follows that transgender women will enter the female division with an inherent advantage because of their prior male physiology.

The current IOC regulations allow transwomen athletes to compete if testosterone levels have been lowered to <10 nmol/L for 12 months prior to competition. While this begins to address the advantageous effects of circulating testosterone on athletic performance, it does not take into account the advantage afforded by testosterone exposure prior to transitioning. The existing data suggests that lowering testosterone to less than 10 nmol/L for 12 months decreases muscle mass but not to biological female levels and despite the decrease in mass, muscle strength can be maintained, especially if concurrently exercising. Estrogen therapy does not affect most of the anatomical structures in the biological male that provide a physiological benefit. Hemoglobin levels are lowered by estrogen therapy, and consequently, maximum aerobic effort may be lower, but this parameter will only be manifested if testosterone levels are suppressed to levels within the biological female range and maintained for extended periods of time. Reported studies show it is difficult to continuously suppress testosterone in transgender women. Given that the percentage difference between medal placings at the elite level is normally less than 1%, there must be confidence that an elite transwoman athlete retains no residual advantage from former testosterone exposure, where the inherent advantage depending on sport could be 10–30%. Current scientific evidence can not provide such assurances and thus, under abiding rulings, the inclusion of transwomen in the elite female division needs to be reconsidered for fairness to female-born athletes.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The author acknowledges the discussions with Lynley Anderson and Taryn Knox (University of Otago, New Zealand) to help provide a balance of science versus sociocultural views during the writing of this manuscript.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Cheuvront, S.N.; Carter, R.; DeRuisseau, K.C.; Moffatt, R.J. Running performance differences between men and women: An update. *Sports Med.* **2005**, *35*, 1017–1024. [\[CrossRef\]](#)
2. Nevill, A.M.; Whyte, G. Are there limits to running world records? *Med. Sci. Sports Exerc.* **2005**, *37*, 1785–1788. [\[CrossRef\]](#)
3. Seiler, S.; de Koning, J.J.; Foster, C. The fall and rise of the gender difference in elite anaerobic performance 1952–2006. *Med. Sci. Sports Exerc.* **2007**, *39*, 534–540. [\[CrossRef\]](#)
4. Berthelot, G.; Thibault, V.; Tafflet, M.; Escolano, S.; El Helou, N.; Jouven, X.; Hermine, O.; Toussaint, J.-F. The citius end: World records progression announces the completion of a brief ultra-physiological quest. *PLoS ONE* **2008**, *3*, e1552. [\[CrossRef\]](#)
5. Thibault, V.; Guillaume, M.; Berthelot, G.; El Helou, N.; Schaal, K.; Quinquis, L.; Nassif, H.; Tafflet, M.; Escolano, S.; Hermine, O.; et al. Women and Men in Sport Performance: The Gender Gap has not Evolved since 1983. *J. Sports Sci. Med.* **2010**, *9*, 214–223.
6. Kennedy, C.L. A New Frontier for Women's Sports (Beyond Title IX). *Gend. Issues* **2010**, *27*, 78–90. [\[CrossRef\]](#)
7. Bretherton, I.; Thrower, E.; Grossmann, M.; Zajac, J.D.; Cheung, A.S. Cross-sex hormone therapy in Australia: The prescription patterns of clinicians experienced in adult transgender healthcare. *Intern. Med. J.* **2019**, *49*, 182–188. [\[CrossRef\]](#)

8. Randolph, J.F., Jr. Gender-Affirming Hormone Therapy for Transgender Females. *Clin. Obstet. Gynecol.* **2018**, *61*, 705–721. [\[CrossRef\]](#)
9. Phoenix, C.H.; Goy, R.W.; Gerall, A.A.; Young, W.C. Organizing action of prenatally administered testosterone propionate on the tissues mediating mating behavior in the female guinea pig. *Endocrinology* **1959**, *65*, 369–382. [\[CrossRef\]](#)
10. McCarthy, M.M. Sex differences in the developing brain as a source of inherent risk. *Dialogues. Clin. Neurosci.* **2016**, *18*, 361–372. [\[CrossRef\]](#)
11. de Vries, G.J.; Sodersten, P. Sex differences in the brain: The relation between structure and function. *Horm. Behav.* **2009**, *55*, 589–596. [\[CrossRef\]](#)
12. Isgor, C.; Sengelaub, D.R. Prenatal gonadal steroids affect adult spatial behavior, CA1 and CA3 pyramidal cell morphology in rats. *Horm. Behav.* **1998**, *34*, 183–198. [\[CrossRef\]](#)
13. Isgor, C.; Sengelaub, D.R. Effects of neonatal gonadal steroids on adult CA3 pyramidal neuron dendritic morphology and spatial memory in rats. *J. Neurobiol.* **2003**, *55*, 179–190. [\[CrossRef\]](#)
14. Schwarz, A.J.; Gozzi, A.; Bifone, A. Community structure and modularity in networks of correlated brain activity. *Magn. Reson. Imaging* **2008**, *26*, 914–920. [\[CrossRef\]](#)
15. Tononi, G.; Sporns, O.; Edelman, G.M. A measure for brain complexity: Relating functional segregation and integration in the nervous system. *Proc. Natl. Acad. Sci. USA* **1994**, *91*, 5033–5037. [\[CrossRef\]](#)
16. Tunç, B.; Solmaz, B.; Parker, D.; Satterthwaite, T.D.; Elliott, M.A.; Calkins, M.E.; Ruparel, K.; Gur, R.E.; Gur, R.C.; Verma, R. Establishing a link between sex-related differences in the structural connectome and behaviour. *Philos. Trans. R Soc. Lond. B Biol. Sci.* **2016**, *371*, 20150111. [\[CrossRef\]](#)
17. Robazza, C.; Bortoli, L. Perceived impact of anger and anxiety on sporting performance in rugby players. *Psychol. Sport Exerc.* **2007**, *8*, 875–896. [\[CrossRef\]](#)
18. Bartlett, M.L.; Abrams, M.; Byrd, M.; Treankler, A.S.; Houston-Norton, R. Advancing the Assessment of Anger in Sports: Gender Differences and STAXI-2 Normative Data for College Athletes. *J. Clin. Sport Psychol.* **2018**, *12*, 114–128. [\[CrossRef\]](#)
19. Ruiz, M.C.; Hanin, Y. Perceived impact of anger on performance of skilled karate athletes. *Psychol. Sport Exerc.* **2011**, *12*, 242–249. [\[CrossRef\]](#)
20. Abrams, M. *Anger Management in Sport*, 1st ed.; Human Kinetics: Champaign, IL, USA, 2010.
21. Bartlett, M.L.; Abrams, M. Anger and aggression in sport. In *APA Handbooks in Psychology Series. APA Handbook of Sport and Exercise Psychology*; Anshel, T.A.P.M.H., Steinfeldt, J.A., Eds.; American Psychological Association: Washington, DC, USA, 2019; pp. 509–528.
22. Deaner, R.O. Physiology does not explain all sex differences in running performance. *Med. Sci. Sports Exerc.* **2013**, *45*, 146–147. [\[CrossRef\]](#)
23. Deaner, R.O. Distance running as an ideal domain for showing a sex difference in competitiveness. *Arch. Sex. Behav.* **2013**, *42*, 413–428. [\[CrossRef\]](#) [\[PubMed\]](#)
24. Ribeiro, E.; Neave, N.; Morais, R.N.; Kilduff, L.; Taylor, S.R.; Butovskaya, M.; Fink, B.; Manning, J.T. Digit ratio (2D:4D), testosterone, cortisol, aggression, personality and hand-grip strength: Evidence for prenatal effects on strength. *Early Hum. Dev.* **2016**, *100*, 21–25. [\[CrossRef\]](#) [\[PubMed\]](#)
25. Kim, T.B.; Kim, K.H. Why is digit ratio correlated to sports performance? *J. Exerc. Rehabil.* **2016**, *12*, 515–519. [\[CrossRef\]](#) [\[PubMed\]](#)
26. Bönke, W.; Procher, V.D.; Urbig, D.; Voracek, M. Digit Ratio (2D:4D) Predicts Self-Reported Measures of General Competitiveness, but Not Behavior in Economic Experiments. *Front. Behav. Neurosci.* **2017**, *11*, 238. [\[CrossRef\]](#)
27. Mailhos, A.; Buunk, A.P.; del Arca, D.; Tuttle, V. Soccer players awarded one or more red cards exhibit lower 2D:4D ratios. *Aggress. Behav.* **2016**, *42*, 417–426. [\[CrossRef\]](#)
28. Voracek, M.; Reimer, B.; Dressler, S.G. Digit ratio (2D:4D) predicts sporting success among female fencers independent from physical, experience, and personality factors. *Scand. J. Med. Sci. Sports* **2010**, *20*, 853–860. [\[CrossRef\]](#)
29. Healy, M.L.; Gibney, J.; Pentecost, C.; Wheeler, M.J.; Sonksen, P.H. Endocrine profiles in 693 elite athletes in the postcompetition setting. *Clin. Endocrinol.* **2014**, *81*, 294–305. [\[CrossRef\]](#)
30. Sale, D.G. Neuromuscular function. In *Gender Differences in Metabolism: Practical and Nutritional Implications*; Tarnopolsky, M., Ed.; CRC Press: Boca Raton, FL, USA, 1999; Chapter 4; pp. 61–86.
31. Handelsman, D.J. Sex differences in athletic performance emerge coinciding with the onset of male puberty. *Clin. Endocrinol.* **2017**, *87*, 68–72. [\[CrossRef\]](#)
32. Bhasin, S.; Storer, T.W.; Berman, N.; Callegari, C.; Clevenger, B.; Phillips, J.; Bunnell, T.J.; Tricker, R.; Shirazi, A.; Casaburi, R. The effects of supraphysiologic doses of testosterone on muscle size and strength in normal men. *N. Engl. J. Med.* **1996**, *335*, 1–7. [\[CrossRef\]](#)
33. Bhasin, S.; Woodhouse, L.J.; Casaburi, R.; Singh, A.B.; Bhasin, D.; Berman, N.; Chen, X.; Yarasheski, K.; Magliano, L.; Dzekov, C.; et al. Testosterone dose-response relationships in healthy young men. *Am. J. Physiol. Endocrinol. Metab.* **2001**, *281*, E1172–E1181. [\[CrossRef\]](#)
34. Hirschberg, A.L. Hyperandrogenism in Female Athletes. *J. Clin. Endocrinol. Metab.* **2019**, *104*, 503–505. [\[CrossRef\]](#)
35. Davidyan, A.; Pathak, S.; Baar, K.; Bodine, S.C. Maintenance of muscle mass in adult male mice is independent of testosterone. *PLoS ONE* **2021**, *16*, e0240278. [\[CrossRef\]](#)

36. Hirschberg, A.L.; Knutsson, J.E.; Helge, T.; Godhe, M.; Ekblom, M.; Berman, S.; Ekblom, B. Effects of moderately increased testosterone concentration on physical performance in young women: A double blind, randomised, placebo controlled study. *Br. J. Sports Med.* **2019**, *54*, 599–604. [\[CrossRef\]](#) [\[PubMed\]](#)
37. Turner, R.T.; Riggs, B.L.; Spelsberg, T.C. Skeletal effects of estrogen. *Endocr. Rev.* **1994**, *15*, 275–300.
38. Orwoll, E.S.; Klein, R.F. Osteoporosis in men. *Endocr. Rev.* **1995**, *16*, 87–116. [\[CrossRef\]](#) [\[PubMed\]](#)
39. Laubach, L.L. Comparative muscular strength of men and women: A review of the literature. *Aviat. Space Environ. Med.* **1976**, *47*, 534–542. [\[PubMed\]](#)
40. Huseynov, A.; Zollikofer, C.P.; Coudyzer, W.; Gascho, D.; Kellenberger, C.; Hinzpeter, R.; Ponce de León, M.S. Developmental evidence for obstetric adaptation of the human female pelvis. *Proc. Natl. Acad. Sci. USA* **2016**, *113*, 5227–5232. [\[CrossRef\]](#)
41. Sutherland, M.A.; Wassersug, R.J.; Rosenberg, K.R. From transsexuals to transhumans in elite athletics—The implications of osteology (and other issues) in leveling the playing field. In *Transgender Athletes in Competitive Sport*; Routledge: London, UK, 2017; p. 238.
42. Fornalski, S.; Gupta, R.; Lee, T.Q. Anatomy and biomechanics of the elbow joint. *Tech. Hand Up. Extrem. Surg.* **2003**, *7*, 168–178. [\[CrossRef\]](#)
43. Carey, M.A.; Card, J.W.; Voltz, J.W.; Arbes, S.J.; Germolec, D.R.; Korach, K.S.; Zeldin, D.C. It's all about sex: Gender, lung development and lung disease. *Trends Endocrinol. Metab.* **2007**, *18*, 308–313. [\[CrossRef\]](#)
44. Townsend, E.A.; Miller, V.M.; Prakash, Y.S. Sex Differences and Sex Steroids in Lung Health and Disease. *Endocr. Rev.* **2012**, *33*, 1–47. [\[CrossRef\]](#)
45. Thurlbeck, W.M. Postnatal human lung growth. *Thorax* **1982**, *37*, 564–571. [\[CrossRef\]](#) [\[PubMed\]](#)
46. Bellemare, F.; Jeanneret, A.; Couture, J. Sex differences in thoracic dimensions and configuration. *Am. J. Respir. Crit. Care Med.* **2003**, *168*, 305–312. [\[CrossRef\]](#) [\[PubMed\]](#)
47. Leinwand, L.A. Sex is a potent modifier of the cardiovascular system. *J. Clin. Investig.* **2003**, *112*, 302–307. [\[CrossRef\]](#) [\[PubMed\]](#)
48. Murphy, W.G. The sex difference in haemoglobin levels in adults—mechanisms, causes, and consequences. *Blood Rev.* **2014**, *28*, 41–47. [\[CrossRef\]](#)
49. Coviello, A.D.; Kaplan, B.; Lakshman, K.M.; Chen, T.; Singh, A.B.; Bhasin, S. Effects of graded doses of testosterone on erythropoiesis in healthy young and older men. *J. Clin. Endocrinol. Metab.* **2008**, *93*, 914–919. [\[CrossRef\]](#)
50. Grossmann, M.; Cheung, A.S.; Zajac, J.D. Androgens and prostate cancer; pathogenesis and deprivation therapy. *Best Pract. Res. Clin. Endocrinol. Metab.* **2013**, *27*, 603–616. [\[CrossRef\]](#)
51. Kenney, W.L.; Wilmore, J.H.; Costill, D.L. *Physiology of Sport and Exercise*, 5th ed.; Human Kinetics: Champaign, IL, USA, 2012.
52. Gardner, I.H.; Safer, J.D. Progress on the road to better medical care for transgender patients. *Curr. Opin. Endocrinol. Diabetes Obes.* **2013**, *20*, 553–558. [\[CrossRef\]](#)
53. Liang, J.; Jolly, D.; Chan, K.J.; Safer, J.D. Testosterone Levels Achieved by Medically Treated Transgender Women in a United States Endocrinology Clinic Cohort. *Endocr. Pract.* **2018**, *24*, 135–142. [\[CrossRef\]](#)
54. Leinung, M.C.; Feustel, P.; Joseph, J. Hormonal Treatment of Transgender Women with Oral Estradiol. *Transgend. Health* **2018**, *3*, 74–81. [\[CrossRef\]](#)
55. SoRelle, J.A.; Jiao, R.; Gao, E.; Veazey, J.; Frame, I.; Quinn, A.M.; Day, P.; Pagels, P.; Gimpel, N.; Patel, K. Impact of Hormone Therapy on Laboratory Values in Transgender Patients. *Clin. Chem.* **2019**, *65*, 170–179. [\[CrossRef\]](#)
56. Jarin, J.; Pine-Twaddell, E.; Trotman, G.; Stevens, J.; Conard, L.A.; Tefera, E.; Gomez-Lobo, V. Cross-Sex Hormones and Metabolic Parameters in Adolescents with Gender Dysphoria. *Pediatrics* **2017**, *139*, e20163173. [\[CrossRef\]](#) [\[PubMed\]](#)
57. Guillamon, A.; Junque, C.; Gil, E.G. A Review of the Status of Brain Structure Research in Transsexualism. *Arch. Sex. Behav.* **2016**, *45*, 1615–1648. [\[CrossRef\]](#) [\[PubMed\]](#)
58. Kreukels, B.P.; Guillamon, A. Neuroimaging studies in people with gender incongruence. *Int. Rev. Psychiatry* **2016**, *28*, 120–128. [\[CrossRef\]](#)
59. Mueller, S.C.; Landré, L.; Wierckx, K.; T'Sjoen, G. A Structural Magnetic Resonance Imaging Study in Transgender Persons on Cross-Sex Hormone Therapy. *Neuroendocrinology* **2017**, *105*, 123–130. [\[CrossRef\]](#)
60. Seiger, R.; Hahn, A.; Hummer, A.; Kranz, G.S.; Ganger, S.; Woletz, M.; Kraus, C.; Sladky, R.; Kautzky, A.; Kasper, S.; et al. Subcortical gray matter changes in transgender subjects after long-term cross-sex hormone administration. *Psychoneuroendocrinology* **2016**, *74*, 371–379. [\[CrossRef\]](#) [\[PubMed\]](#)
61. Zubiaurre-Elorza, L.; Junque, C.; Gómez-Gil, E.; Guillamon, A. Effects of cross-sex hormone treatment on cortical thickness in transsexual individuals. *J. Sex. Med.* **2014**, *11*, 1248–1261. [\[CrossRef\]](#) [\[PubMed\]](#)
62. Burke, S.M.; Manzouri, A.H.; Savic, I. Structural connections in the brain in relation to gender identity and sexual orientation. *Sci. Rep.* **2017**, *7*, 17954. [\[CrossRef\]](#)
63. Mueller, S.C.; Wierckx, K.; Jackson, K.; T'Sjoen, G. Circulating androgens correlate with resting-state MRI in transgender men. *Psychoneuroendocrinology* **2016**, *73*, 91–98. [\[CrossRef\]](#)
64. Kranz, G.; Hahn, A.; Kaufmann, U.; Tik, M.; Ganger, S.; Seiger, R.; Hummer, A.; Windischberger, C.; Kasper, S.; Lanzenberger, R. Effects of testosterone treatment on hypothalamic neuroplasticity in female-to-male transgender individuals. *Brain Struct. Funct.* **2018**, *223*, 321–328. [\[CrossRef\]](#)
65. Linn, M.C.; Petersen, A.C. Emergence and characterization of sex differences in spatial ability: A meta-analysis. *Child. Dev.* **1985**, *56*, 1479–1498. [\[CrossRef\]](#)

66. Voyer, D.; Voyer, S.; Bryden, M.P. Magnitude of sex differences in spatial abilities: A meta-analysis and consideration of critical variables. *Psychol. Bull.* **1995**, *117*, 250–270. [\[CrossRef\]](#) [\[PubMed\]](#)
67. Hedges, L.V.; Nowell, A. Sex differences in mental test scores, variability, and numbers of high-scoring individuals. *Science* **1995**, *269*, 41–45. [\[CrossRef\]](#)
68. Miles, C.; Green, R.; Hines, M. Estrogen treatment effects on cognition, memory and mood in male-to-female transsexuals. *Horm. Behav.* **2006**, *50*, 708–717. [\[CrossRef\]](#) [\[PubMed\]](#)
69. Karalexi, M.A.; Georgakis, M.K.; Dimitriou, N.G.; Vichos, T.; Katsimpris, A.; Petridou, E.T.; Papadopoulos, F.C. Gender-affirming hormone treatment and cognitive function in transgender young athletes: A systematic review and meta-analysis. *Psychoneuroendocrinology* **2020**, *119*, 104721. [\[CrossRef\]](#) [\[PubMed\]](#)
70. Van Goozen, S.H.; Cohen-Kettenis, P.T.; Gooren, L.J.; Frijda, N.H.; Van De Poll, N.E. Gender differences in behaviour: Activating effects of cross-sex hormones. *Psychoneuroendocrinology* **1995**, *20*, 343–363. [\[CrossRef\]](#)
71. Pol, H.E.H.; Schnack, H.G.; Mandl, R.C.; Brans, R.G.; van Haren, N.E.; Baaré, W.F.; van Oel, C.; Collins, D.L.; Evans, A.C.; Kahn, R.S. Gray and white matter density changes in monozygotic and same-sex dizygotic twins discordant for schizophrenia using voxel-based morphometry. *Neuroimage* **2006**, *31*, 482–488.
72. Kim, T.-H.; Kim, G.-W.; Kim, S.-K.; Jeong, G.-W. Brain activation-based sexual orientation in female-to-male transsexuals. *Int. J. Impot. Res.* **2016**, *28*, 31–38. [\[CrossRef\]](#)
73. Kim, T.H.; Kim, S.K.; Jeong, G.W. Cerebral gray matter volume variation in female-to-male transsexuals: A voxel-based morphometric study. *Neuroreport* **2015**, *26*, 1119–1125. [\[CrossRef\]](#)
74. McCarthy, M.M. Multifaceted origins of sex differences in the brain. *Philos. Trans. R Soc. Lond. B Biol. Sci.* **2016**, *371*, 20150106. [\[CrossRef\]](#)
75. Beking, T.; Geuze, R.; van Faassen, M.; Kema, I.; Kreukels, B.; Groothuis, T. Prenatal and pubertal testosterone affect brain lateralization. *Psychoneuroendocrinology* **2018**, *88*, 78–91. [\[CrossRef\]](#)
76. Nguyen, T.-V.; Lew, J.; Albaugh, M.D.; Botteron, K.N.; Hudziak, J.J.; Fonov, V.S.; Collins, D.L.; Ducharme, S.; McCracken, J.T. Sex-specific associations of testosterone with prefrontal-hippocampal development and executive function. *Psychoneuroendocrinology* **2017**, *76*, 206–217. [\[CrossRef\]](#) [\[PubMed\]](#)
77. Grimshaw, G.; Sitarenios, G.; Finegan, J. Mental rotation at 7 years: Relations with prenatal testosterone levels and spatial play experiences. *Brain Cogn.* **1995**, *29*, 85–100. [\[CrossRef\]](#) [\[PubMed\]](#)
78. Elbers, J.M.H.; Asscheman, H.; Seidell, J.; Gooren, L.J.G. Effects of sex steroid hormones on regional fat depots as assessed by magnetic resonance imaging in transsexuals. *Am. J. Physiol.* **1999**, *276*, E317–E325. [\[CrossRef\]](#)
79. Wiik, A.; Lundberg, T.R.; Rullman, E.; Andersson, D.P.; Holmberg, M.; Mandić, M.; Brismar, T.B.; Leinhard, O.D.; Chanpen, S.; Flanagan, J.N.; et al. Muscle strength, size and composition following 12 months of gender-affirming treatment in transgender individuals: Retained advantage for the transwomen. *bioRxiv* **2019**, *105*, e805–e813.
80. Roberts, T.A.; Smalley, J.; Ahrendt, D. Effect of gender affirming hormones on athletic performance in transwomen and transmen: Implications for sporting organisations and legislators. *Br. J. Sports Med.* **2020**, *55*, 577–583. [\[CrossRef\]](#)
81. Harper, J. Race times for transgender athletes. *J. Sport. Cult. Identities* **2015**, *6*, 1–9. [\[CrossRef\]](#)
82. van Kesteren, P.; Lips, P.; Gooren, L.J.; Asscheman, H.; Megens, J. Long-term follow-up of bone mineral density and bone metabolism in transsexuals treated with cross-sex hormones. *Clin. Endocrinol.* **1998**, *48*, 347–354. [\[CrossRef\]](#)
83. Lee, H.; McGovern, K.; Finkelstein, J.S.; Smith, M.R. Changes in bone mineral density and body composition during initial and long-term gonadotropin-releasing hormone agonist treatment for prostate carcinoma. *Cancer* **2005**, *104*, 1633–1637. [\[CrossRef\]](#)
84. Galvao, D.A.; Nosaka, K.; Taaffe, D.R.; Spry, N.; Kristjansson, L.J.; McGuigan, M.R.; Suzuki, K.; Yamaya, K.; Newton, R.U. Resistance training and reduction of treatment side effects in prostate cancer patients. *Med. Sci. Sports Exerc.* **2006**, *38*, 2045–2052. [\[CrossRef\]](#)
85. Segal, R.J.; Reid, R.D.; Courneya, K.S.; Malone, S.C.; Parliament, M.B.; Scott, C.G.; Venner, P.M.; Quinney, H.A.; Jones, L.W.; D'Angelo, M.E.S.; et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. *J. Clin. Oncol.* **2003**, *21*, 1653–1659. [\[CrossRef\]](#)
86. Fu, X.; Wang, H.; Hu, P. Stem cell activation in skeletal muscle regeneration. *Cell Mol. Life Sci.* **2015**, *72*, 1663–1677. [\[CrossRef\]](#)
87. Bruusgaard, J.C.; Johansen, I.B.; Egner, I.M.; Rana, Z.A.; Gundersen, K. Myonuclei acquired by overload exercise precede hypertrophy and are not lost on detraining. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 15111–15116. [\[CrossRef\]](#) [\[PubMed\]](#)
88. Egner, I.M.; Bruusgaard, J.C.; Eftestøl, E.; Gundersen, K. A cellular memory mechanism aids overload hypertrophy in muscle long after an episodic exposure to anabolic steroids. *J. Physiol.* **2013**, *591*, 6221–6230. [\[CrossRef\]](#) [\[PubMed\]](#)
89. Gundersen, K. Excitation-transcription coupling in skeletal muscle: The molecular pathways of exercise. *Biol. Rev. Camb. Philos. Soc.* **2011**, *86*, 564–600. [\[CrossRef\]](#) [\[PubMed\]](#)
90. Gundersen, K. Muscle memory and a new cellular model for muscle atrophy and hypertrophy. *J. Exp. Biol.* **2016**, *219* Pt 2, 235–242. [\[CrossRef\]](#)
91. Staron, R.S.; Leonardi, M.J.; Karapondo, D.L.; Malicky, E.S.; Falkel, J.E.; Hagerman, F.C.; Hikida, R.S. Strength and skeletal muscle adaptations in heavy-resistance-trained women after detraining and retraining. *J. Appl. Physiol.* **1991**, *70*, 631–640. [\[CrossRef\]](#)
92. Taaffe, D.; Marcus, R. Dynamic muscle strength alterations to detraining and retraining in elderly men. *Clin. Physiol.* **1997**, *17*, 311–324. [\[CrossRef\]](#)

93. Neal, A.; Boldrin, L.; Morgan, J.E. The satellite cell in male and female, developing and adult mouse muscle: Distinct stem cells for growth and regeneration. *PLoS ONE* **2012**, *7*, e37950. [[CrossRef](#)]
94. Seaborne, R.; Strauss, J.; Cocks, M.; Shepherd, S.; O'Brien, T.D.; Van Someren, K.A.; Bell, P.G.; Murgatroyd, C.; Morton, J.P.; Stewart, C.E.; et al. Methylome of human skeletal muscle after acute & chronic resistance exercise training, detraining & retraining. *Sci. Data* **2018**, *5*, 180213.
95. Seaborne, R.A.; Strauss, J.; Cocks, M.; Shepherd, S.; O'Brien, T.D.; Van Someren, K.A.; Bell, P.G.; Murgatroyd, C.; Morton, J.P.; Stewart, C.E.; et al. Human Skeletal Muscle Possesses an Epigenetic Memory of Hypertrophy. *Sci. Rep.* **2018**, *8*, 1898. [[CrossRef](#)]
96. Karunasena, N.; Han, T.S.; Mallappa, A.; Elman, M.; Merke, D.P.; Ross, R.J.; Daniel, E. Androgens correlate with increased erythropoiesis in women with congenital adrenal hyperplasia. *Clin. Endocrinol.* **2017**, *86*, 19–25. [[CrossRef](#)] [[PubMed](#)]
97. Hicks, B.M.; Klil-Drori, A.; Yin, H.; Campeau, L.; Azoulay, L. Androgen Deprivation Therapy and the Risk of Anemia in Men with Prostate Cancer. *Epidemiology* **2017**, *28*, 712–718. [[CrossRef](#)] [[PubMed](#)]
98. Snyder, P.J.; Peachey, H.; Berlin, J.A.; Hannoush, P.; Haddad, G.; Dlewati, A.; Santanna, J.; Loh, L.; Lenrow, D.A.; Holmes, J.H.; et al. Effects of testosterone replacement in hypogonadal men. *J. Clin. Endocrinol. Metab.* **2000**, *85*, 2670–2677. [[CrossRef](#)] [[PubMed](#)]

The Biological Basis of Sex Differences in Athletic Performance: Consensus Statement for the American College of Sports Medicine

SANDRA K. HUNTER¹, SIDDHARTHA S. ANGADI², ADITI BHARGAVA³, JOANNA HARPER⁴, ANGELICA LINDÉN HIRSCHBERG⁵, BENJAMIN D. LEVINE⁶, KERRIE L. MOREAU⁷, NATALIE J. NOKOFF⁸, NINA S. STACHENFELD⁹, and STÉPHANE BERMON¹⁰

¹Exercise Science Program, Department of Physical Therapy, and Athletic and Human Performance Center, Marquette University, Milwaukee, WI; ²Department of Kinesiology, University of Virginia, Charlottesville, VA; ³Department of Obstetrics and Gynecology, Center for Reproductive Sciences, University of California, San Francisco, CA; ⁴Loughborough University, Loughborough, UNITED KINGDOM; ⁵Department of Women's and Children's Health, Karolinska Institutet, and Department of Gynecology and Reproductive Medicine, Karolinska University Hospital, Stockholm, SWEDEN; ⁶Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital Dallas, and the Department of Internal Medicine, Division of Cardiology, University of Texas Southwestern Medical Center, Dallas, TX; ⁷Department of Medicine, Division of Geriatric Medicine, University of Colorado Anschutz Medical Campus, and Eastern Colorado Health Care System, Geriatric Research Education and Clinical Center, Aurora, CO; ⁸Department of Pediatrics, Section of Endocrinology, University of Colorado Anschutz Medical Campus, Aurora, CO; ⁹The John B. Pierce Laboratory and Department of Obstetrics, Gynecology and Reproductive Sciences, Yale School of Medicine, New Haven, CT; and ¹⁰Health and Science Department, World Athletics, Monaco and the LAMHESS, University Côte d'Azur, Nice, FRANCE

ABSTRACT

HUNTER, SANDRA K., S. S. ANGADI, A. BHARGAVA, J. HARPER, A. L. HIRSCHBERG, B. D. LEVINE, K. L. MOREAU, N. J. NOKOFF, N. STACHENFELD, and S. BERMON. The Biological Basis of Sex Differences in Athletic Performance: Consensus Statement for the American College of Sports Medicine. *Med. Sci. Sports Exerc.*, Vol. 00, No. 00, pp. 00–00, 2023. Biological sex is a primary determinant of athletic performance because of fundamental sex differences in anatomy and physiology dictated by sex chromosomes and sex hormones. Adult men are typically stronger, more powerful, and faster than women of similar age and training status. Thus, for athletic events and sports relying on endurance, muscle strength, speed, and power, males typically outperform females by 10%–30% depending on the requirements of the event. These sex differences in performance emerge with the onset of puberty and coincide with the increase in endogenous sex steroid hormones, in particular testosterone in males, which increases 30-fold by adulthood, but remains low in females. The primary goal of this consensus statement is to provide the latest scientific knowledge and mechanisms for the sex differences in athletic performance. This review highlights the differences in anatomy and physiology between males and females that are primary determinants of the sex differences in athletic performance and in response to exercise training, and the role of sex steroid hormones (particularly testosterone and estradiol). We also identify historical and nonphysiological factors that influence the sex differences in performance. Finally, we identify gaps in the knowledge of sex differences in athletic performance and the underlying mechanisms, providing substantial opportunities for high-impact studies. A major step toward closing the knowledge gap is to include more and equitable numbers of women to that of men in mechanistic studies that determine any of the sex differences in response to an acute bout of exercise, exercise training, and athletic performance.

INTRODUCTION

Biological sex is a primary determinant of performance in many athletic events and physical tasks. In athletic events and sports relying on endurance, muscle strength, speed, and power, men typically outperform women because of fundamental sex differences dictated by their sex chromosomes and sex hormones at puberty, in particular, testosterone. For example, the advantages of men over women in athletic performance that require muscle power and endurance are illustrated in the comparison of the best times of men 400-m runners and the top 3 women running times in 2019 where

Address for correspondence: Sandra K. Hunter, Ph.D., Marquette University, Milwaukee, WI 53233 (E-mail: Sandra.hunter@marquette.edu).

This article is being simultaneously published in *Translational Journal of the American Journal of Sports Medicine*® (DOI:10.1249/TJX.0000000000000236)

0195-9131/23/0000-0000/0

MEDICINE & SCIENCE IN SPORTS & EXERCISE®

Copyright © 2023 by the American College of Sports Medicine

DOI: 10.1249/MSS.00000000000003300

motivation does not differ between sexes (Fig. 1). Over 10,000 men (including boys <18 yr) ran faster than the three fastest recorded women in that year (2019), illustrating no overlap in the performance of men and women at the top level. These numbers underscore the historical and current rationale for biological sex-based categories in many athletic events because the top adult males almost always outperform the top females in events that rely on muscle power, strength, speed, and/or endurance. In contrast, in sporting events and physical tasks where performance relies more on skill than muscle power and endurance, such as archery, the sex differences among the world's best is minimal. This variation in the magnitude of the sex difference in performance across sports and physical tasks is a consequence of the difference in the timing and effects of sex steroid hormones during growth and development and their varying effects on the different biological systems that are most utilized during athletic events (e.g., muscle vs central nervous system). Understanding the latest science for the differences in performance between males and females can inform policies of governing sports and athletic organizations on the inclusion of athletes who are transgender (1,2) and/or have disorders (or differences) of sex development (DSD), also referred to as intersex, within sex-based categories of competition. Thus, we provide definitions of sex and gender (see discussion hereinafter), and a clear picture of the science that dictates those factors that differentiate sexes in athletic performance across different events, as we address the role and inclusion of males and females, men and women in sports, and professions that require physical performance (3,4). Such information will also provide a rationale for sex-specific requirements of tactical athletes in professions with an historically strong male presence (e.g., law enforcement, military, and firefighters) as their professions open to the inclusion of more females (5,6). Lastly, because males and females

can respond differently to acute exercise bouts, and historically exercise and sports-based research has concentrated on males, more information is needed particularly on the female response during exercise and adaptations to training and rehabilitation.

The primary goal of this consensus statement is to provide the latest scientific knowledge for the sex-based differences in athletic performance. To do this, we highlight the following:

1. The magnitude of the sex differences in performance across various athletic pursuits and events that differ in their physiological and anatomical demands, and the historical and nonphysiological factors that influence these sex differences
2. The differences in anatomy and physiology between males and females that are primary determinants for the sex differences in response to acute exercise, exercise training, and athletic performance and across the life span from infancy to adulthood
3. The role of sex steroid hormones (particularly testosterone and estrogen) in the sex differences and their effect on physiology and anatomy that determine athletic performance and adaptability to exercise training in males and females
4. Models that provide insight into the role of sex steroid hormones in athletic performance including the addition and suppression of sex steroid hormones
5. Gaps in the knowledgebase of the sex differences in performance during exercise and athletic performance and the underlying mechanisms, and strategies to fill these gaps

This is a comprehensive review, yet there are many related and important topics that cannot be covered, leaving opportunity for more detailed analysis and reviews to answer key questions, with some that are covered in recent reviews including sex differences in performance fatigability and sex differences in basic science and clinical studies (7–12). Additional topics not covered in detail by this review but deserve attention include *sex differences* in i) performance in people with clinical conditions, ii) performance in the tactical athlete and requirements of their profession, iii) cellular and molecular underpinnings in response to exercise training, iv) recovery from acute exercise bouts, v) injuries and illnesses, vi) thermoregulation during exercise, and vii) social determinants that enhance or diminish athletic performance. Other related topics where key questions remain that potentially influence sex differences in performance but not covered in detail include the effects of oral contraceptives and hormone therapy in women's performance and training adaptations. Although sex differences during growth transitions such as puberty and aging have been addressed in several places in this review, more extensive analysis is warranted in other areas. Finally, the DSD (intersex) individual (defined more thoroughly in later sections), and the implications on athletic performance, should be addressed in greater detail in further publications.

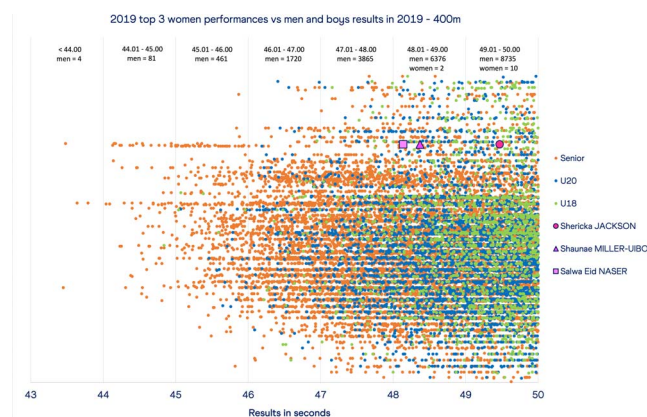


Figure 1—Top 400-m track running performances of women (top 3) and men (senior, U20, and U18) in 2019 who ran faster than 50s. Each data point represents a single performance (time plotted on the x axis) with faster times on the left-hand side of the figure. The y axis represents the spread of the performances and does not have a unit of measure. The times of the fastest three women in 2019 are shown as pink symbols (square, triangle, and circle) among the times of the men as seniors, under 20 (U20), and under 18 (U18), illustrating that >10,000 men ran faster than the top 3 women for the 400-m event in 2019.

In this statement, the terms *sex* and *gender* are defined according to the US National Institutes of Health (NIH) (13). *Sex* refers to biological differences between females and males, including chromosomes, sex organs, and endogenous sex hormone profiles (which include peptide and sex steroid hormones secreted from the pituitary and the gonads). *Gender* refers to socially constructed and enacted roles and behaviors that occur in a historical and cultural context and vary across societies and over time. Box 1 elaborates and provides other definitions including cisgender and transgender. Most relevant to athletic performance and the underlying rationale for the male and female categories in sport (also often categorized as men and women) is the sex of the person. Every cell in the body has a sex determined by the presence of sex chromosomes (typically XX for females and XY for males) (14), which fundamentally affects development and growth, and contributes to an individual's athletic ability. The sex differences in athletic performance involving strength, power, and endurance are related to the potent effects of testosterone, which is ~15-fold higher in adult males than females (9,15–17), and is a major theme in this consensus statement. Figure 2 shows the range and bimodal distribution of circulating testosterone

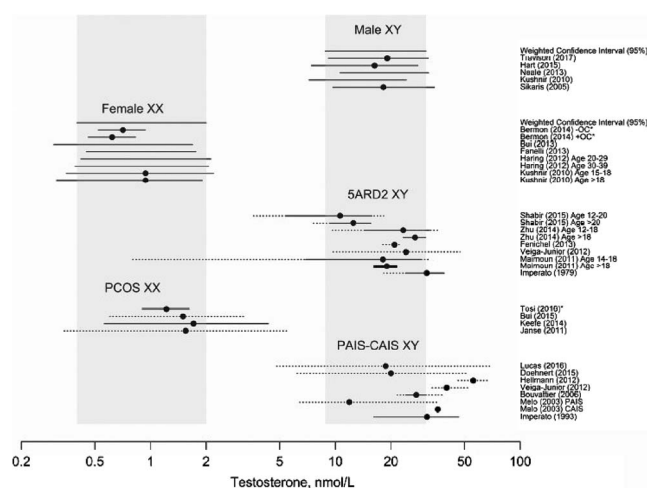


Figure 2—Circulating testosterone concentrations in adult males and females. Forest plot of testosterone ranges for women and men from the reference articles. X-axis log scale for testosterone values in $\text{nmol}\cdot\text{L}^{-1}$ ($\text{ng}\cdot\text{dL}^{-1}=\text{nmol}\cdot\text{L}^{-1}$ multiplied by 28.82), Y-axis ranges of testosterone levels for each group of women or men. Top solid line for each column is the weighted 95% confidence interval for normal men and women, solid line for each study is 95% confidence interval, and dotted line is absolute range. *Solid lines for the studies by Bermon et al. (42) and Tosi et al. (28) represent interquartile ranges, as these were the only data available in the references. 5ARD2, men with 5-alpha-reductase type 2 deficiency; CAIS, men with CAIS, -OC, women not taking oral contraceptives, +OC, women taking oral contraceptives. PAIS, men with partial androgen insensitivity; PCOS, women with polycystic ovarian syndrome. Solid circles represent median or mean values as reported in the tables of the erratum of Clark et al. (16) to Clark et al. (17). References in this figure include the following: Bermon et al. (18), Bouvattier et al. (19), Bui et al. (20), Bui et al. (21), Doehnert et al. (22), Fanelli F, Gambineri A, Belluomo I et al. (23), Fénichel et al. (24), Haring et al. (25), Hart et al. (26), Hellmann et al. (27), Imperato-McGinley et al. (28), Imperato-McGinley et al. (29), Janse et al. (30), Keefe et al. (31), Kushnir et al. (32), Lucas-Herald et al. (33), Maimoun et al. (34), Melo et al. (35), Neale et al. (36), Shabir et al. (37), Sikaris et al. (38), Tosi et al. (39), Travison et al. (40), Veiga-Junior et al. (41), Zhu et al. (42).

in the human body of adult males and females (16,17). Also shown are the testosterone concentrations in people with various DSDs and females with polycystic ovary syndrome (PCOS) that can affect testosterone concentrations and influence athletic performance. PCOS and DSD are discussed later in this review. Understanding the role of different levels and exposure of testosterone on athletic performance is important because of the central role this information can play in informing policy on inclusion into categories of athletic competition such as male, female, or open, and across different sports.

Box 1: Definitions

Sex is a multidimensional biological construct based on anatomy, physiology, genetics, and hormones (sex traits). (7,13) (NIH framework). *Sex* is an objective term, defined for the purposes of reproduction with distinct, fixed facets, notably genetic, chromosomal, gonadal, hormonal, and phenotypic (including genital) sex. Biological sex is typically dichotomous as male and female; the classical definition can be applied across most animals. Two percent of humans are intersex, harboring both male and female reproductive organs, and are reproductively fertile. Females (mammals) of a species possess XX chromosomes, have ovaries, and produce oocytes, whereas males (mammals) possess XY chromosomes, have testes, and produce spermatozoa (7).

Gender is a multidimensional construct that encompasses gender identity and expression, as well as social and cultural expectations about status, characteristics, and behavior as they are associated with certain sex traits. Gender can vary between societies and over time (13) (NIH framework). Gender involves perception of the individual as male, female, or someone who does not fit into one of these constructs, both by the individual and by society. Human gender is a spectrum from feminine to gender-neutral to masculine and includes individuals who do not fit readily on a simple linear continuum (7).

Cisgender individuals are those whose gender identity corresponds with their biological sex (or the sex designated at birth).

Transgender individuals are those whose gender identity differs or is opposite from their biological sex (or the sex designated at birth).

Sex hormones refers to peptide and steroid sex hormones secreted by the pituitary and the gonads. Many other organs, such as the liver, brain, adipose, adrenals, and the placenta, also can make *de novo* steroid sex hormones from cholesterol (7); however, after puberty (and until menopause in women), gonads are the major site for synthesis and secretion of sex steroid hormones.

HISTORICAL PERSPECTIVES

Athletic performance of men and women has progressively improved over the last century owing to factors such as enhanced training strategies, equipment, nutrition, opportunity, access, and inclusion (43). This performance improvement is observed in Olympic and World Championship competitions every 2–4 yr for a wide range of aerobic, power, and skill-based events including running, swimming, skiing, rowing, and jumping. The rate of performance improvement in women, however, has exceeded that of men (43–46) and is primarily

driven by an increase in participation and the talent pool of women and illustrated in Figure 3. This figure shows the initial rapid improvement in the marathon (Fig. 3A) and 100-m sprint (Fig. 3C) in the years that women were first permitted to compete in each of these events. The sex difference in performance for many events leveled off after 20–30 yr of “catch up” for women, although a lack of depth of talent among women in some events where participation is more limited for women can still inflate the sex difference above the differences expected due to physiology (44,48). Women did not compete in the first games of the modern Olympiad (Athens, Greece, 1896), and they were banned from competing in numerous Olympic athletic events for many years, including the marathon (first included in the women’s Olympic program in 1984). Participation rates for women in the Olympics have gradually increased with near equity in the Tokyo 2020 Summer Games (contested in 2021), although were still lacking in the 2022 Beijing Winter Olympic Games (45% women). Gender/sex equity in numbers and opportunity is important to ensure a representative talent pool of men and women (44) in all athletic events. Table 1 highlights some key benchmarks and policies that have influenced the participation of women, advancing the inclusion of women in competitive athletic events and equity in sports and health research.

Globally, and in the United States, women still do not participate regularly in physical activity (Centers for Disease Control and Prevention (50), World Health Organization (51)), and in many athletic events; e.g., (44,52), at the same rate as men. A consequence of insufficient participation in physical activity and exercise is that women are more vulnerable to diseases that are preventable with physical activity (53,54). The reasons for low participation of women are multifactorial, and some include socialization (55), lower incentives, and access to training facilities and resources (56,57) for women than men at the elite, subelite, and recreational levels in schools, colleges, and professional leagues. These social determinants potentially have a high impact on performance of women and influence the sex differences in performance. A 25-yr study, for example, indicated elite youth female track and field athletes were more likely to drop out from athletics than age-matched male athletes (58), with the potential ripple effect leading to a reduced depth and talent pool among females relative to males. Thus, inclusion and equity for women within many athletic events are not yet achieved, and even more so for women in marginalized groups, such as transgender individuals and para-athletes. Women represented 38% of the athletes competing at the Tokyo 2020 Paralympics.

Another consequence is that low participation of women limits our understanding of the physiological sex differences that determine performance. Studies on women and their inclusion as research participants, particularly those published in the exercise and sports science journals, have been vastly inadequate (8,10,59–63). An underrepresentation of women led to an overestimation of the sex differences in marathon performance that could be attributed to physiological and anatomic

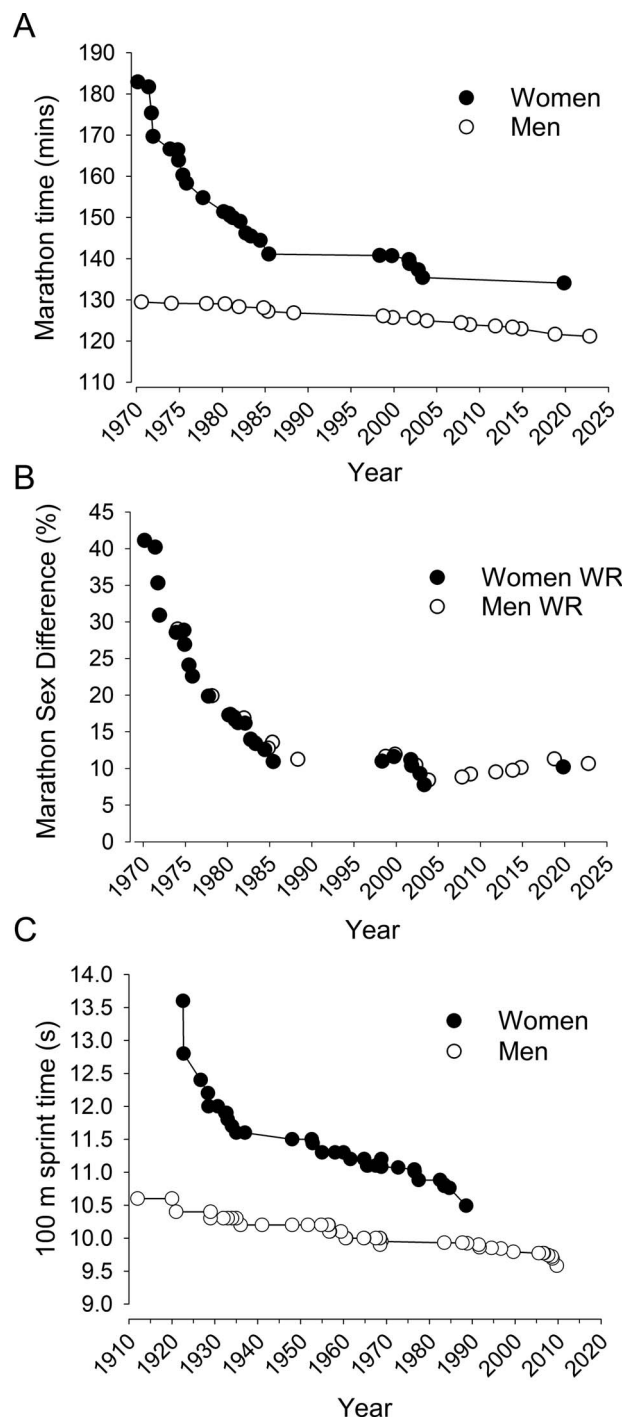


Figure 3—Progression of world record (WR) performances by men and women for the marathon and 100-m sprint. A, WR times in marathon for men and women from when women could legally compete (1970 onward). The decline in the women’s WR was dramatic in the first 15 yr until ~1985 as more women competed. Adapted from Figure 1B in Hunter et al. (47). B, The sex difference in the WR marathon times (Sex difference = $[\text{women} - \text{men}] / \text{men} \times 100$) declined markedly until the mid-1980s with a plateau of 10%–12% thereafter. The filled circles represent the new calculated sex difference when the women’s WR was broken and the unfilled circle (white) when the men’s world record was broken. C, WR times in the outdoor 100-m sprint for men and women from when women could legally compete (1922 onward). The trends for both events (A and C) show an initial rapid improvement in performance in the WR times by women relative to men, once women were permitted to compete. Data from World Athletics (worldathletics.org).

TABLE 1. Historical Events and Policy Influencing Participation and Equity in Women's Sport and Health Research.

Year	Historical Moments Influencing Participation and Equity in Women's Sport
1884	First women's tennis champion was crowned at Wimbledon, England.
1896	No women were permitted to compete in any Olympic event at the first Olympic Games in the modern era (Athens, Greece).
1900	Twenty-two females of 997 athletes competed the Summer Olympic Games (Paris, France).
1912	Women were allowed to compete in swimming for the first time at the Olympics (2 events).
1924	One women's sporting event (figure skating) was held at the First Winter Olympics (Chamonix, France).
1928	Women were first allowed to compete in Athletics (track and field) at the Olympics. Five events were contested, but the 800 m was dropped after 1928 because it was perceived as too stressful for women.
1937	Two-time Olympic track and field gold medalist Babe Didrikson played in a men's professional golf tournament.
1948	First woman (30-yr-old Fanny Blankers-Koen, Netherlands) won four gold medals in a single Olympic Games in track and field (London, UK), helping to make sports more acceptable for women.
1960	Women's Olympic 800-m track race was reinstated in the Olympics (Rome, Italy).
1967	First woman (Kathrine Switzer) ran the Boston marathon as an officially registered competitor (Boston, MA).
1972	Title IX legislation passed in the US congress legislated equal education opportunity for females and males including athletic scholarships and educational institutions such as universities.
1984	Women's Olympic marathon competed for the first time (Los Angeles, USA).
1999	Serena Williams' first Grand Slam (top 4) tennis championship propels her into the top money earners among all athletes.
2007	Equal pay for women and men in the Grand Slam professional tennis tournaments was achieved.
2021	Women's Olympic 1500-m swimming was competed for the first time (Tokyo, Japan).
2021	Similar numbers of women and men for the first time participated in the summer Olympics (Tokyo, Japan).
2022	Lia Thomas becomes the first transgender athlete to win an NCAA DI title, leading to significant discussion over eligibility requirements for women's sports.
2022	Equal pay for US women's and men's soccer was achieved.
Year	Policy and Declarations in Research
1990	NIH established the Office of Women's Health Research.
1993	NIH Revitalization Act mandating the inclusion of women in human studies (or the justification for lack of inclusion). The Advisory Committee on Research on Women's Health and Federal Advisory Committee Act committee was established to advise and make recommendations on priority issues affecting women's health and sex differences research.
2001	Institute of Medicine published a report titled "Exploring the Biological Contributions of Sex" (49).
2016	NIH enacted a policy of including sex as a biological variable for research involving humans, animals, and cells (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-102.html).

sex differences (44) (Fig. 4). Both past and present research studies of athletic performance, acute exercise, and exercise training involve more men than women, or a lack of distinction between the sexes (10,59,60). Many studies are underpowered to understand the sex differences or simply do not include women (8,59–61,63). Consequently, because of the historical predominance of research and athletic participation of men compared with women, less is known about the physiology of women athletes, limits in their athletic ability, and the acute and adaptive response of women to exercise and training relative to men. This is also true, in general, within biomedical research of human, animal, and basic cell studies (14,49,64–66). Key events and national funding policies outlined in Table 1 have promoted the involvement of females in biomedical research in the United States, and ultimately increased awareness of the sex differences in athletic performance and other important areas of the health sciences.

SEX DIFFERENCES IN ATHLETIC PERFORMANCE

Sex differences in athletic performance that involve strength, power, and/or endurance are sizable and determined by biological differences between males and females. Adult men on average are stronger, more powerful, and faster over short and long distances than women of similar age and training status. The sex differences emerge with the onset of puberty, coinciding with the increase in endogenous sex hormones, in particular testosterone in males (9,67–69) as discussed in the Biological Mechanisms for Sex Differences in Athletic Performance section. The sex difference in the world records and best performances of many athletic events that rely on endurance and muscular power ranges from ~10% to 30% (Table 2 and Figure 5)

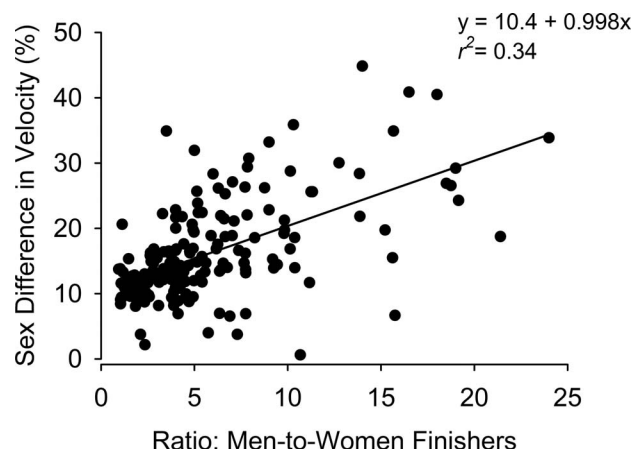


Figure 4—Sex differences in New York City marathon performance and the ratio of the number of male to female finishers over 31 yr. Shown is the association between the ratio of the number of men-to-women finishers within an age group in the New York City marathon between 1981 and 2010. Data points represent the ratio of men-to-women finishers for a 10-yr age group (between 20 and 79 yr) for each year (between 1980 and 2010) on the x axis plotted against the sex difference in running velocity for the first-placed finisher (y axis). A ratio larger than 1 on the x axis indicates more men than women runners competed within an age group. For example, a ratio of 6 indicates that for every female runner in a 10-yr age group, there were six male runners. There was a positive association for the first-place finishers between the ratio of men-to-women and the sex difference in velocity ($r=0.58$, $r^2=0.34$, $P<0.001$). Linear regression showed the best prediction with $y=10.4+0.998x$ ($n=184$ pairs). A ratio of equal numbers of men and women in an age group (ratio of 1) predicts a sex difference of 11.4% in performance, which is similar to the sex differences in performance because of physiological and anatomical sex differences. When all the first-placed runners are averaged, however, the sex difference was 16.9%. These data indicate that most of variability in the sex difference in performance among the first-placed runners that was not due to the physiological and anatomical sex differences (11.4%, which is ~66% of the variability) was explained by the greater number of male runners relative to females in an age group (34%). Figure adapted and reprinted with permission from Hunter and Stevens (44).

TABLE 2. Sex Differences in the World Records and Best Performances of Various Athletic Events (January 2023).

Event	Men	Women	Sex Difference (%)
Running (outdoor)			
100m (s)	9.58	10.49	9.5
200m (s)	19.19	21.34	11.2
400m (s)	43.03	47.60	10.6
800m (min:s)	1:40.91	1:53.28	12.3
1500m (min:s)	3:26.00	3:50.07	11.7
5000m (min:s)	12:35.36	14:06.62	12.1
10,000m (min:s)	26:11.00	29:01.03	10.8
Marathon (h:min:s)	2:01:09	2:14:04	10.7
Jumping (outdoor)			
High jump (m)	2.45	2.09	14.7
Long jump (m)	8.95	7.52	16.0
Triple jump (m)	18.29	15.67	14.3
Pole vault (m)	6.21	5.06	18.5
Swimming freestyle			
50m (s)	20.91	23.67	13.2
100m (s)	46.91	51.71	10.2
200m (min:s)	1:42:00	1:52:98	10.8
400m (min:s)	3:40.07	3:56.40	7.4
800m (min:s)	7:32.12	8:04.79	7.2
1500m (min:s)	14:31.02	15:20.48	5.7
10,000m open water ^a (h:min:s)	1:50:56.80	2:02:29.20	10.4
Cycling (track)			
Flying 200-m time trial (s)	9.10	10.15	11.6
Flying 500-m time trial (s)	24.76	28.97	17.0
1-h record (km)	56.79	49.21	13.3
Speed skating			
500m (s)	33.61	36.36	8.2
1000m (min:s)	1:05.69	1:11.61	9.0
1500m (min:s)	1:40.17	1:49.83	9.6
3000m (min:s)	3:37.28	3:52.02	6.8
5000m (min:s)	6:01.56	6:39.02	10.4
10,000m (min:s)	12:30.74	13:48.33	10.3
Weightlifting			
55 kg category (kg): total ^b	294	227	22.8
Heaviest category (kg): Total ^b (men, +109kg; women, +87kg)	492	335	31.9
Archery (recurve)			
1440 round (points)	1391	1405	-1.0
70m/72 arrows (points)	702	692	1.4

^a World Championships; Budapest, Hungary; June 29, 2022.

^b Total weightlifting is the world record for the total kilograms lifted in the snatch and the clean and jerk events.

Data updated (January 2023) from several websites: <https://www.iaaf.org/records/by-category/world-records>; <http://www.fina.org/fina-rankings/filter/overall-rankings>; <https://www.fina.org/open-water/results?year=2022&month=1&disciplines=OW>; https://en.wikipedia.org/wiki/List_of_world_records_in_track_cycling; <https://speedskatingresults.com/index.php?p=9>; <https://iifw.sport/results/world-records/>; <https://worldarchery.sport/world-records?category=Recurve%20Men&discipline=Outdoor%20Archery>.

(9,67,68,70–72). The largest sex differences are apparent for sports and events relying more on muscular power such as in weightlifting, jumping events, and short distance swimming. In such events, men outperform women, even when body weight is matched between the sexes (e.g., 55-kg weight class comparison in weightlifting; Table 2). In swimming, for example, the sex difference gap occurs in the shortest events (e.g., 50m) and the smallest gap for the longer events (73) (Table 2). These differences primarily represent the physical and anatomical abilities and limitations of males and females, largely independent of motivation, and access/opportunity to training at the elite level.

In ultraendurance events that are performed at relatively low percentages of oxygen utilization, the sex difference in running performance is still apparent for most events and in the range of the sex difference in the marathon (52,74–76). Although women may seem to have fewer physiological disadvantages

than they typically do in running events (fatigue-resistant muscles (10), higher reliance on lipid metabolism (77), and more even pacing strategies than men (78)), these factors do not overcome the physiological advantages of men. Other factors, such as nutrition, equipment, race conditions, and environment, can dominate performance similarly for the sexes, and overall men outperform women at the elite level in running events (52,74,75). Only in ultradistance open swimming events women have outperformed men when water temperatures are cold (<20°C) and greater than 30km in distance (79). In long-distance open water swimming events less than 30km, the best men typically outperform the best women. For example, the first-placed man was 10.4% faster than the first-placed woman in the open water 10-km event at the 2022 World Championship in Budapest, Hungary (Table 2).

Sports relying primarily on technical skill, however, such as archery and shooting, have minimal sex differences in performance (80) (Table 2). Thus, in competitive sports and athletic events where skill is the predominant performance factor, differences between men and women are small, whereas in other sports where aerobic or anaerobic power are predominant factors (even in skillful events such as pole vault), the differences between men and women are significant. Figure 4 shows the advantage of men (relative to the performance of women) among the top 100 men and women athletes in each of the Track and Field events.

This section describes the primary physiological predictors of endurance and power-based athletic performance in both males and females, and highlights some of the known sex differences in these predictors that are central to many athletic events and sports.

Primary Physiological Predictors of Athletic Performance in Cisgender Men and Women

Athletic performance in both men and women is primarily due to several major attributes, and the dominance of each attribute will vary with the demands of the athletic discipline/event. For example, endurance performance such as distance running (distances >3000m) is predicted by (i) maximal oxygen uptake ($\dot{V}O_{2max}$), (ii) the maximal running intensity (or percentage of $\dot{V}O_{2max}$) that can be sustained during long time periods and is related to the critical velocity, and (iii) running economy (a surrogate for efficiency because calculations of true mechanical efficiency during running are difficult to achieve) (43,81). Of these three primary determinants, faster distance running speeds of men compared with women are primarily explained by a larger $\dot{V}O_{2max}$ of males with minimal differences in the relative maximal sustainable running intensity or running economy. Although, even in long-distance races, anaerobic capacity can be decisive for victory in the event of a final acceleration. In contrast, sports such as weightlifting and jumping performance are determined primarily by lean body mass and muscular power (82,83) with large sex differences in both (Table 2). Many sports, however, require a variety of attributes with those that are potentially the

% MEN ADVANTAGE FOR THE TOP 100 ATHLETES IN HISTORY (%)

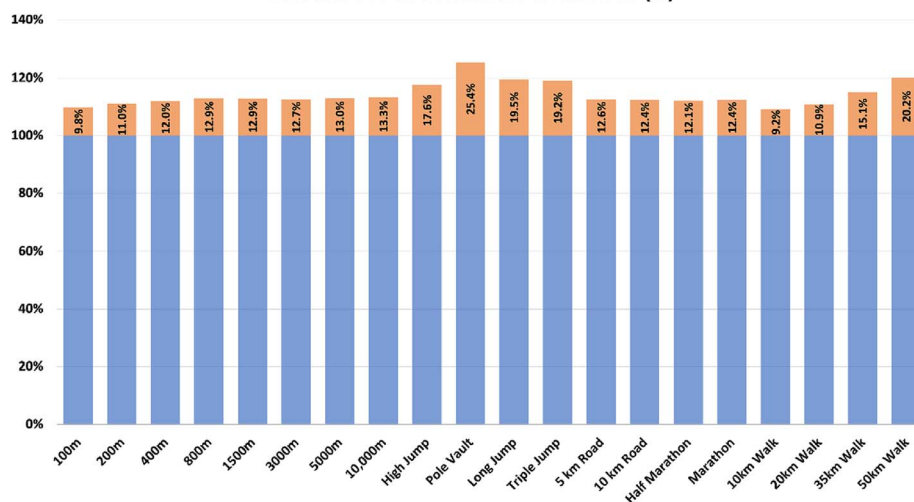


Figure 5—Sex differences in performance between the top 100 men and top 100 women in track and field outdoor events. Shown is the mean advantage men have relative to women in 20 track and field events. Data from World Athletics (worldathletics.org).

most influential on sex differences in athletic performance summarized hereinafter.

Muscular and Anaerobic Power. Males have larger, stronger, faster, and more powerful skeletal muscles than females (84–88). Muscle power is the product of strength (force or torque) and contraction velocity, both of which are larger in males than females (84). Males produce greater maximal limb torque because their muscles have a larger cross-sectional area (and thus force) and they have longer limbs than females (89,90). Muscle force is also dependent on the nervous system and its ability to activate the available skeletal muscle via alpha motor neurons (maximality of activation) and the speed of neural activation. The ability and motivation to optimally activate the available motor neurons and the muscle fibers they innervate (the motor unit) during a maximal strength contraction while rested (not fatigued) do not differ between males and females (84,85,91–98). Thus, the sex differences in muscular strength and power are primarily due to larger skeletal muscle mass and faster contracting skeletal muscle of males relative to females (84,86,99).

The larger skeletal muscle of males is primarily due to the muscle fibers that have a bigger cross-sectional area (84,100–105), particularly type II fibers (expressing type II myosin heavy chain (MHC) isoforms) (101,104–109). It is important to note that the specific force and power (force or power normalized to the fiber size) of both MHC type I and type II fibers are similar between males and females (110,111). MHC type II fibers, however, have up to twice the maximal shortening velocity of MHC type I fibers in both sexes (108,112,113). Because, in general, recreationally active males have larger type II fibers than females, the whole muscle of males have a larger proportional MHC type II area, and females have a larger proportional area with type I fibers than males (e.g., (101, 104,107, 114,115); Fig. 6). Contractile speed of skeletal muscle is dependent on the muscle fiber type compositional area. Thus,

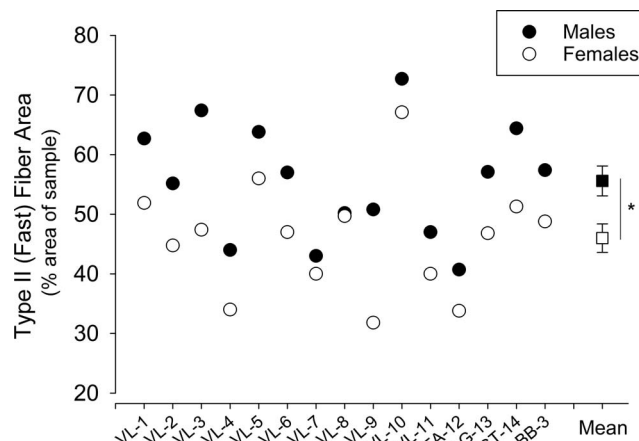


Figure 6—Type II (fast) fiber area (% area of sample) of the cross section of the sample) of skeletal muscle in males and females. The cross sections of muscle were histochemically analyzed for myosin ATPase activity from muscle biopsy samples of vastus lateralis (VL; quadriceps), tibialis anterior (TA), lateral gastrocnemius (LG), semitendinosus (ST; hamstring), and biceps brachii (BB) in males and females who were sampled in the same study. All studies included biopsies of young adults with a mean age between 21 and 26yr for 12 of the 14 studies and 49yr (<57 yr) for one study (102) and 35yr <50yr for another (104). The proportional area (% area of sample) shown for the males and females in each study was calculated from the percentage number of fibers within a sample and the mean cross-sectional area of each fiber type within the sample. Fourteen studies identified on the x axis are coded by the muscle that was biopsied (VL, TA, LG, ST, or BB) and a number that corresponds to the study as follows: VL-1 (114), VL-2 (116), VL-3 and BB-3 (84), VL-4 (117), VL-5 (101), VL-6 (118), VL-7 (119), VL-8 (102), VL-9 (107), VL-10 (115), VL-11 (120), TA-12 (106), LG-13 (121), and ST-14 (104). The mean ($\pm$ SEM) proportional area of type II fibers of all the muscles from the 14 studies is plotted on the right side of the figure. Males had greater type II (fast) fiber area (%) than females for the studies pooled ($P<0.05$). References in this figure include the following: Toft et al. (102), Fournier et al. (104), Simoneau et al. (114), Simoneau Bouchard (116), Miller et al. (84), Esbjornsson-Liljedahl et al. (117), Staron et al. (101), Carter et al. (118), Esbjornsson-Liljedahl Bodin (119), Roepstorff et al. (107), Maher et al. (115), Esbjornsson et al. (120), Porter et al. (106), Larsson et al. (121).

this sex difference in fiber type proportional area is consistent with faster contracting whole muscle of males than females, and conversely slower contractile properties, such as slower rates of relaxation, and a more fatigue-resistant muscle in females when contracting at the same relative intensity as males (91,103,122,123).

These aforementioned studies have been performed predominantly on sedentary or recreationally active males and females but few studies on well-trained or elite athletes (124,125). Fiber type compositions are congruent with the requirements of the sport/event of the athlete such that endurance runners possess a larger relative percentage and proportional muscle volume of fatigue-resistant type I fibers than controls, whereas sprinters and power athletes have a predominance of type II fibers (125,126). Although males possess larger fiber types than similarly trained or sedentary females, a key question is whether the sex differences in proportional area of fiber types are also observed among elite athletes within a given sport. Inspection of the limited data suggests that even among elite athletes, males persist in possessing a larger area of type II fibers compared with females, including endurance and power athletes and body builders (100, 124,125). Consistent with these observations, satellite cells, which are involved in muscle fiber repair and also support hypertrophy of fibers, are more numerous in males than females, but only for type II fibers; satellite cell content is similar between the sexes for type I fibers (105). Sex differences in fiber types and their adaptations to training in elite athletes are an area of opportunity for further studies.

The muscle mass and limb power of males can be twice that of females across many age groups (84,86,87,93,100,108) with larger sex differences in muscle mass and strength in the upper body than the lower body (84,86,127–130). The strength of arm muscles in females range from 50% to 60% that of males such as the elbow flexor muscles, and ~60% to 80% in the lower limb muscles such as the knee extensor and ankle dorsiflexor muscles of similarly active adults (84,128,129,131,132). In healthy males and females, maximal isometric muscle force is primarily dependent on the cross-sectional area of the skeletal muscle (133). Thus, males are stronger than females because they have a larger skeletal muscle mass such that there are minimal sex differences in the force/cross-sectional area of muscle (84,133–136).

Sex differences in the power of limb muscles are even larger than the differences in maximal isometric strength (93,128) possibly because maximal contraction velocity is typically slower in females for a given load (92). Peak power during cycling and knee extensor single limb exercise of females, for example, was 63% to 67% that of males (93,137,138). This sex difference in strength and limb power persists into very old age (92,93). Thus, the sex difference in sports that require power can be substantial, particularly upper body power, such as throwing and sprint swimming (Table 2).

Similarly, *anaerobic power* (work per unit time), which is developed and assessed during maximal, short-term physical effort during exercise such as cycling, running, skiing, jump-

ing, arm-cranking, and swimming (139,140), is greater in men compared with women (119,141–148). Anaerobic power reflects energy-output capacity of intramuscular high-energy phosphates (ATP and PCr) and/or anaerobic glycolysis and is highly associated with body size and the volume of muscle utilized (143,144). Maximal anaerobic power of men during lower-limb maximal exercise is ~15%–50% greater than women, depending on the major muscle groups assessed with the largest sex differences in the upper body (119,140–148). Most of the sex difference in anaerobic power is accounted for by muscle mass, although some difference remains, particularly in tests involving arm muscles (130,143,144,149). Limb size and the glycolytic capacity of skeletal muscle are larger in men than women (146,150–152) and likely account for most of these differences in anaerobic power between men and women when muscle mass is normalized (144,149). Thus, during short bursts of exercise that require muscular and anaerobic power, men outperform women, largely because they have bigger bodies and limbs, and larger and faster muscles than women.

Body Composition and Anthropometrics. Males are taller and heavier than females and also have also greater lean body mass (muscle and bone) and less percentage of fat mass (90,127,153–159). Adult males (>20yr) are 8% taller than females with longer upper and lower limbs (90,160), allowing them to produce greater torque of the limbs, for example, when throwing, jumping, and swimming. They are also ~17%–18% heavier than adult females (160) because they have greater lean body mass despite less body fat. Female athletes typically have ~5%–10% more body fat than similarly trained males and ~85% the lean body mass as male athletes (154).

Larger muscle mass is directly associated with greater muscular strength and power; hence, males are stronger and more powerful than females. Coupled with lower body fat percentage and larger and stronger muscles (101), males have a larger power (anaerobic or aerobic) to body mass ratio than females. Lower body fat is of considerable advantage for males during weight-bearing exercises such as sustained running (161) and jumping (162). Greater body fat percentage of females and a lower power to lean mass ratio can account for up to 70% of the sex differences in weight-bearing exercises involving vertical and horizontal jumping (162).

Aerobic Power. Aerobic power is a primary predictor of athletic endurance performance, for example, during distance running and swimming, road cycling, and cross-country skiing (81,163). Superior aerobic performance is associated with a high $\text{VO}_{2\text{max}}$. $\text{VO}_{2\text{max}}$ is the product of the maximal blood volume transported through the heart in a given time (maximal cardiac output, $\text{L}\cdot\text{min}^{-1} = \text{heart rate} \times \text{stroke volume}$) and the oxygen utilized in the peripheral tissues (mostly skeletal muscle arteriovenous oxygen difference: $a-v \text{ O}_2 \text{ diff}$) (Fick equation: (163)). Therefore, $\text{VO}_{2\text{max}}$ depends on total blood volume, cardiac size/mass/compliance and stroke volume, and maximal heart rate and in the periphery on the skeletal muscle blood flow, capillary density, and mitochondrial content (81,163).

Males, on average, have a higher $\dot{V}O_{2\max}$ than females in trained and untrained adults (161,164,165). In absolute capacity ($L \cdot \min^{-1}$), female athletes are in the range of 60%–70% of similarly trained males (161), and when normalized to body mass ~80%–85% that of males, with smallest differences in long distance runners (161,166). Elite male runners usually have a $\dot{V}O_{2\max}$ of ~70–85 $mL \cdot kg^{-1} \cdot \min^{-1}$, and elite female runners and cyclists ~60–75 $mL \cdot kg^{-1} \cdot \min^{-1}$ (81,166–172) representing ~10%–14% difference between the sexes when normalized to body mass. Males, on average, have a larger heart size and thus greater stroke volume, greater blood hemoglobin concentration and mass, larger muscle mass, less percentage body fat to carry, and consequently a higher $\dot{V}O_{2\max}$ than females (173–176). There are minimal sex differences in maximal heart rates between equally trained and untrained individuals (164,167,172,174,175,177–179). Furthermore, even when normalized to fat-free mass, sex differences in $\dot{V}O_{2\max}$ remain in the range of ~5%–10% (70,166,180) presumably due to the larger hearts and greater hemoglobin mass in males than females, which is strongly correlated with $\dot{V}O_{2\max}$ (181). $\dot{V}O_{2\max}$ sets the upper limit of aerobic metabolism that can be achieved by an individual. Thus, even when normalized to body weight, males utilize more oxygen at greater rates and thus move large muscles groups faster than females.

Although the sex differences in $\dot{V}O_{2\max}$ are largely due to males possessing larger heart size and hemoglobin mass than females, the contribution to this sex difference of the peripheral components in the muscle, such as capillary density, is not clear. For example, capillary density was greater in the tibialis anterior of males compared with females but only for type II fibers (106). In contrast, there was no sex difference in capillary density in the vastus lateralis (both young and old adults), although the numbers of females relative to males in the study were small and possibly underpowered (109). Furthermore, the capillary density from vastus lateralis muscle biopsies was greater in females than males because the fibers were larger in males with no difference between the sexes in the number of fibers contacting each fiber (107). Thus, the studies are few and contrasting and do not provide a clear picture of a large sex difference in the ability of the muscle to utilize oxygen. Despite the need for clarity, the most pronounced sex differences in $\dot{V}O_{2\max}$ are likely due to the larger heart size and hemoglobin mass of males.

Fuel Metabolism and Exercise Performance. Energy substrate stores (i.e., intramuscular triglycerides, free fatty acids, glycogen, plasma glucose, protein, ATP+PCr) play a key role in the regulation of fuel metabolism during exercise and are a determining factor of exercise performance. The relative contribution of these fuel sources is determined primarily by the intensity and duration of exercise, but it is also affected by diet, environmental conditions, training status, and participant sex. Short-duration, high-intensity anaerobic exercise such as sprinting will rely primarily on stored ATP and glucose for energy (182). For longer-duration aerobic exercise, carbohydrate and fat sources are heavily relied upon for energy (183–185). At low-intensity exercise (<40% $\dot{V}O_{2\max}$)

fat is the predominant fuel source, but as exercise intensity increases, energy from fat sources decreases and increases from carbohydrate sources (183). Trained individuals utilize substrates more efficiently than untrained individuals, with untrained relying more on carbohydrates at moderate and higher intensities than trained (186). At the same relative intensities of exercise however, there are sex differences in whole-body substrate utilization during endurance exercise: females oxidize more fat and fewer carbohydrates and amino acids than males during similar-intensity endurance exercise (77,179,187–189) originating in part from sex differences within the muscle typology (190). Males have greater glycolytic capacity than females (146,150–152) who demonstrate greater oxidative capacity of whole muscle than males (146,191). Males also exhibit an earlier dependency on carbohydrate during exercise (i.e., lower crossover threshold) (179) and use proportionally more protein than females during prolonged exercise (192). This sex difference in whole muscle energy metabolism is related to differences in the proportional area of type II (and I) fibers in the skeletal muscle affecting both aerobic and anaerobic power (Fig. 6). These sex differences in fuel metabolism may also explain why subelite and recreational male athletes slow more than females during long-distance events such as the marathon (78).

Among highly trained and elite athletes, these factors are unlikely to result in performance advantages for females. The fat oxidation advantage in females largely exists at low work rates (i.e., 41%–61% of $\dot{V}O_{2\text{peak}}$) (179). However, many elite athletic events are likely performed at a substantially higher $\dot{V}O_{2\text{peak}}$ ($\geq 85\%$ $\dot{V}O_{2\max}$) where fuel utilization is largely carbohydrates and thus unlikely to favorably affect elite athletic performance in females more than males. Indeed, maximal rates of fat oxidation in recreationally active females were ~7–8 $kcal \cdot \min^{-1}$, whereas the maximal rates of carbohydrate oxidation at 85% of $\dot{V}O_{2\text{peak}}$ were ~25 $kcal \cdot \min^{-1}$ (179). Even in ultramarathon events conducted at lower levels of $\dot{V}O_{2\text{peak}}$ and where females may seem to have the fat oxidation advantage, men outperform women at the elite level (52,74,75).

The sustained athletic performances required in distance running, cycling, and swimming can be performed at the highest sustainable oxidative metabolic rate and are related to the “critical velocity” and the “lactate threshold” (81, 193,194). Critical velocity or power (sometimes referred to as threshold) represents the highest intensity of exercise that $\dot{V}O_2$, blood lactate, and intramuscular metabolites such as H^+ , PCr, and P_i can be stabilized for a prolonged period (195). Although absolute $\dot{V}O_{2\max}$ and the highest sustainable performance velocities are larger in males than females, there is minimal sex difference in the relative critical velocity between highly trained male and female distance runners who sustain running for several hours at ~85%–90% $\dot{V}O_{2\max}$ (196–199). Similarly, the absolute critical threshold of running speed or cycling power in nonelite athletes is typically higher for males compared with females; however, the hyperbolic relationship between the relative limb power and task duration (195,200,201) is similar, suggesting that men and women have similar

rate-limiting muscular mechanisms at the same relative intensity of dynamic exercise above and below the critical threshold during exercise (137).

There are two instances, however, where women seem to have the advantage in performance compared with men, and which are likely related to the sex differences in fiber types and a greater reliance on oxidative metabolism in women:

1. Isometric exercise and slow dynamic contractions: For isometric exercise of a single limb (sustained and intermittent contractions), females have a higher relatively critical threshold of exercise intensity than males (202). These findings are consistent with the large number of studies that show greater fatigue resistance of females compared with males during isometric fatiguing contractions in upper and lower limb muscles for intensities normalized to maximal strength (10–12,123,132,203) and some slow-to-moderate velocity dynamic contractions (123,204) in humans and also in animal models (103). These sex differences do not occur during fast dynamic contractions (93,128). The fatigue resistance of females reflects differences in proportional type I fiber area (percentage area of the muscle) that is larger in some limb muscles of females compared with males (10,103). Thus, during select exercises that involve isometric exercise (e.g., wall sit exercises), women often outperform men. The mechanisms for the sex difference are dependent on the details of the isometric and dynamic task as reviewed elsewhere (10,205).
2. Short-term recovery from dynamic exercise. Females seem to recover from fatiguing dynamic and isometric exercise more quickly than males (85) because of faster recovery of contractile function related to anaerobic fuel metabolism during dynamic tasks. Females exhibit less muscle fatigue during or after single bouts of exercise (85) and after multiple-sprint exercise (190), including cycling (206) and running (207). Again, the sex differences in sprint exercise are likely due to faster recovery of muscle metabolism (85,190) and also related to maximal power or torque (206). However, there were no sex differences in the number of repetitions until failure of biceps curls or leg extension at 4–48 h after resistance exercise in a small study of resistance-trained men and women (208). Most of these studies cited previously are conducted on recreationally active males and females, with less known about recovery in highly trained and elite male and female athletes. Thus, recovery of performance may extend for less than several hours but presents as an area of opportunity for further study in well-trained and elite male and female athletes.

Economy of Motion. More efficient movement patterns during athletic performance result in less metabolic cost for a given performance velocity and contribute to superior athletic performance. Running or cycling economy is quantified by determining the oxygen uptake at a set speed (81). Running economy, and to a lesser extent cycling economy, varies considerably

between individuals (30%–40% in running and 20%–30% cycling) (81,209,210) and can improve with training for some athletes (168,211). Regardless of individual differences, running economy does not differ markedly between trained male and female runners (166,197,199,212,213) and thus does not explain the sex differences in performance across elite runners. In recreational runners, however, females had a slightly lower gross oxygen cost of running at submaximal velocities (214). In swimming, females exhibit greater economy of movement than males (215,216). The higher percentage body fat of females and lower resistance due to smaller surface areas may be beneficial relative to males, allowing less drag and less resistance in the water and a lower oxygen consumption at a given speed (173,215–217). The greater economy of swimming for females compared with males may in part explain the narrowing of the sex difference in swim performance in the long-distance events in the pool (>400m) (Table 2) and ultra-distance open water swimming (79).

BIOLOGICAL MECHANISMS FOR SEX DIFFERENCES IN ATHLETIC PERFORMANCE

Many of the sex differences of the major attributes that determine performance are dictated by the strong effect of endogenous sex hormones during and after growth and development.

Direct Effects of Endogenous Sex Hormones

DEVELOPMENT *Fetal Life.* Early in the first trimester, reproductive structures (including gonads, internal reproductive structures, and external genitalia) are undifferentiated and identical between XX and XY fetuses (218,219). Expression genes on autosomes and sex chromosomes (with *SRY* being a key gene in testicular development), along with certain hormonal actions, cause sex differentiation in either a male or female direction, a process that is complete by about 13 wk of gestation (218,219). DSD are congenital conditions in which the development of chromosomal, gonadal, or phenotypic sex falls outside the typical male/female binary (220).

Minipuberty and Childhood. Minipuberty is characterized as a transitory surge of gonadotropins (peptide sex hormones that stimulate or act on the gonads, testes or ovaries) and sex steroid hormones during infancy in both boys and girls (221). In infant boys, serum luteinizing hormone (LH) rises at 1 wk of age to the pubertal range, followed by an increase in serum testosterone, which peaks at 1–3 months and then declines to prepubertal ranges by 6–9 months of age. Minipuberty in girls may last several months longer than boys, during which time they experience increases in gonadotropins and estradiol (E2) (221). During the minipuberty, growth velocity is greater in boys than girls, with the biggest difference at 1 month of age, when peak minipuberty and the rise in testosterone in boys occurs (222). Studies evaluating the influence of minipuberty on growth are limited and conflicting (223). There are, however, associations between sex steroids and body composition in this time period. The impact of testosterone exposure

during fetal development and early infancy on future growth, and development including muscle mass and other factors remains an opportunity for further study.

On average, newborn boys weigh more and have more fat-free mass than girls (224). During childhood, accumulation of fat-free mass is similar between the sexes; however, in mid-childhood, girls accumulate more fat mass than boys, a difference that becomes more pronounced during puberty (224). In general, there are no clear sex differences in athletic performance and fitness assessments before the onset of puberty (67,68,225–230), although some studies (detailed hereinafter) indicate small differences with boys outperforming girls. Numerous studies, however, demonstrate that overall girls are less active and have lower sports participation than boys throughout childhood (229,231–234). The sex differences in activity levels are possibly due to social factors such as positive reinforcement of physical activity that differ between girls and boys (234,235). These differences in activity may also account for small sex differences (~3%–5%) in athletic performance in childhood before 10yr observed in some studies (236) because lower activity levels in children are associated with lower metrics of fitness (229). Accordingly, cardiorespiratory fitness assessments increased in girls but not in boys in response to school-based fitness interventions (237). Other studies show that boys outperformed girls for tasks such as handgrip strength, modified pull ups (226), 30-m dash and long jump (238), although there was no sex difference observed in knee extensor strength and planks (226). Comparison of the top 10 boys and girls USA running track records (2019–2021) in 100, 200, 400, and 800m also show that boys were ~4%–5% faster than girls in the age categories of 7–8, 9–10, and 11–12yr and rose to >8% by 13–14yr (239). At the elite level in swimming where participation and motivation are typically similar in boys and girls, boys do not outperform girls until puberty (>12yr) (68). Key ongoing questions include 1) whether sex differences in physical activity and social influences drive some of the small sex differences in athletic performance before puberty, and 2) whether there is an influence of the testosterone surges during infancy in males (minipuberty) on their development, growth, and athletic performance over the life span (including puberty and into adulthood) compared with females.

Puberty. From the minipuberty period until puberty, testosterone concentrations are similar between the sexes, and then diverge with up to 30-fold increases in boys by 18yr (Fig. 7). The onset of puberty typically occurs around age 10yr for girls (range, 8–13yr) and at age 11.5yr in boys (range, 9–14yr) in the United States. Pubertal development before age 7yr in White girls and before age 6yr in Black girls is considered precocious or early (240); more research is needed to understand contributions of minority stress and environmental factors on pubertal timing (241). Puberty is characterized by rising sex steroid concentrations, reproductive and psychological maturation, development of secondary sex characteristics, a growth spurt (peak height velocity age 11.5yr in girls and 13.5yr in boys), changes in body composition, and a strength spurt in males (242). Sex differences in body composition emerge in early-to-mid puberty, with females having more fat mass and males more fat-free mass (224). Puberty development requires coordination of various hormones including growth hormone (GH), insulin-like GH, gonadotropins, in addition to sex steroids (224).

The onset of puberty aligns with the large sex divergence in athletic performance, differences not typically seen, or that are minimal before puberty (67,68,225–228). Growing sex differences in running, jumping, swimming, and hand-grip strength emerge at age 12–13yr and parallel the increase in serum testosterone in boys in puberty (67,69). This sex difference is clearly observed in elite youth swimming (69) (Fig. 8) where participation is high for both sexes. The sex difference in performance is highly correlated with the increase in total testosterone in boys (explaining 98% of the variability in the sex difference in swim performance between 11 and 17 years), with the sex difference increasing at 11–12yr of age (69) (Fig. 9). Other sports relying on strength, power, or endurance show similar divergence performance between boys and girls at the onset of puberty (67,227,228,243). Accordingly, dynamic balance, which is minimally reliant on muscle power or endurance, does not differ between boys and girls after puberty (227). Thus, it is clear that the divergence in athletic performance that involves strength, power, and endurance is tightly aligned with increased testosterone in males during puberty, particularly in elite swimmers. Key ongoing opportunities for research involve determining the association between

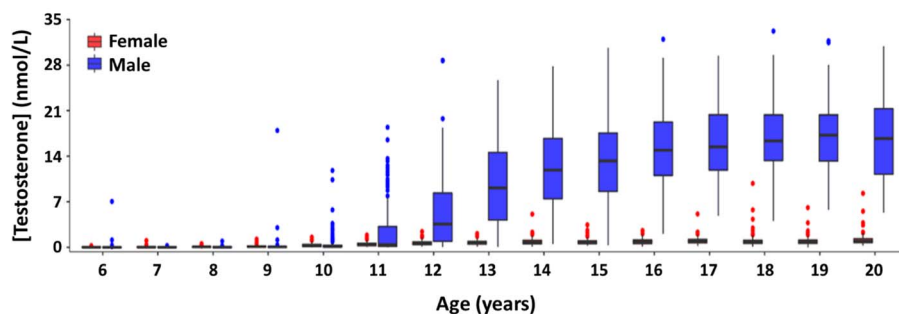


Figure 7—Total testosterone concentrations of the US population aged 6 to 20yr. The horizontal line in the middle of each box indicates the median; top and bottom borders, 75th and 25th percentiles; whiskers above and below the box, 90th and 10th percentiles; and circles beyond the whiskers, outliers beyond the 90th or 10th percentiles. Adapted with permission from Seneff et al. (69).

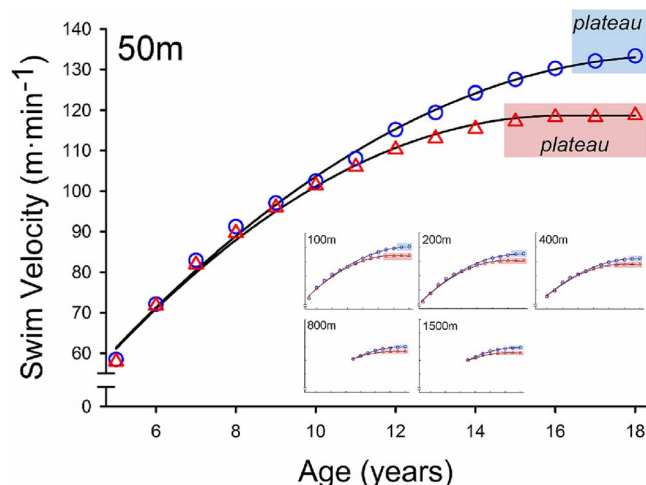


Figure 8—Elite youth swimming performance of boys and girls across age groups (5–18yr) in the United States. Mean swimming velocity from athletes aged 5 to 18yr of the top 100 fastest US boys (blue circles) and girls (red triangles) for the 50-, 100-, 200-, 400-, 800-, and 1500-m freestyle swimming distances. The performance of girls and boys is similar until age 10–11yr, and noticeably diverges at 12yr and older, with boys outperforming girls thereafter. Girls plateau in performance at a younger age (16–17yr) than boys who continue to improve until at least 17–18yr. Reprinted from Senefeld et al. (68).

the sex differences in testosterone concentration during puberty and the sex differences of both youth and into adulthood in athletic performance that rely on varying contributions of muscle power and endurance.

Adulthood. Testosterone. The primary cause for the large sex difference in athletic performance is exposure to high levels of endogenous testosterone in males at the onset of puberty (9,69). Testosterone is synthesized from cholesterol in the gonads and other tissues such as the adrenal glands, prostate, and liver (244). Testosterone mediates its effect by binding to the androgen receptor and the hormone-receptor complex serves as a transcription factor to modulate gene expression. Circulating testosterone concentrations increase in males because the testes produce ~20- to 30-fold more testosterone than before puberty with circulating testosterone more than 15-fold that of females at any age in adulthood (9,67,69) (Fig. 7). The distribution of testosterone between males and females is non-overlapping and bimodal (9) as shown in Figures 2 and 7 (69). In males, both nonathletes and athletes, endogenous testosterone levels produce potent anabolic effects on muscle mass and bone mass, circulating hemoglobin mass, and ultimately power and endurance-based sports performance (9,245,246) (Table 3). Advantages associated with higher testosterone provide the justification for sex-segregated sports (4,9).

Testosterone can be measured in its free or bound form (bound to proteins including sex hormone-binding globulin and others). There are several methods for measuring serum testosterone, many with significant pitfalls, leading the Endocrine Society to recommend that measurement by mass spectrometry is preferred (247). Measurements based on liquid chromatography–tandem mass spectrometry, the gold standard for steroid hormone determination, indicate that the normal

female range of circulating testosterone is 0.1–1.8nmol·L⁻¹ and that in men is 7.7–29.4nmol·L⁻¹ (9). Measured serum testosterone concentration can be impacted by aging, circadian rhythm, geography, genetics, lifestyles, comorbidities, and daily variability (247,248).

In females, much less is known about the role of their normal endogenous androgen concentrations and physical performance. One reason for this could be the need to take into consideration the hormonal variations of the menstrual cycle and use of hormonal contraception. However, national- and international-level female sprinters and team sports athletes showed superior performances that correlated with serum levels of testosterone (249). Androgen precursors have been shown to be associated with enhanced performance in physical fitness tests of female Olympic athletes (250). Furthermore, in a large study involving more than 1000 female track and field athletes, women with the highest tertile of testosterone performed significantly better than those with the lowest tertile in specific events (251,252). Thus, mild variations of endogenous testosterone within the normal female range may be advantageous for athletic performance. Important remaining questions include understanding the sensitivity of the varying ranges of endogenous testosterone concentrations within females, and effects on different aspects of physical performance and the body systems most influenced.

Estrogen. There are four major estrogens: estrone (E1), 17-β-estradiol (E2), estriol (E3), and estetrol (E4), which differ from each other in the number of hydroxyl groups or ketones, mode

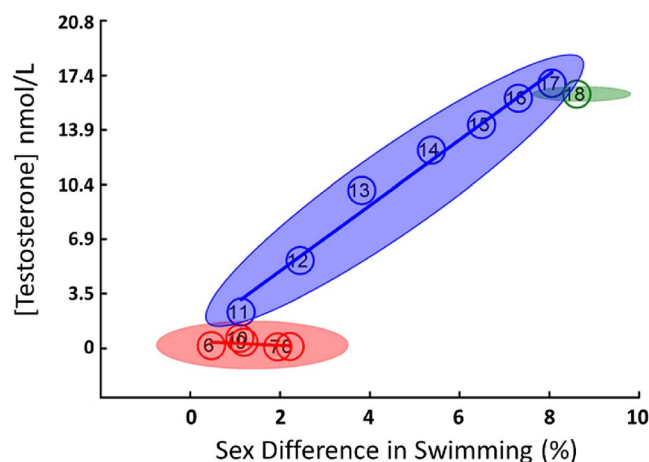


Figure 9—Correlation of boy's serum testosterone and sex differences in swimming performance of the top 100 US elite youth swimmers aged between 5 and 18yr. The mean circulating testosterone concentrations from the National Health and Nutrition Examination Survey database were, linearly correlated with the mean sex difference in swimming performance (%) during the years of rapidly increasing testosterone levels for boys (11–17yr; $P < 0.001$, $r = 0.99$, blue shading), but not during the years of low testosterone for boys (6–10yr; $P = 0.50$, red shading). Each circle represents the mean sex difference in swimming for each age group pooled for all race distances (50, 100, 200, 400, 800, and 1500m freestyle) and top 100 places (x axis) and mean circulating testosterone level for boys (y axis), with the age group denoted using corresponding Arabic numeral within each circle. The colored ellipses represent the standard error of three separate groupings for the correlation analysis, low-testosterone group (6–10yr, red), increasing testosterone group (11–17yr, blue), and plateaued testosterone group (18yr, green). Adapted from Senefeld et al. (68).

TABLE 3. Actions of Sex Steroid Hormones.

Actions of Sex Steroids		
Hormone	Synthesis, Action	Effect on Growth and Development
Estrogens		
Estrone (E1)	Synthesized from cholesterol and rostenedione intermediate in gonads and adipose tissue; formed from estradiol by 17 β HSD in the liver, uterus, and mammary gland; binds to ER α and ER β receptors (less potent than estradiol)	Unclear, main actions through conversion to estradiol
Estradiol (E2)	Synthesized from cholesterol in ovarian follicles, testicles, adrenal glands, fat, liver, breasts, and brains; binds to ER α and ER β receptors, the most potent estrogen	Breast development, female fat distribution, regulation of menstrual cycle, also on mammary glands, uterus, vagina, bone, fat, skin, liver, brain
Estriol (E3)	Synthesized by placenta in pregnancy, low levels in nonpregnant state; binds to ER α and ER β receptors (far less potent than estradiol)	Uterine growth during pregnancy
Estetrol (E4)	Synthesized exclusively in the liver by the human fetus	Its biological function remains unknown
Androgens		
Testosterone	Synthesized from cholesterol in the testes (Leydig cells), adrenal glands, and ovaries (theca cells); binds to the androgen receptor	External genital, prostate, and seminal vesicle development in the male fetus; in puberty genital growth, bone and muscle mass, body hair, voice deepening
Dihydrotestosterone	Synthesized from testosterone by 5 α -reductase in the prostate, seminal vesicles, epididymides, skin, hair follicles, liver, and brain; binds to the androgen receptor (more potent than testosterone)	External genital development and virilization in fetus; maturation of penis and scrotum at puberty, facial and pubic hair growth

of action, and site of synthesis (242,253,254) (Table 3). In humans, all four estrogens are synthesized from cholesterol in several tissues besides the gonads, including the liver, adrenal glands, uterus, mammary glands, brain, adipose, skin, and the placenta. Estrogens bound to their nuclear receptors, ER α / β , serve as transcription factors to modulate gene expression. Circulating E2, the primary female sex steroid hormone, increases during puberty and, on average, is ~4-fold higher in adult females than males until menopause. Fluctuations of E2 occur monthly during the menstrual cycle in females, along with LH, follicle-stimulating hormone, progesterone, and other hormones (Fig. 10).

Estrogen is crucial for the health and survival in both males and females in glucose homeostasis, immune function, bone

health, cardiovascular health, fertility, and neural functions (256). Although estrogen is important in maintenance of bone mass, skeletal muscle, and tendon protein metabolism in females (257), it does not have the same anabolic effects of testosterone that dictates the large sex differences in athletic performance. The significance of endogenous estrogen for physical performance in women has been investigated in menstrual cycle studies by comparing performance at high levels of E2 in late follicular phase with low E2 levels in the early follicular phase or with high levels of E2 and progesterone in the midluteal phase. See the subsequent paragraph on menstrual cycle.

In males, circulating E2 is in the range of early follicular phase of premenopausal females and higher than in postmenopausal females (258). Although endogenous E2 is important for numerous actions in males, including reproductive function, bone growth and skeletal health, body composition, and glucose metabolism (258), little is known about its role in physical performance. Estradiol concentrations do not seem to be related to muscle strength and bone microarchitecture in older men (259). Furthermore, overtraining in male athletes was associated with increased E2 and decreased testosterone levels (260). On the other hand, increased skeletal muscle expression of estrogen receptors was demonstrated in endurance-trained males compared with moderately active males, suggesting a role of estrogen receptors in the adaptation of skeletal muscle to endurance training (261).

Menstrual Cycle. Direct effects of the menstrual cycle on exercise performance are difficult to assess and found to be highly variable and dependent on how the menstrual cycle is determined (262–264). Figure 10 illustrates the fluctuations in hormones over the regular menstrual cycle in females (255). Studies indicating physiological factors influenced by hormonal changes across the menstrual cycle can impact exercise performance including estradiol-associated increases in free fatty acid use (265,266), glycogen sparing (267,268), and muscle glycogen storage capacity (265,266). In contrast, progesterone counteracts some of the estradiol-associated effects on carbohydrate metabolism (269) and increases heart rate (270), body temperature (271), sweating (272), and set points for sweating and vasodilation (273–276). However, systematic reviews and

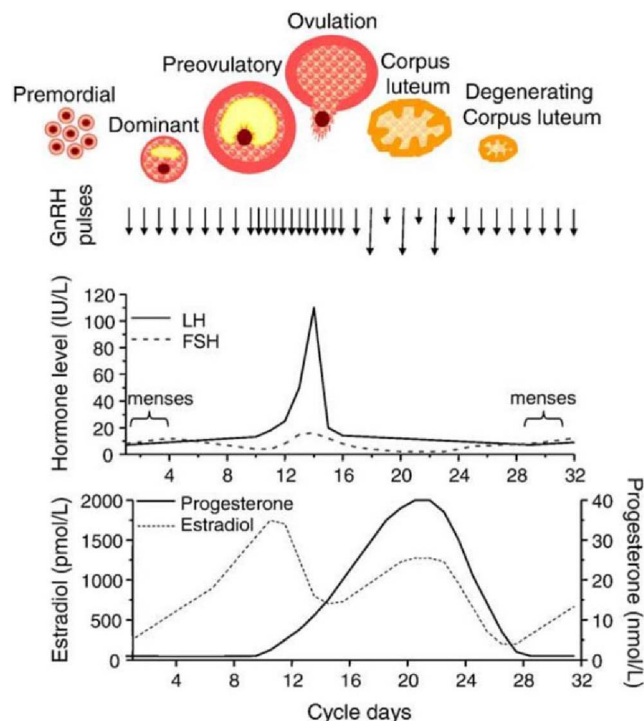


Figure 10—Diagram of the hormonal levels across the menstrual cycle. FSH, follicle-stimulating hormone. LH, luteinizing hormone. Adapted from Sims et al. (255).

meta-analyses have reported conflicting results, possibly explained by methodological issues (263,264,277). Most important, data from a recent large meta-analysis (263) indicate that despite the physiological effects of hormone exposure on metabolic and thermoregulation, effects on actual sports performance of menstrual phase are small and unlikely to overcome the more powerful factors that seem on the day of competition, including environmental temperature, type of exercise, training status, or individual characteristics. A caveat to consider is that menstrual cycle-related symptoms including menstrual pain and premenstrual symptoms (278–280) can have profound impacts on performance if a woman suffers physical or psychological consequences. Individual responses to menstrual cycle related symptoms among females can be quite varied. Although hormonal fluctuations across the menstrual cycle can alter physiological responses in some females, the average effect on performance is likely small relative to the large differences in athletic performance between males and females (10,138) and other environmental factors that affect both males and females. Key questions on the influence of the menstrual cycle and conditions affecting menstruation on athletic performance remain and certainly deserve more detailed analysis and reviews. Regardless of the effects, the menstrual cycle should not be used as an excuse to not include females in studies on acute exercise, exercise training, and the effects on athletic performance (281). Rather the menstrual cycle in women presents as another opportunity for high-impact studies to provide a rationale for inclusion of females into exercise science and sports-based studies.

Oral Contraceptives. The use of hormonal contraceptives does not differ among athletes compared with the general population (250). One of the most common types is combined oral contraceptives containing both estrogen and progestin. Oral contraceptives have a profound effect on the hypothalamic–pituitary–gonadal axis leading to suppressed levels of gonadotropins and sex steroid hormones, and thereby prevent ovulation (282). A recent meta-analysis concluded that combined oral contraceptives may slightly reduce exercise performance compared with nonhormonal contraceptive use (283). However, because the effect was minor and variable, the practical significance of the results is unclear. Future research studies in this area present as an excellent opportunity to solidify and clarify the knowledge needed before any general recommendations. At present, however, the evidence suggests that use of contraceptives by women does not play a large role in explaining the large sex difference in athletic performance between men and women.

Menopause and Aging. Surprisingly, there is little information about how the menopausal transition may affect physical performance in women and thus either adds variability between women or changes the magnitude of the sex differences in performance with aging. Population-based studies demonstrate reduced muscle strength and balance in postmenopausal women compared with premenopausal women of the same age (284,285). There may be a greater loss in physical performance in women who have undergone surgical menopause

compared with natural menopause (286). However, there is minimal evidence that menopausal hormone therapy protects against impaired physical performance in women (287). Understanding the possible role of estradiol and progesterone in skeletal muscle protein metabolism (257) presents opportunities to further explore the role of declines in these hormones after menopause and their contribution to age-related loss of muscle mass and function in women.

Effects of Sex Hormones on Various Physiological Systems

Central Nervous System

Brain development is modulated by steroid and peptide hormones *in utero* as well as during minipuberty in humans. Although brain regions involved in reproduction are sexually dimorphic, there are specific brain regions that are either influenced by or influence gender (288) as well, not just biological sex. Sex differences in brain size, height, and skeletal muscle mass even after controlling for body size are well documented, showing that males are larger than females, but sex differences in functional tasks associated with specific brain regions are not shown in large studies arguing for a continuum, rather than discrete male versus female differences in brain function (7).

However, some functional tasks such as visuospatial abilities and targeting objects with hand–eye coordination are important in many sports and may be influenced by exposure to androgens. Here, individuals with known DSD provide an opportunity to distinguish the effects of hormones from those of X or Y chromosomes for brain function (289). Functional magnetic resonance imaging studies involving 46,XY individuals with complete androgen insensitivity syndrome (CAIS) showed activation pattern in mental rotation-related brain areas that were more aligned with patterns in control females (289). Thus, the sexual differentiation of visuospatial neural activation is not directly influenced by sex chromosomal composition but is determined by exposure to androgens, as individuals with CAIS cannot respond to androgens (290–292). CAIS is explained more thoroughly in the later section on hormonal disorder. Similarly, studies focusing on hand–eye coordination found that 46,XX individuals with congenital adrenal hyperplasia (CAH), a medical condition associated with increased concentrations of circulating androgens, were able to target both darts and ball throwing more accurately than control females (293,294). Such results concur with the experimental results found in 46,XY individuals with CAIS and show that exposure to androgens *in utero* or during early childhood enables enhanced targeting coordination lasting at adult age. Whether this exposure to androgens in boys drives large or any sex differences in sports requiring visuospatial skills with development is difficult to determine. Shooting and archery, for example, show minimal sex differences in performance at the elite level (Table 2).

Although the link between testosterone and aggression in animals is known (295), the relationship is less clear in humans. In the context of competitive contact or combat

sports, aggressiveness can be a determinant of final performance. In a recent meta-analysis, Geniole et al. (296) reported a weak relationship between endogenous testosterone and aggressive behavior. Baseline testosterone and changes in serum testosterone shared a weak, although significant association with aggression in men but not in women. Moreover, results from exogenous testosterone administration in both males and females did not provide compelling evidence for a causal role of testosterone in promoting aggression. It is interesting to note, however, that gender-atypical behaviors have been reported in young girls and women with CAH (297), providing an opportunity for future well-controlled studies.

Finally, during a nonfatiguing motor task, adult males and females have similar and near maximal neural drive from central nervous system during maximal voluntary contractions of limb muscles as indicated in the Muscular and Anaerobic Power section (84,85,91–96). Neural drive is often quantified during a maximal voluntary contraction of a limb muscle by simultaneously superimposing a brief twitch or tetani evoked with either electrical stimulation at the motor nerve or transcranial magnetic stimulation over the motor cortex (298–300). Furthermore, excitability of the motor cortex and spinal cord (301) is similar in males and females (302,303) and during maximal voluntary contractions (91,93,94,304). Collectively, these studies indicate that sex differences in maximal strength contractions are due to greater muscle mass of males than females and not due to sex differences in excitability of the central nervous system and its ability to drive the muscle maximally.

During low-force submaximal tasks, however, emerging evidence indicates that females exhibit greater variability of motor unit activation (discharge rates) and lower force steadiness of limb muscles than males (305–309). Furthermore, imposing a stressful or demanding cognitive challenge during the motor task can decrease force control and increase fatigability of the limb muscles more so in females than males (305,306, 309–312). The reduced force control during a dual task (motor and cognitive tasks) may be related to more variable motor unit activation and oscillations in the common synaptic input to motor units originating from the central nervous system (305,306). The mechanisms for the sex differences, however, are not fully understood, or the role of the sex steroid hormones, testosterone, and estrogen. Further research on the reductions in force control during a dual task in females will provide a better understanding on its possible involvement in sex-related differences in sports injury patterns and the involved mechanisms.

Fat and Fat-Free Masses

Males and females have marked differences in fat and fat-free mass, because of the potent effects of androgens, primarily testosterone (158). The direct effects of testosterone in males include more muscle mass due to larger fibers cross-sectional area, larger bones, and less fat than females resulting in greater muscle power and strength (313,314). Estradiol has minimal

anabolic effects on skeletal muscle relative to testosterone (315). Estradiol does, however, aid in regulation of adipose tissue in both males and females (316) and maintenance of skeletal muscle mass in females, possibly in combination with progesterone (257).

Testosterone and dihydrotestosterone exert anabolic effects in skeletal muscle tissue by binding to the androgen receptor (103,317) resulting in increased protein synthesis and decreased protein degradation. This leads to increases in muscle fiber numbers and size, muscle satellite cell numbers, numbers of myonuclei, and size of motor neurons (317). Experimental evidence shows that testosterone increases skeletal muscle myostatin expression, mitochondrial biogenesis, myoglobin expression, and insulin-like growth factor content (103).

Testosterone administration in both males and females is responsible for increased muscle mass, muscle fiber size, and capillarization (318–320). In males, there are positive correlations between endogenous testosterone levels, muscle mass, and physical performance (249,315,321). Furthermore, increasing exogenous doses of testosterone over 12–20 wk caused a dose-dependent increase in lean mass and muscle strength in relation to increasing levels of serum testosterone (318,319). Testosterone administration for 20 wk in males also induces an increase in cross-sectional area of both type I and type II muscle fibers in a dose-dependent manner (322). Testosterone administration increased lean mass in postmenopausal females (323) and induced type II muscle fiber hypertrophy and increased capillarization in skeletal muscle of young females (320) (see the Models that Provide Insight into the Role of Sex Steroid Hormones section).

Testosterone is also responsible for less adipose tissue in males than females (317,324). Lowering testosterone to hypogonadal levels in young men (20–35 yr) for 20 wk using a gonadotropin-releasing hormone (GnRH) agonist caused a dose-dependent increase in total body adipose tissue in the trunk and limbs (arms and legs) (324). In contrast, increasing testosterone both in young females and males reduced total body adipose tissue mass with losses in the trunk and limbs (324,325). Administering various testosterone doses with and without concurrent aromatase inhibition demonstrated that the effects of testosterone on lean mass are mediated by testosterone effects, whereas the effect on adipose tissue is primarily related to aromatization to estradiol (318). Thus, testosterone, via both direct and indirect effects through aromatization to estradiol, is a powerful modulator of body composition.

To achieve the exercise-induced skeletal muscle hypertrophy, muscle cells recruit nuclei from helper satellite cells to increase protein synthesis and thus muscle fiber hypertrophy (326). Even after a detraining period, the number of nuclei acquired during the training process remains stable and will boost further episodes of protein synthesis, and muscle growth should training be resumed. This concept represents the so-called muscle memory (327). Because testosterone is known to stimulate satellite cell proliferation as well as the number of nuclei in males or in female muscles exposed to moderate levels of exogenous testosterone (320,326), longer-term testosterone

exposure contributes to the sex gap in muscle physiology (328) through the muscle memory phenomenon.

Estrogen, specifically estradiol, contributes to the regulation of adipose tissue in both males and females (316,329,330) and is important in fat distribution and maintenance of bone health (159). Estrogen is thought to have an important role in the maintenance and repair of skeletal muscle mass in females (331,332), and possibly muscle growth in response to resistance training in both young and postmenopausal women despite no direct effect on muscle protein synthesis at rest (257). Estrogens mediate their action by binding to receptors within adipose tissue, skeletal muscle tissue (333,334), tendons, and ligaments (335,336). Despite the role of estrogen in males and females, their actions and altered levels after menopause have important implications for females, but do not contribute to large sex differences in athletic performance.

Cardiovascular System

$\dot{V}O_{2\max}$ is a predictor of cardiovascular performance (163). Males have notable cardiac and hematological adaptations compared with females resulting in a significant performance gap in endurance events. These sex differences include the following: greater cardiac mass (absolute and relative to lean mass) and blood volume, and higher cardiac output and hemoglobin concentrations and thus larger $\dot{V}O_{2\max}$ (Fig. 11) (172,176,337–339). Importantly, the greater cardiac mass reflects the larger cardiac chamber dimensions in males and appropriate exercise-induced cardiac remodeling in males, which in turn results in substantially larger end-diastolic volumes and greater stroke volumes leading to higher cardiac than in females (176,339).

Evidence suggests that sex steroid hormones affect exercise training adaptations on cardiac structure (i.e., chamber size, ventricular mass) and function (i.e., contractility, stroke volume). Exercise training does not increase maximal heart rate, and if anything, endurance athletes have lower maximal heart rates than sedentary males and females (177,340). However,

males have higher stroke volume and stroke volume index compared with females at rest, and this difference persists through submaximal and maximal exercise (339,341). This larger stroke volume is likely driven by larger hearts, with higher blood volumes in males (338), which results in significant increases in central blood volume and thus end-diastolic volume during exercise (339). Because males have an enhanced ability to use the Frank–Starling mechanism compared with females (a mechanism ensuring stroke volume changes proportionally with end-diastolic volume), this results in significant increases in stroke volume compared with females (339,342). It is important to emphasize that cardiovascular regulation of heart rate is remarkably identical in males and females, and the cardiac output response for a given metabolic demand is exactly the same (177). Thus, for the same absolute work, females have the same cardiac output, a smaller stroke volume, and higher heart rate, but for the same relative work (reflecting cardiovascular regulation), the heart rate is the same between sexes. Furthermore, estrogens seem to have ergolytic effects on stroke volume. Specifically, estradiol reduces norepinephrine-induced vasoconstriction while increasing nitric oxide bioavailability (341). Lower norepinephrine in females at rest and during submaximal exercise limits cardiac contractility, whereas enhanced nitric oxide bioavailability results in a vasodilatory state reducing vasoconstriction in nonactive vascular bed. In turn, these factors work concurrently to depress stroke volume due to compromised venous return (thus, reduced preload) in the setting of reduced cardiac contractility. Finally, estrogens directly compromise cardiac contractility and result in a lower contractile reserve due to downregulation of L-type calcium channels (343), which inhibits calcium loading-dependent increases in contractility with increased stimulation (344).

In contrast, testosterone is associated with greater ventricular mass and myocardial contractility. Orchiectomy in rodents depresses ventricular weights in males, whereas testosterone administration enhances ventricular weights in females (345). In fact, exogenous testosterone analogues result in significant left ventricular (LV) hypertrophy in athletes along with an elevated risk of developing cardiomyopathy (346). Furthermore, low testosterone states are associated with attenuations in myocardial contractility (347). The beneficial effects of testosterone on contractility are likely due to favorable effects on calcium handling in the cardiomyocyte.

Evidence also suggests that testosterone has significant ergogenic effects on peripheral determinants of $\dot{V}O_{2\max}$. As a potent inducer of erythropoiesis, testosterone recalibrates the set-point of erythropoietin in relation to hemoglobin levels and results in improvements in hemoglobin and hematocrit, raising the oxygen carrying capacity of blood (348). Sex differences in blood volume and hemoglobin mass (males > females) act synergistically to augment LV filling (and stroke volume) and enhance peripheral oxygen delivery in males allowing for a higher $\dot{V}O_{2\max}$ (338). Females partially compensate for this by increasing oxygen extraction; however, arteriovenous oxygen extraction remains lower at submaximal

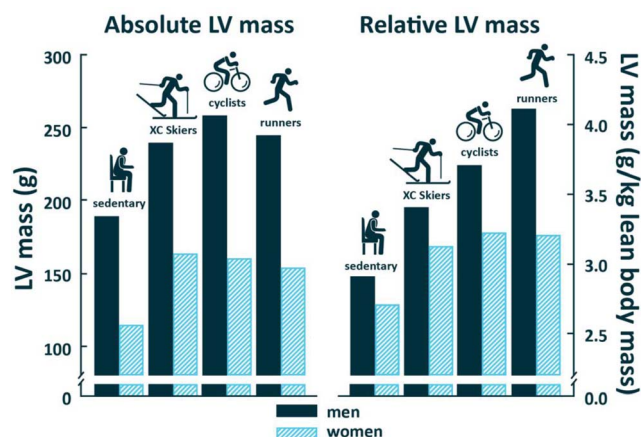


Figure 11—Cardiac mass (absolute and relative to lean body mass) of male and female athletes and sedentary controls. LV, left ventricular. Data adapted from Milliken et al. (337) and Riley-Hagan et al. (172).

exercise (341). Testosterone administration in females result in improvements in mitochondrial respiration and 8% greater capillary to fiber ratio compared with placebo, which further underscores the primacy of testosterone with regard to developing this phenotype (349).

Pulmonary function at rest and during exercise is different between males and females. Compared with males, females have smaller lungs when matched for height (350,351) and smaller conductive airways when matched for lung size (352,353) and irrespective of fitness (354). The larger lung and airway size of healthy males compared with females emerge by 14 yr of age, with small differences remaining when normalized to height (351). As a result, females have lower maximum expiratory flows compared with males at rest (355). Furthermore, females also exhibit lower diffusion capacity for carbon monoxide (corrected for hemoglobin) that is likely driven by lower pulmonary capillary blood volume and alveolar capillary diffusion capacity compared with males (356). However, there is no sex difference in the diffusion capacity for carbon monoxide when normalized to alveolar volume, indicating that it is likely that the difference is driven by sex differences in lung size (356).

These differences described at rest have implications for exercise. Because airway size affects airway resistance, females have a higher work of breathing (357) and exhibit shallower breathing with greater breathing frequency compared with males (358,359). Furthermore, endurance trained females have a higher propensity toward expiratory flow limitation. This is principally observed when ventilatory demand approaches maximal ventilatory capacity during exercise (360). Finally, females have a blunted inspiratory muscle metaboreflex (the reflex increases blood pressure in response to metabolite accumulation in the muscle during exercise), which is likely due to the effect of estradiol on β -adrenergic receptors on the leg muscle vasculature (361).

Fuel Metabolism

The observed sex differences in fuel metabolism during endurance exercise (77,179,187–189) are attributed in part to sex differences in estrogen (362–364) with minimal effects of testosterone (365). Preclinical studies show that male and ovariectomized female rats treated with estradiol have greater fat and lower carbohydrate utilization during endurance (i.e., treadmill) exercise compared with animals treated with placebo or estradiol plus progesterone (366). In addition, the glycogen-sparing effect and shift toward lipid utilization during endurance exercise in the presence of higher circulating levels of estradiol may be antagonized by the addition of progesterone (367,368). Similarly, in studies conducted in young men and amenorrheic women, short-term estradiol treatment reduced the rate of glucose utilization but had no effect on whole-body lipolysis or substrate oxidation during exercise (362–364). In a study that administered a GnRH antagonist in eumenorrheic premenopausal women to suppress estradiol and progesterone levels, fat utilization was increased and

carbohydrate (i.e., muscle glycogen) utilization was decreased during endurance exercise when estradiol was added-back. However, when progesterone was combined with estradiol, the muscle glycogen-sparing effect of estradiol alone was prevented, consistent with preclinical observational studies (269).

The mechanisms by which estrogen promotes fat utilization during exercise may be related to increases in mitochondrial enzymes that favor fat utilization, including carnitine palmitoyl-transferase 1 and β -hydroxyacyl dehydrogenase (369). Interestingly, progesterone alone or combined with estradiol reduces the activity of these enzymes (369).

In contrast to the effects of estrogen on fuel metabolism during exercise, testosterone may not significantly impact substrate utilization during exercise in males or females. Studies that either suppressed testosterone with a GnRH antagonist or administered high doses of testosterone had little impact on the balance between blood glucose, glycogen, or fat utilization during exercise in young men (365). These data contrast with animal studies that show that testosterone treatment reduced glycogen utilization during exercise in female rats (370) and reversed the elevated rates of glycogenolysis induced by castration in male animals (371).

It is important to note that age and menopause status may modulate the influence of estrogen on fuel metabolism during exercise. Premenopausal women have higher fat oxidation rates at rest and during exercise compared with postmenopausal women (372), whereas the percentage of fat and carbohydrate utilization during 30 min of high-intensity (80% VO_2 max) treadmill exercise was not different between postmenopausal women using estrogen-based hormone therapy and those not using hormone therapy (373).

Models that Provide Insight into the Role of Sex Steroid Hormones

TESTOSTERONE SUPPRESSION/ADDITION CONDITIONS (ESTROGEN SUPPRESSION/ADDITION CONDITIONS)

Testosterone Addition in Females. Except for some of the classified documents extracted from the former German Democratic Republic archives, which meticulously describes its state doping program (374), few studies have investigated the effect of testosterone treatment on physical performance in healthy females, possibly related to ethical concerns about potential adverse effects. In postmenopausal women however, increased testosterone administration up to 24 wk was associated with a dose-dependent increase in lean mass and muscle performance (323). The highest dose resulted in a mean testosterone concentration of $7.3 \text{ nmol} \cdot \text{L}^{-1}$ and caused an increase in lean mass of 4.4% in these postmenopausal females (323). A moderate increase in testosterone also induced type II muscle fiber hypertrophy and increased capillarization in skeletal muscle of young females (320,349). In a randomized clinical trial, young healthy exercising females were treated with testosterone (10 mg daily) or placebo for 10 wk (325). In the treated group, testosterone rose to a mean concentration of

4.3 nmol·L⁻¹, muscle mass increased, and aerobic performance (treadmill running time to exhaustion) improved by 8.5% compared with placebo. Anaerobic power (Wingate test) improved minimally (3.2%) and was not significantly different from placebo. Thus, the few studies conducted in nonathletes indicate that testosterone can increase muscle mass via muscle fiber hypertrophy and aerobic performance in females after 2–3 months of testosterone administration.

Testosterone Suppression in Males. Endogenous testosterone blockade in males with a GnRH agonist or antagonist to castrate concentrations results in increased body fat and decreased lean mass (329,375). A randomized controlled trial in adult males (treated with GnRH antagonist plus one of the following: placebo, low-dose testosterone, typical-dose testosterone, or testosterone with letrozole) showed decreases in lean mass primarily due to androgen withdrawal, whereas changes in fat mass were secondary to estrogen withdrawal (329). Furthermore, after treatment with a GnRH agonist, add-back of testosterone injections at low, moderate, and high doses showed that fat-free mass, muscle volume, and strength have a dose-dependent relationship with testosterone (319,375). Androgen deprivation therapy is often proposed to male patients with prostate cancer. Although these studies involve older men, several meta-analyses and randomized control trials (376–378) show that resistance training programs are able to maintain body composition, muscle strength, and aerobic capacity in these hypogonadal individuals, despite very low levels of circulating testosterone.

Gender-Affirming Hormone Therapy. Transgender youth treated with a puberty blocker such as GnRH agonist have higher percent body fat than age-, assigned sex- and body mass index-matched controls (379). Longitudinal studies show that transgender women treated with estradiol have increased body fat and decreased lean mass, whereas transgender men on testosterone experience opposite effects (380). Cross-sectional studies, however, show that individuals treated with testosterone or estradiol have body composition (fat, lean mass) that are intermediate between body mass index-matched cisgender controls after ~12 months of treatment (381). Hence, more is known about effects of gender-affirming hormone therapy (GAHT) in nonathletic transgender individuals than GAHT effects on athletic performance. Because many of these studies are conducted on nonathletes, key questions remain about the effects of GAHT on athlete populations where the effects of hormonal status and the addition of exercise training may influence body composition, adaptations with training, and performance.

Transgender Men (Female Sex, Male Gender Identity). GAHT in transgender men involves testosterone treatment aiming at testosterone levels in the male range and results in increased hemoglobin levels, lean body mass, and muscle cross-sectional area, and reductions in body fat but no changes in height if administered after puberty (380,382–384). Increased muscle mass, strength, and power are consistent with insight gained on the strong effects of anabolic steroids such as testosterone in athletes (385). After 1 yr of transition, transgender men had increased handgrip strength (18.4%) (383),

pushups repetitions (19.8%) (386), and leg strength (19%) (384) and these changes were associated with an increase in muscle mass/lean mass (383,384).

Endurance performance also increases in transgender men after GAHT. Run speed over 1.5-mile distance increased 11.6% in transgender men in the US Air Force after a 2.0-yr period of GAHT but only 2.8% after 1 yr of GAHT (386). Although there is little evidence that transgender men can outperform cisgender men who are typically taller with larger limbs, they can increase performance levels within the range of cisgender males (386). A key question is to what extent testosterone usage in transgender men can overcome any disadvantages with respect to cisgender men.

Transgender Women (Male Sex, Female Gender Identity). Several longitudinal studies in transgender women show a reduction in hemoglobin/hematocrit (the latter equivalent to cisgender women after ~4 months), and lean body mass, muscle cross-sectional area, and muscle strength, but are typically stronger than cisgender women (387) even 14 yr after initiation of GAHT (388). For example, nonathletic transgender women who underwent estrogen treatment for 12 months decreased muscle volume by 5% but maintained muscle strength (384).

Cross-sectional and longitudinal studies show reductions in endurance performance in transgender women, although not always to the level of cisgender women. A retrospective observational study of eight transgender women runners showed they had slower race times after GAHT and their age-graded performances were relatively constant (389). In longitudinal observations (386), transgender women in the US Air Force performed a slower 1.5-mile run time (~8%) at 2–2.5 yr of follow-up but maintained a performance advantage of 12% over cisgender women. Given that 1.5-mile run times are highly correlated ($r=-0.89$) with VO_{2max} (390), it is possible that the greater endurance performance is associated with a larger aerobic capacity and is advantageous for transgender women. Following up, on a similar population, the same research group recently studied a larger cohort of military Air Force transgender people for up to 4 yr of GAHT to address the question of unified and evidence-based fitness testing policy for a growing number of transgender servicemembers (391). Transgender women had better performance than cisgender women on the 1.5-mile run until 2 yr of GAHT (13:51 vs 14:36 min:s, respectively, at 2 yr). At least 4 yr was necessary to show minimal differences between transgender women and cisgender women on assessments of muscular endurance (sit-ups in 1 min, 44 vs 41, respectively), but transgender women outperformed cisgender women in push-ups (30 vs 35) after 4 yr of GAHT. However, these results must be considered with caution as they are probably subject to a survivorship bias (approximate 94% dropout rate in transgender women after 2 yr of observation).

Consistent with some retained advantage of performance in transgender women, effects of ~2 yr of GAHT on swimming performance (50–1500 m) in an elite transgender woman (1) resulted in a reduction in performance, but retention of a 5% performance advantage compared with a historical database

of competitive times in cisgender women. Because oxygen uptake and muscle power are important predictors of swimming velocity (392), it is plausible that advantages in performance associated with endogenous testosterone were retained.

Key questions and opportunities remain for high-quality, well-controlled, and impactful longitudinal studies on the trajectory of performance changes in transgender athletes and the physiological and anatomical mechanisms involved.

HORMONAL DISORDERS (PCOS, DSD)

Hyperandrogenism is a key component of PCOS diagnosis (according to the Rotterdam consensus), so hypothetically, PCOS may imply competitive advantages to sport activities. PCOS presents as a combination of signs and symptoms of androgen excess and ovarian dysfunction (oligo-ovulation/anovulation and/or polycystic ovaries) in the absence of other specific diagnoses (15). Such women are biological females with XX chromosomal complement and ovaries and have a feminizing puberty. Although they may have testosterone above the normal range for biological females, their testosterone levels are typically well below the male range (Fig. 2). Indeed, most hyperandrogenic female athletes show polycystic ovaries on ultrasound. Hagmar et al. (393) demonstrated that PCOS was the primary predictor of menstrual dysfunction in female Olympic athletes. However, relative energy deficiency is probably the most common cause of amenorrhea among exercising women overall (394). Greater hyperandrogenism in athletes is suggested to confer an athletic advantage because the combination of hyperandrogenism and exercise may help athletic women with PCOS maintain their lean phenotype (395). It is also proposed that women with PCOS are drawn to sports such as swimming in which high testosterone may provide an advantage because the hyperandrogenism precedes sports participation (396,397). However, among the general population of women with PCOS, most are not athletes, with estimates showing that 38%–88% are either overweight or obese (398).

DSDs are rare conditions in which the development of chromosomal, gonadal, and anatomic sex is atypical (outside the

binary of male/female) (9,399) (Table 4). Specific examples of DSD follow with Figure 2 displaying ranges of testosterone concentrations in these populations.

- a. Androgen-insensitivity syndrome (AIS) is a 46, XY DSD caused by a hemizygous mutation in the androgen receptor (*AR*) gene in XY individuals, leading to resistance to androgens, including testosterone. The condition results in partial (partial AIS, or PAIS) or CAIS inability of cells to respond to androgens. This unresponsiveness can impair or prevent the development of typical male genitalia and male secondary sexual characteristics at puberty. Clinical phenotypes in these individuals range from a typical male habitus with mild spermatogenic defect or reduced secondary terminal hair, to a full female habitus, despite the presence of a Y-chromosome (CAIS). Individuals with CAIS have typical external female genitalia and internal testes, and undergo breast development at puberty (due to aromatization of testosterone to estradiol) but do not have a uterus, so they do not menstruate. There is a wide-ranging phenotype for PAIS (400).
- b. 5 α -reductase deficiency type 2 is a 46, XY DSD caused by biallelic mutations in *SRD5A2*, a gene encoding the enzyme 5 α -reductase type 2, which converts testosterone to dihydrotestosterone. In this rare condition, XY individuals have undervirilized genitalia. At puberty, when the testes start to produce high amounts of androgens, these individuals will undergo virilization and develop various degrees of male-like phenotype (401).
- c. CAH refers to a group of autosomal recessive genetic disorders in which the two adrenal glands lack the proteins and enzymes involved in cortisol biosynthesis. The most common mutation is in the gene encoding the adrenal 21-hydroxylase, which is an enzyme responsible for converting cholesterol to cortisol within the adrenal glands. Without this enzyme, the adrenal glands may produce too little cortisol and/or aldosterone and too much androgens leading to varying degrees of hyperandrogenism in XX individuals (402,403).

TABLE 4. Examples of Conditions of Endogenous Hyperandrogenism and Differences (or Disorders) of Sex Development (DSD) and the Potential Advantage for Physical Performance in Women.

Condition	Prevalence/Incidence	Karyotype	Phenotype	Testosterone Concentrations ^a	Advantage in Sports?
PCOS	~10%	XX	- Mild symptoms of hyperandrogenism (e.g., hirsutism) - No virilization^b	Most often within the upper normal female range or just above ^a	Yes, possibly in normal-weight individuals
CAH	- Classic: 1/10,000–1/16,000 - Nonclassic: 1/100–1/1000	XX	- Classic form: virilized at birth - Nonclassic: not virilized, symptoms at puberty	High testosterone levels reaching the male range if untreated with glucocorticoids	Yes, but only if undertreated
5 α -Reductase deficiency type 2	Extremely rare with geographical regions of higher incidence	XY	- Female or ambiguous-appearing genitalia, testes - Virilization proceeds at puberty	Testosterone levels in the male range	Yes
CAIS	1/50,000	XY	- Completely female external genitalia - No effect of high testosterone levels	Testosterone levels in the male range	Not because of androgenic effects
PAIS	1/130,000	XY	- Ambiguous genitalia at birth - From puberty high testosterone, but with variable clinical effect	Testosterone levels in the male range	Possibly depending on the degree of androgenic effects

^a Normal female range of serum testosterone is 0.1–1.8 nmol·L⁻¹ and normal male range is 7.7–29.4 nmol·L⁻¹, as determined by liquid chromatography–tandem mass spectrometry (9).

^b Virilizing symptoms: muscle growth, increase in body hair (hirsutism), hair loss of male type, deepening of the voice, breast atrophy, and enlargement of the clitoris.

Individuals with 46,XY DSD who are born with female or ambiguous genitalia and functioning testes, such as in the case of 5- α reductase deficiency, will produce testosterone concentrations in the typical male range (9,325) (Fig. 2). Except in cases of androgen resistance (CAIS), the individual will respond to testosterone made during puberty and adult life with increased virilization and muscle development (9,325). The prevalence of 46,XY DSD is estimated to be ~140 times greater (7.1/1000 vs 0.05/1000) among elite women athletes than the general population (18,404). These findings, together with an increased occurrence of mild forms of hyperandrogenism (PCOS) among elite female athletes (393), support an advantageous role of endogenous hyperandrogenism for athletic performance in women.

Monitoring competition performances obtained from athletes with 46,XY DSD before and after they had their testosterone level lowered from the normal male range to the normal female range is also a valuable and unique source of information. Three elite middle-distance runners, for example, had an average decrease of their best chronometric performance of 5.7% over a 2-yr period (405). Finally, not all individuals with 46,XY DSD identify as women, many identify as men, including over half with 5- α -reductase deficiency, or may identify as nonbinary (399,406,407).

The Hypothalamic–Pituitary–Somatotrophic and Corticotrophic Axes

In addition to androgens, the GH superfamily and the insulin-like growth factor superfamily play a role in muscle growth and repair (408). The interplay between sex steroids and GH and insulin-like growth factor-1 (IGF-1) are complex and previously reviewed (9,409). Short-term administration of GH results in increased protein synthesis, muscle repair, and lean body mass (410,411) but does not result in significant increases in strength, exercise capacity (411), and muscle function (412). IGF-1 levels, however, are associated with improvements in handgrip strength in old age (413). Moreover, higher circulating IGF-1 has been linked to increased muscle protein synthesis, muscle-free fatty acid utilization, and better insulin sensitivity (414), which may promote training adaptations. However, these ergogenic effects of GH and IGF-1 *per se* remain small compared with the effects of testosterone. Relevant to this review, the primary evidence suggests that the sex differences in performance are not due to GH or IGF-1 (9) because endogenous GH secretion in young females is consistently higher (typically twice as high) than young males. Moreover, intervention studies show minimal changes in performance with administration of GH, but GH may rather amplify the effects of testosterone (9). Indeed, during resistance training, testosterone increases IGF-1 gene expression (415). Both testosterone and estrogen (416) blunt IGF-1 feedback-dependent inhibition of GH secretion. Lastly, despite their important roles in the integrated communication for anabolic/catabolic signaling, effects of glucocorticosteroids are not discussed in this review because their effects on athletic capacity do not seem

to be significantly influenced by sex (9). Thus, the evidence suggests that impact of GH, IGF-1, and glucocorticosteroids on the sex difference in athletic performance is minimal relative to the effects of testosterone.

TRAINING ADAPTATIONS TO EXERCISE IN MALES AND FEMALES

Males and females show robust physiological adaptations and improvement in performance in response to exercise training (417–419). Several key questions are as follows: 1) whether males and females differ in trainability, that is, their relative improvements in performance and physiological adaptations in response to a similar exercise training dosage, and 2) do gonadal sex steroid hormones contribute to potential differences in training adaptations between males and females? It is important to note that a vast majority of training studies are short-term, whereas elite athletes train for years and often decades including during growth and development to achieve maximal performance. Although we will not review in detail the effects of oral contraceptive use on training adaptations, the results are discordant. Collectively, the limited number of studies show that oral contraceptive use does not markedly impair or enhance adaptations to exercise training in females (420–425) and thus relative to males. However, as noted earlier, more nuanced guidance for women could be gained by answering key questions around the types of events and athletic attributes that may be most affected by hormonal contraceptives, as well as the effects of specific oral contraceptive hormones on training adaptations (283).

Fat-Free Mass: Resistance and High-Intensity Training

Exercise training affects the production of gonadal sex steroid hormones, with some studies reporting increases in total and free testosterone levels after a bout of heavy resistance exercise in men, whereas responses in women are not clear (426–428). This effect varies by age, training status, mode, intensity, and volume of exercise training. Increased testosterone, however, is not always needed for muscle hypertrophy (429) and may be more important for males in conditions of low testosterone, such as aging (430). Although females can but often do not display acute increases in testosterone after resistance exercise (426), males typically do (431). Greater total testosterone levels, however, have been reported after 24 wk of resistance training in females (432). Thus, males and females may experience increased anabolic hormones in response to high-resistance training; however, their roles in consequently promoting hypertrophy are key questions that remain.

Males and females exhibit similar relative (percentage) magnitudes of muscle hypertrophy, muscle strength, and power improvements in response to high-load resistance training (~6–12 wk) in young adults (e.g., (419,433–436)) and adults older than 50 yr (437), with the expected moderating effects of frequency, volume, and intensity (419,436). Males and females also adapted similarly (relatively) to 12-wk high-intensity

interval training on the bike with similar muscle hypertrophy (5%) and increased fatigue resistance (4.8%) (438). Because males are typically stronger than females at baseline, their absolute increase in muscle mass and strength is often larger than females. Clarification of these adaptations are needed, however, because of the considerably larger number of men assessed and tested relative to females (419) and the nuanced sex differences reported in individual studies. In addition, whether males exhibit even greater relative skeletal muscle hypertrophy than females (as occurs with cardiac mass: Fig. 11) with long-term high-resistance training is not clear.

Cardiovascular Adaptations and Endurance Training

Both males and females exhibit similar relative increases in cardiovascular function ($\text{VO}_{2\text{max}}$) and aerobic performance with short-term training, but long-term cardiac adaptations may be larger in males than females, possibly moderated by endogenous testosterone (339). In young adults, increases in stroke volume, a-vO₂ difference and $\text{VO}_{2\text{max}}$ were similar between the sexes 3 months after endurance exercise training; however, thereafter, males continued to improve $\text{VO}_{2\text{max}}$ for up to 9 months after initiation of exercise training, whereas females plateaued after 3 months of training (339). Males also demonstrated increases in LV mass up to 6 months after initiating endurance exercise training, but female plateaued after 3 months. Both sexes achieve LV mass values after 1 yr of training equivalent to cross-sectional studies in elite athletes where females consistently have smaller LV mass across multiple training modalities (including sedentary) than males (172,337). In males, 1 yr of endurance training resulted in a balanced increase in both LV mass and volume, and thus, the LV mass-to-volume ratio was similar to baseline. However, in females, the volume increased more than LV mass so that the LV mass-to-volume ratio was below their baseline ratio (339). This relatively greater increase in volume compared with mass indicates a greater contribution of eccentric remodeling in females versus males. Importantly, males have larger increases in stroke volume for a given filling pressure than females. Although exercise training adaptations in LV end-diastolic volume are similar between young males and females, young males have a greater augmentation of the Frank-Starling mechanism (339,439), which is a hallmark feature of endurance athletes (440).

The reason for the sex differences in cardiovascular adaptations in LV structure (i.e., mass) is not completely understood, but differences in gonadal sex steroid hormones are likely involved (441). The increase in circulating testosterone with exercise may contribute to the increase in LV mass due to both anabolic and anticatabolic effects (345,442). In females, circulating estrogens could attenuate the increase in LV mass with exercise training through estrogen receptor β signaling and antihypertrophic effects of atrial natriuretic factor (441). Furthermore, estrogen likely affects the Akt/PI3K pathway, which blocks ventricular hypertrophy associated with exercise training (339). Testosterone in males and estrogen in females could

also influence exercise-induced LV hypertrophy through opposing effects on the cardiac renin-angiotensin system (441,443). This adaptation is not necessarily all beneficial: concomitant with the larger cardiovascular adaptations in males with training, the rate of sudden cardiac death in men during exercise is considerably greater compared with women (444,445).

In older adults, $\text{VO}_{2\text{max}}$ increases similarly with endurance training in males and females, although cardiovascular adaptations differ between the sexes (446,447). Older males increased stroke volume during maximal exercise with endurance exercise training, whereas greater a-vO₂ difference accounted for all the increase in $\text{VO}_{2\text{max}}$ for older females (446,447). The difference in adaptations is not understood, but lack of ventricular remodeling and blood volume expansion may be responsible for blunted cardiac adaptations to exercise training in older women (441). Menopause-related declines in estrogen may also be involved (446). However, in women, endurance exercise training improved submaximal central responses (i.e., lower HR and VO_2 at the same intensity), regardless of hormone therapy use (448–451).

Fuel Utilization during Exercise

Endurance exercise training is associated with an increase in the proportion of lipid oxidized during exercise at the same absolute intensity, as well as in intramyocellular lipid and mitochondrial content, and higher β -oxidation enzyme capacity in both sexes (452). Plasma glucose uptake during exercise is also reduced after endurance exercise training at both absolute and relative exercise intensity (453). Although both sexes demonstrate greater lipid oxidation during moderate-intensity exercise at the same absolute intensity, females have an increased rate of lipolysis and oxidize proportionally more lipid and less carbohydrate before and after training (452,453). Compared with males, females also have greater intramyocellular lipid content in the vastus lateralis before and after exercise training because of a greater number of individual droplets (452). We are not aware of any data on the modulatory influence that gonadal sex steroid hormones may have on endurance exercise training effects on fuel utilization in males or females. Thus, this is also an area ripe for future research.

NONHORMONAL FACTORS CONTRIBUTING TO SEX DIFFERENCES IN ATHLETIC PERFORMANCE: Y AND X CHROMOSOMES

It has been hypothesized that the Y chromosome could be associated with a higher level of physical performance in males compared with females because of a taller stature that is advantageous in many athletic events, and this mechanism is independent from the circulating testosterone concentration (454). This chromosomal contribution to height (455) was reported in 1985, along with information that individuals with a 46,XY gonadal dysgenesis (an atypical development of the gonads in the embryo with reproductive tissue replaced with functionless, fibrous tissue producing very few or no sex

steroids) were, on average, 6.6 cm taller than individuals with a 46,XX gonadal dysgenesis. Interestingly, the X chromosome is also involved in the observed difference in height between males and females (456). Indeed, an incomplete silencing mechanism of the *ITM2A* gene, a gene associated with a short stature, often occurs, and the expression of its two copies in females (vs one in males) is believed to account for only a small percentage of the observed difference in height between sexes. As far as the Y chromosome is concerned, there is little other evidence supporting dosage-dependent Y chromosomal gene effects on height other than the copy number of the short stature homeobox gene (*SHOX*) carried by the short arms of X and Y chromosomes (9,457).

SUMMARY AND CONCLUSIONS

Males outperform females in sports and athletic endeavors that require aerobic endurance, muscle strength, power, and speed. The biological differences between males and females result in ~10%–30% sex difference in athletic performance, although the magnitude depends on the demands of the event/sport and which biologic systems are most involved. Males are taller with longer limbs, stronger, more powerful, and faster than females over short and long distances. Males have a larger skeletal muscle mass, less percentage body fat, and faster contracting muscle due to a larger proportional area and volume of fast contracting muscle fibers than females. Sex differences in endurance performance such as distance running (~10% among the world's best) is dictated by the higher aerobic power of males compared with females. This is because males have a larger heart size, and thus greater stroke volume, blood hemoglobin concentration, and mass, larger muscle mass, larger airways and lung volume, less body fat, and consequently a higher $\text{VO}_{2\text{max}}$ than females. Sex differences in athletic events that are reliant primarily on muscular power, including weightlifting and jumping events, can be as high as 30% because males have more muscle mass and faster contracting muscles, with longer limbs and taller stature that together generate more limb power for males compared with females.

The primary cause for the large sex difference in athletic performance is exposure to high levels of endogenous testosterone in boys at the onset of puberty (~12 yr) that will rise 30-fold in males but remains low in females. Females, on the other hand, experience the menstrual cycle and monthly fluctuations in endogenous hormones including estradiol, which is important in maintenance of bone mass, skeletal muscle, and tendon protein metabolism. However, estradiol does not have the same anabolic effects as testosterone, which dictates the large sex differences in performance. The effects of the sex steroid hormones, in particular the potent, quick-acting, and long-lasting effects of testosterone, are evident in 1) experiments/studies where sex steroid hormones have been added or suppressed in both males and females, 2) studies of the physiology and performance of individuals with various

TABLE 5. Key Points and Future Directions.

Key points

- Biological sex is a determinant of athletic performance: adult males are faster, stronger, and more powerful than females. The fastest and most powerful males outperform the fastest and most powerful females.
- The sex difference in athletic performance where endurance or muscular power is required is ~10%–30% and varies depending on the requirements of the event. The largest sex difference in performance occurs in sports that rely on muscular power such as weightlifting and jumping.
- Historically, the sex difference in performance is larger than explained by physiological and anatomical differences between males and females, particularly among lower-ranked athletes. This is in part due to women having less opportunity and inequitable access to sports, facilities, and training than men, and higher dropout rates of female athletes than males.
- Both past and present research studies of athletic performance, acute exercise, and exercise training involve the testing of more men than women, or a lack of distinction between the sexes. Consequently, less is known about the physiology of women athletes, limits in their athletic ability, and the acute and adaptive response of women to exercise and training relative to men.
- The rate of improvement in athletic performance of women has exceeded that of men in the last 100 yr across a multitude of sports, as women have gained access to training, equipment, facilities, and opportunities.
- Exposure to high levels of endogenous testosterone in males at the onset of puberty (~12 yr) is the primary determinant for the large sex difference in athletic performance during puberty and in adulthood. Before puberty, the sex difference in athletic performance is minimal.
- Testosterone, a powerful anabolic steroid, increases ~20–30-fold in males during puberty and is 15× higher than adult females.
- The direct and indirect effects of testosterone in males (relative to females) during puberty that impact athletic performance include increased skeletal muscle mass due to larger muscle fiber cross-sectional area especially fast, type II MHC fibers, lower percentage body fat, higher hemoglobin concentration and mass, larger ventricular mass and myocardial contractility, larger airways and lungs, greater body height, and longer limbs.
- Estradiol (E2), which fluctuates during the menstrual cycle in females, does not have the same anabolic effects as testosterone but is important in maintenance of body composition including bone mass, skeletal muscle, fat mass, and tendon protein metabolism.
- Models that provide insight into the role of testosterone in athletic performance include the following:
 - Testosterone addition in females resulting in increased muscle mass and muscle fiber size, increased hemoglobin concentration and mass, improved strength, and endurance performance.
 - Testosterone suppression in adult males resulting in initial decreases in muscle mass, increased fat mass, although the loss of lean mass and strength is not to the levels of adult females at least up to 3 yr post.
 - Biologic males who undergo partial or complete male puberty followed by testosterone suppression retain some advantage in power and endurance performance over biological females, at least up to 2 yr post.
- GH and IGF-1 are associated with increased protein synthesis, muscle repair, and some improvements in strength but do not explain the large sex differences in athletic performance.
- DSDs are rare conditions in which the development of chromosomal, gonadal, and anatomic sex is atypical, but their prevalence is overrepresented in elite women athletes by 140-fold relative to the general population.
- Males and females exhibit similar relative (percentage) increases in performance and adaptations in response to short-term (6–12 wk) high-resistance and endurance training.
- “Muscle memory” may play an important role in individuals who have been previously exposed to high levels of testosterone (e.g., male puberty) and who undergo suppression of testosterone but retain the ability to hypertrophy in response to resistance training and more so than those not exposed to testosterone.
- Males exhibit larger adaptations of ventricular mass than females after long-term endurance training (>9 mo) possibly facilitated by high concentrations of endogenous testosterone.
- Nonhormonal factors that may impact the sex differences in height determination and thus athletic performance include possession of the Y chromosome (greater height) and/or the X chromosome (shorter height).

Future directions and opportunities

- A mandate to include sex as a biological variable across all studies of athletic performance and exercise science. This would involve including women at all levels and studies to be adequately powered to understand sex differences in the acute and chronic exercise responses.
- Declare the sex of the participants in the title and abstract of published studies.

Continued next page

Studies to determine:

- The long and short consequences and reasons for lower participation of women in sports relative to men.
- The impact and identification of social determinants that influence the sex difference in performance including poor access to resources and athletic discouragement among females, and training based on male only studies.
- The role of minipuberty (transient increases in testosterone in boys and estradiol in girls in infancy) in the growth, development, exercise training, and athletic performance of children, and males and females during puberty and into adulthood.
- Long-term trainability and mechanisms of endurance and resistance strength training in both sexes.
- The effects of sex steroid hormones including testosterone and estradiol on trainability (improvements in performance and physiological adaptations in response to a similar exercise training dosage) in males and females.
- Sex differences in short-term and long-term recovery from intense and long-duration exercise including recovery from races/competitions/events.
- Sex differences in physical performance in people with clinical conditions of various abilities including diabetes, metabolic syndrome, stroke, and other clinical conditions.
- Sex differences in brain function and motor control that may affect athletic performance.
- The long-lasting effects of testosterone supplementation and suppression in DSD and transgender athletes.
- Mechanisms for the differences in injury rates to male and female athletes (e.g., ACL in females).
- Performance effects of the menstrual cycle and hormone therapy after during and menopause in females.
- The effects of oral contraceptive use on long-term training adaptations, although collectively, the limited number of studies show oral contraceptive use does not markedly impair or enhance adaptations to short-term exercise training in females.
- The short- and long-term consequences of pregnancy, childbirth, and childbearing on the female athlete body and performance.
- How aging and its hormonal consequences during and after menopause can change the sex-related difference in response to acute exercise, exercise training, and athletic performance.
- The trajectory of performance changes in transgender athletes and the physiological and anatomical mechanisms involved.
- The effects and role of muscle memory on retention of strength, power, and endurance in transgender athletes who have been previously exposed to high levels of testosterone (e.g., male puberty).

DSDs, and 3) studies of transgender men and transgender women in response to GAHT.

Although it is clear that biologic males outperform biologic females in muscular power, strength, and endurance, primarily

REFERENCES

1. Senefeld JW, Hunter SK, Coleman D, Joyner MJ. Case studies in physiology: male to female transgender swimmer in college athletics. *J Appl Physiol* (1985). 2023;134(4):1032–7.
2. Nokoff NJ, Senefeld J, Krausz C, et al. Sex differences in athletic performance: perspectives on transgender athletes. *Exerc Sport Sci Rev*. 2023;51(3):85–95.
3. Giersch GEW, Charkoudian N, McClung HL. The rise of the female warfighter: physiology, performance, and future directions. *Med Sci Sports Exerc*. 2022;54(4):683–91.
4. Hilton EN, Lundberg TR. Transgender women in the female category of sport: perspectives on testosterone suppression and performance advantage. *Sports Med*. 2021;51(2):199–214.
5. Bloodgood AM, Dawes JJ, Orr RM, et al. Effects of sex and age on physical testing performance for law enforcement agency candidates: implications for academy training. *J Strength Cond Res*. 2021;35(9):2629–35.
6. Xu J, Haigney MC, Levine BD, Dineen EH. The tactical athlete: definitions, cardiovascular assessment, and management, and “fit for duty” standards. *Cardiol Clin*. 2023;41(1):93–105.
7. Bhargava A, Arnold AP, Bangasser DA, et al. Considering sex as a biological variable in basic and clinical studies: an endocrine society scientific statement. *Endocr Rev*. 2021;42(3):219–58.
8. O'Bryan SM, Connor KR, Drummer DJ, et al. Considerations for sex-cognizant research in exercise biology and medicine. *Front Sports Active Living*. 2022;4:903992.

due to the potent effects of testosterone, there remain knowledge gaps in our understanding of the sex and gender differences in athletic performance and the training response of males and females across many different events/sports. Table 5 highlights several areas for opportunity and future directions. Many of the acute exercise and training studies are conducted on men, often with the assumption that the effects are similar in women. The suggested future directions in Table 5 are opportunities for high-impact studies, with the goal of providing a more complete understanding of the sex differences in athletic performance and the adaptations associated with training.

This article is being published as an official pronouncement of the American College of Sports Medicine. This pronouncement was reviewed for the American College of Sports Medicine by members-at-large and the Pronouncements Committee.

Care has been taken to confirm the accuracy of the information present and to describe generally accepted practices. However, the authors, editors, and publisher are not responsible for errors or omissions or for any consequences from application of the information in this publication and make no warranty, expressed or implied, with respect to the currency, completeness, or accuracy of the contents of the publication. Application of this information in a particular situation remains the professional responsibility of the practitioner; the clinical treatments described and recommended may not be considered absolute and universal recommendations.

Click here (<http://links.lww.com/TJACSM/A234>) to download a slide deck that summarizes this American College of Sports Medicine expert consensus statement on The Biological Basis of Sex Differences in Athletic Performance.

S.K.H. reports a financial relationship with the National Institutes of Health (NIH). S.S.A. reports financial relationships with the Grain Foods Foundation, Quality Carbohydrate Coalition, and the US Air Force. K.L.M. has received funding from NIH. N.J.N. reports a financial relationship with Neurocrine Biosciences, Inc, and has received funding from NIH. N.S.S. has received funding from NIH. The other authors have nothing to declare.

9. Handelsman DJ, Hirschberg AL, Berman S. Circulating testosterone as the hormonal basis of sex differences in athletic performance. *Endocr Rev*. 2018;39(5):803–29.
10. Hunter SK. The relevance of sex differences in performance fatigability. *Med Sci Sports Exerc*. 2016;48(11):2247–56.
11. Ansdell P, Thomas K, Hicks KM, et al. Physiological sex differences affect the integrative response to exercise: acute and chronic implications. *Exp Physiol*. 2020;105(12):2007–21.
12. Hunter SK. Sex differences in human fatigability: mechanisms and insight to physiological responses. *Acta Physiol*. 2014;210(4):768–89.
13. National Institutes of Health Office of Research on Women's Health. *Sex & Gender* [Internet]. Bethesda (MD): National Institutes of Health; [cited 2022 Sep 26]. Available from: <https://orwh.od.nih.gov/sex-gender>.
14. Miller VM. Why are sex and gender important to basic physiology and translational and individualized medicine? *Am J Physiol Heart Circ Physiol*. 2014;306(6):H781–8.
15. Teede HJ, Misso ML, Costello MF, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Fertil Steril*. 2018;110(3):364–79.
16. Clark RV, Wald JA, Swerdloff RS, et al. Erratum. *Clin Endocrinol*. 2019;91(3):471–3.

17. Clark RV, Wald JA, Swerdloff RS, et al. Large divergence in testosterone concentrations between men and women: frame of reference for elite athletes in sex-specific competition in sports, a narrative review. *Clin Endocrinol*. 2019;90(1):15–22.
18. Berman S, Garnier PY, Hirschberg AL, et al. Serum androgen levels in elite female athletes. *J Clin Endocrinol Metab*. 2014;99(11):4328–35.
19. Bouvattier C, Mignot B, Lefèvre H, et al. Impaired sexual activity in male adults with partial androgen insensitivity. *J Clin Endocrinol Metab*. 2006;91(9):3310–5.
20. Bui HN, Sluss PM, Blincko S, et al. Dynamics of serum testosterone during the menstrual cycle evaluated by daily measurements with an ID-LC-MS/MS method and a 2nd generation automated immunoassay. *Steroids*. 2013;78(1):96–101.
21. Bui HN, Sluss PM, Hayes FJ, et al. Testosterone, free testosterone, and free androgen index in women: reference intervals, biological variation, and diagnostic value in polycystic ovary syndrome. *Clin Chim Acta*. 2015;450:227–32.
22. Doehnert U, Bertelloni S, Werner R, et al. Characteristic features of reproductive hormone profiles in late adolescent and adult females with complete androgen insensitivity syndrome. *Sex Dev*. 2015;9(2):69–74.
23. Fanelli F, Gambineri A, Belluomo I, et al. Androgen profiling by liquid chromatography–tandem mass spectrometry (LC-MS/MS) in healthy normal-weight ovulatory and anovulatory late adolescent and young women. *J Clin Endocrinol Metab*. 2013;98(7):3058–67.
24. Fénichel P, Paris F, Philibert P, et al. Molecular diagnosis of 5 α -reductase deficiency in 4 elite young female athletes through hormonal screening for hyperandrogenism. *J Clin Endocrinol Metab*. 2013;98(6):E1055–9.
25. Haring R, Hannemann A, John U, et al. Age-specific reference ranges for serum testosterone and androstenedione concentrations in women measured by liquid chromatography–tandem mass spectrometry. *J Clin Endocrinol Metab*. 2012;97(2):408–15.
26. Hart RJ, Doherty DA, McLachlan RI, et al. Testicular function in a birth cohort of young men. *Hum Reprod*. 2015;30(12):2713–24.
27. Hellmann P, Christiansen P, Johannsen TH, et al. Male patients with partial androgen insensitivity syndrome: a longitudinal follow-up of growth, reproductive hormones and the development of gynaecomastia. *Arch Dis Child*. 2012;97(5):403–9.
28. Imperato-McGinley J, Gautier T, Cai LQ, et al. The androgen control of sebum production. Studies of subjects with dihydrotestosterone deficiency and complete androgen insensitivity. *J Clin Endocrinol Metab*. 1993;76(2):524–8.
29. Imperato-McGinley J, Peterson RE, Gautier T, Sturla E. Androgens and the evolution of male-gender identity among male pseudohermaphrodites with 5 α -reductase deficiency. *N Engl J Med*. 1979;300(22):1233–7.
30. Janse F, Eijkemans MJ, Goverde AJ, et al. Assessment of androgen concentration in women: liquid chromatography–tandem mass spectrometry and extraction RIA show comparable results. *Eur J Endocrinol*. 2011;165(6):925–33.
31. Keefe CC, Goldman MM, Zhang K, Clarke N, Reitz RE, Welt CK. Simultaneous measurement of thirteen steroid hormones in women with polycystic ovary syndrome and control women using liquid chromatography–tandem mass spectrometry. *PLoS One*. 2014;9(4):e93805.
32. Kushnir MM, Blamires T, Rockwood AL, et al. Liquid chromatography–tandem mass spectrometry assay for androstenedione, dehydroepiandrosterone, and testosterone with pediatric and adult reference intervals. *Clin Chem*. 2010;56(7):1138–47.
33. Lucas-Herald A, Bertelloni S, Juul A, et al. The long-term outcome of boys with partial androgen insensitivity syndrome and a mutation in the androgen receptor gene. *J Clin Endocrinol Metab*. 2016;101(11):3959–67.
34. Maimoun L, Philibert P, Cammas B, et al. Phenotypical, biological, and molecular heterogeneity of 5 α -reductase deficiency: an extensive international experience of 55 patients. *J Clin Endocrinol Metab*. 2011;96(2):296–307.
35. Melo KF, Mendonça BB, Billerbeck AE, et al. Clinical, hormonal, behavioral, and genetic characteristics of androgen insensitivity syndrome in a Brazilian cohort: five novel mutations in the androgen receptor gene. *J Clin Endocrinol Metab*. 2003;88(7):3241–50.
36. Neale SM, Hocking R, Biswas M, et al. Adult testosterone and calculated free testosterone reference ranges by tandem mass spectrometry. *Ann Clin Biochem*. 2013;50(2):159–61.
37. Shabir I, Khurana ML, Joseph AA, et al. Phenotype, genotype and gender identity in a large cohort of patients from India with 5 α -reductase 2 deficiency. *Andrology*. 2015;3(6):1132–9.
38. Sikaris K, McLachlan RI, Kazlauskas R, et al. Reproductive hormone reference intervals for healthy fertile young men: evaluation of automated platform assays. *J Clin Endocrinol Metab*. 2005;90(11):5928–36.
39. Tosi F, Fiers T, Kaufman JM, et al. Implications of androgen assay accuracy in the phenotyping of women with polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2016;101(2):610–8.
40. Travison TG, Vesper HW, Orwoll E, et al. Harmonized reference ranges for circulating testosterone levels in men of four cohort studies in the United States and Europe. *J Clin Endocrinol Metab*. 2017;102(4):1161–73.
41. Veiga-Junior NN, Rodrigues Medaets PA, Petroli RJ, et al. Clinical and laboratorial features that may differentiate 46,XY DSD due to partial androgen insensitivity and 5 α -reductase type 2 deficiency. *Int J Endocrinol*. 2012;2012:964876.
42. Zhu H, Liu W, Han B, et al. Phenotypic and molecular characteristics in eleven Chinese patients with 5 α -reductase type 2 deficiency. *Clin Endocrinol*. 2014;81(5):711–20.
43. Joyner MJ, Hunter SK, Lucia A, Jones AM. Physiology and fast marathons. *J Appl Physiol* (1985). 2020;128(4):1065–8.
44. Hunter SK, Stevens AA. Sex differences in marathon running with advanced age: physiology or participation? *Med Sci Sports Exerc*. 2013;45(1):148–56.
45. Seiler S, De Koning JJ, Foster C. The fall and rise of the gender difference in elite anaerobic performance 1952–2006. *Med Sci Sports Exerc*. 2007;39(3):534–40.
46. Whipp BJ, Ward SA. Will women soon outrun men? *Nature*. 1992;355(6355):25.
47. Hunter SK, Joyner MJ, Jones AM. The two-hour marathon: what's the equivalent for women? *J Appl Physiol*. 2015;118(10):1321–3.
48. Hunter SK, Stevens AA, Magennis K, et al. Is there a sex difference in the age of elite marathon runners? *Med Sci Sports Exerc*. 2011;43(4):656–64.
49. Institute of Medicine (US) Committee on Understanding the Biology of Sex and Gender Differences. *Exploring the Biological Contributions to Human Health: Does Sex Matter?* Witzmann TM, Pardue M-L, editors. Washington (DC): National Academy Press; 2001.
50. Rosenfeld CS. Sex-dependent differences in voluntary physical activity. *J Neurosci Res*. 2017;95(1-2):279–90.
51. World Health Organization. *Prevalence of insufficient physical activity among adults aged 18+ years (age-standardized estimate) (%)* [Internet]. [cited 2023 Jan 24]. Available from: [https://www.who.int/data/gho/data/indicators/indicator-details/GHO/prevalence-of-insufficient-physical-activity-among-adults-aged-18-years-\(age-standardized-estimate\)-\(-\)](https://www.who.int/data/gho/data/indicators/indicator-details/GHO/prevalence-of-insufficient-physical-activity-among-adults-aged-18-years-(age-standardized-estimate)-(-)).
52. Senefeld J, Smith C, Hunter SK. Sex differences in participation, performance, and age of ultramarathon runners. *Int J Sports Physiol Perform*. 2016;11(7):635–42.
53. Pedersen BK, Saltin B. Exercise as medicine—evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand J Med Sci Sports*. 2015;25(Suppl 3):1–72.
54. Vaccarezza M, Papa V, Milani D, et al. Sex/gender-specific imbalance in CVD: could physical activity help to improve clinical outcome targeting CVD molecular mechanisms in women? *Int J Mol Sci*. 2020;21(4):1477.

55. Kilpatrick M, Hebert E, Bartholomew J. College students' motivation for physical activity: differentiating men's and women's motives for sport participation and exercise. *J Am Coll Heal*. 2005;54(2):87–94.
56. Suggs W. *A Place on the Team: The Triumph and Tragedy of Title IX*. Princeton (NJ): Princeton University Press; 2005.
57. Perras C. Moving towards equal pay for professional female athletes: what we can learn from equal pay legislation in Iceland. *Ind Intl Comp L Rev*. 2019;30:319–48.
58. Enoksen E. Drop-out rate and drop-out reasons among promising Norwegian track and field athletes: a 25 year study. *Scand Sport Stud Forum*. 2011;2:19–43.
59. Costello JT, Bieuzen F, Bleakley CM. Where are all the female participants in Sports and Exercise Medicine research? *Eur J Sport Sci*. 2014;14(8):847–51.
60. Smith ES, McKay AKA, Kuikman M, et al. Auditing the representation of female versus male athletes in sports science and sports medicine research: evidence-based performance supplements. *Nutrients*. 2022;14(5):953.
61. O'Halloran KD. Mind the gap: widening the demographic to establish new norms in human physiology. *J Physiol*. 2020;598(15):3045–7.
62. Devries MC, Jakobi JM. Importance of considering sex and gender in exercise and nutrition research. *Appl Physiol Nutr Metab*. 2021;46(6):iii–vii.
63. Cowan SM, Kemp JL, Arden CL, et al. Sport and exercise medicine/physiotherapy publishing has a gender/sex equity problem: we need action now! *Br J Sports Med*. 2023;57(7):401–7.
64. Beery AK, Zucker I. Sex bias in neuroscience and biomedical research. *Neurosci Biobehav Rev*. 2011;35(3):565–72.
65. Garcia-Sifuentes Y, Maney DL. Reporting and misreporting of sex differences in the biological sciences. *Elife*. 2021;10:e70817.
66. Arnegard ME, Whitten LA, Hunter C, Clayton JA. Sex as a biological variable: a 5-year progress report and call to action. *J Womens Health*. 2020;29(6):858–64.
67. Handelsman DJ. Sex differences in athletic performance emerge coinciding with the onset of male puberty. *Clin Endocrinol*. 2017;87(1):68–72.
68. Senefeld JW, Clayburn AJ, Baker SE, et al. Sex differences in youth elite swimming. *PLoS One*. 2019;14(11):e0225724.
69. Senefeld JW, Lambelet Coleman D, Johnson PW, et al. Divergence in timing and magnitude of testosterone levels between male and female youths. *JAMA*. 2020;324(1):99–101.
70. Sandbakk Ø, Solli GS, Holmberg HC. Sex differences in world-record performance: the influence of sport discipline and competition duration. *Int J Sports Physiol Perform*. 2018;13(1):2–8.
71. Schlegel P, Křehký A. Performance sex differences in CrossFit®. *Sports (Basel)*. 2022;10(11):165.
72. Keenan KG, Senefeld JW, Hunter SK. Girls in the boat: sex differences in rowing performance and participation. *PLoS One*. 2018;13(1):e0191504.
73. Senefeld J, Joyner MJ, Stevens A, Hunter SK. Sex differences in elite swimming with advanced age are less than marathon running. *Scand J Med Sci Sports*. 2016;26(1):17–28.
74. Tiller NB, Elliott-Sale KJ, Knechtle B, et al. Do sex differences in physiology confer a female advantage in ultra-endurance sport? *Sports Med*. 2021;51(5):895–915.
75. Besson T, Macchi R, Rossi J, et al. Sex differences in endurance running. *Sports Med*. 2022;52(6):1235–57.
76. Lepers R, Knechtle B, Stapley PJ. Trends in triathlon performance: effects of sex and age. *Sports Med*. 2013;43(9):851–63.
77. Tamopolsky MA. Sex differences in exercise metabolism and the role of 17-beta estradiol. *Med Sci Sports Exerc*. 2008;40(4):648–54.
78. Deaner RO, Carter RE, Joyner MJ, Hunter SK. Men are more likely than women to slow in the marathon. *Med Sci Sports Exerc*. 2015;47(3):607–16.
79. Knechtle B, Dalamitros AA, Barbosa TM, et al. Sex differences in swimming disciplines—can women outperform men in swimming? *Int J Environ Res Public Health*. 2020;17(10):3651.
80. Hamilton BR, Guppy FM, Barrett J, et al. Integrating transwomen athletes into elite competition: the case of elite archery and shooting. *Eur J Sport Sci*. 2021;21(11):1500–9.
81. Joyner MJ, Coyle EF. Endurance exercise performance: the physiology of champions. *J Physiol*. 2008;586(1):35–44.
82. Hydren JR, Borges AS, Sharp MA. Systematic review and meta-analysis of predictors of military task performance: maximal lift capacity. *J Strength Cond Res*. 2017;31(4):1142–64.
83. Joffe SA, Tallent J. Neuromuscular predictors of competition performance in advanced international female weightlifters: a cross-sectional and longitudinal analysis. *J Sports Sci*. 2020;38(9):985–93.
84. Miller AE, MacDougall JD, Tarnopolsky MA, Sale DG. Gender differences in strength and muscle fiber characteristics. *Eur J Appl Physiol Occup Physiol*. 1993;66(3):254–62.
85. Senefeld J, Pereira HM, Elliott N, et al. Sex differences in mechanisms of recovery after isometric and dynamic fatiguing tasks. *Med Sci Sports Exerc*. 2018;50(5):1070–83.
86. Hubal MJ, Gordish-Dressman H, Thompson PD, et al. Variability in muscle size and strength gain after unilateral resistance training. *Med Sci Sports Exerc*. 2005;37(6):964–72.
87. Alcazar J, Aagaard P, Haddock B, et al. Age- and sex-specific changes in lower-limb muscle power throughout the lifespan. *J Gerontol A Biol Sci Med Sci*. 2020;75(7):1369–78.
88. Suetta C, Haddock B, Alcazar J, et al. The Copenhagen Sarcopenia Study: lean mass, strength, power, and physical function in a Danish cohort aged 20–93 years. *J Cachexia Sarcopenia Muscle*. 2019;10(6):1316–29.
89. Brinckmann P, Hoefert H, Jongen HT. Sex differences in the skeletal geometry of the human pelvis and hip joint. *J Biomech*. 1981;14(6):427–30.
90. Gallagher D, Visser M, De Meersman RE, et al. Appendicular skeletal muscle mass: effects of age, gender, and ethnicity. *J Appl Physiol*. 1997;83(1):229–39.
91. Hunter SK, Butler JE, Todd G, et al. Supraspinal fatigue does not explain the sex difference in muscle fatigue of maximal contractions. *J Appl Physiol*. 2006;101(4):1036–44.
92. Delgadillo JD, Sundberg CW, Kwon M, Hunter SK. Fatigability of the knee extensor muscles during high-load fast and low-load slow resistance exercise in young and older adults. *Exp Gerontol*. 2021;154:111546.
93. Sundberg CW, Kuplic A, Hassanlouei H, Hunter SK. Mechanisms for the age-related increase in fatigability of the knee extensors in old and very old adults. *J Appl Physiol*. 2018;125(1):146–58.
94. Keller ML, Pruse J, Yoon T, et al. Supraspinal fatigue is similar in men and women for a low-force fatiguing contraction. *Med Sci Sports Exerc*. 2011;43(10):1873–83.
95. Kent-Braun JA, Ng AV. Specific strength and voluntary muscle activation in young and elderly women and men. *J Appl Physiol*. 1999;87(1):22–9.
96. Jo D, Goubran M, Bilodeau M. Sex differences in central and peripheral fatigue induced by sustained isometric ankle plantar flexion. *J Electromyogr Kinesiol*. 2022;65:102676.
97. Rozand V, Senefeld JW, Hassanlouei H, Hunter SK. Voluntary activation and variability during maximal dynamic contractions with aging. *Eur J Appl Physiol*. 2017;117(12):2493–507.
98. Molenaar JP, McNeil CJ, Bredius MS, Gandevia SC. Effects of aging and sex on voluntary activation and peak relaxation rate of human elbow flexors studied with motor cortical stimulation. *Age (Dordr)*. 2013;35(4):1327–37.
99. Hosler WW, Morrow JR Jr. Arm and leg strength compared between young women and men after allowing for differences in body size and composition. *Ergonomics*. 1982;25(4):309–13.
100. Alway SE, Grumbt WH, Gonyea WJ, Stray-Gundersen J. Contrasts in muscle and myofibers of elite male and female bodybuilders. *J Appl Physiol*. 1989;67(1):24–31.
101. Staron RS, Hagerman FC, Hikida RS, et al. Fiber type composition of the vastus lateralis muscle of young men and women. *J Histochem Cytochem*. 2000;48(5):623–9.

102. Toft I, Lindal S, Bonaa KH, Jenssen T. Quantitative measurement of muscle fiber composition in a normal population. *Muscle Nerve*. 2003;28(1):101–8.
103. Haizlip KM, Harrison BC, Leinwand LA. Sex-based differences in skeletal muscle kinetics and fiber-type composition. *Physiology*. 2015;30(1):30–9.
104. Fournier G, Bernard C, Cieviet-Bonfils M, et al. Sex differences in semitendinosus muscle fiber-type composition. *Scand J Med Sci Sports*. 2022;32(4):720–7.
105. Horwath O, Moberg M, Larsen FJ, et al. Influence of sex and fiber type on the satellite cell pool in human skeletal muscle. *Scand J Med Sci Sports*. 2021;31(2):303–12.
106. Porter MM, Stuart S, Boij M, Lexell J. Capillary supply of the tibialis anterior muscle in young, healthy, and moderately active men and women. *J Appl Physiol*. 2002;92(4):1451–7.
107. Roepstorff C, Thiele M, Hillig T, et al. Higher skeletal muscle alpha2AMPK activation and lower energy charge and fat oxidation in men than in women during submaximal exercise. *J Physiol*. 2006;574(Pt 1):125–38.
108. Trappe S, Gallagher P, Harber M, et al. Single muscle fibre contractile properties in young and old men and women. *J Physiol*. 2003; 552(1):47–58.
109. Barnouin Y, McPhee JS, Butler-Browne G, et al. Coupling between skeletal muscle fiber size and capillarization is maintained during healthy aging. *J Cachexia Sarcopenia Muscle*. 2017;8(4): 647–59.
110. Teigen LE, Sundberg CW, Kelly LJ, et al. Ca²⁺ dependency of limb muscle fiber contractile mechanics in young and older adults. *Am J Physiol Cell Physiol*. 2020;318(6):C1238–51.
111. Grosicki GJ, Zepeda CS, Sundberg CW. Single muscle fibre contractile function with ageing. *J Physiol*. 2022;600(23):5005–26.
112. Sundberg CW, Hunter SK, Trappe SW, et al. Effects of elevated H⁺ and P_i on the contractile mechanics of skeletal muscle fibres from young and old men: implications for muscle fatigue in humans. *J Physiol*. 2018;596(17):3993–4015.
113. Krivickas LS, Suh D, Wilkins J, et al. Age- and gender-related differences in maximum shortening velocity of skeletal muscle fibers. *Am J Phys Med Rehabil*. 2001;80(6):447–55 quiz 56–7.
114. Simoneau JA, Lortie G, Boulay MR, et al. Skeletal muscle histochemical and biochemical characteristics in sedentary male and female subjects. *Can J Physiol Pharmacol*. 1985;63(1):30–5.
115. Maher AC, Fu MH, Isfort RJ, et al. Sex differences in global mRNA content of human skeletal muscle. *PLoS One*. 2009;4(7):e6335.
116. Simoneau JA, Bouchard C. Human variation in skeletal muscle fiber-type proportion and enzyme activities. *Am J Phys*. 1989; 257(4 Pt 1):E567–72.
117. Esbjornsson-Liljedahl M, Sundberg CJ, Norman B, Jansson E. Metabolic response in type I and type II muscle fibers during a 30-scycle sprint in men and women. *J Appl Physiol* (1985). 1999;87(4):1326–32.
118. Carter SL, Rennie CD, Hamilton SJ, Tamopolsky MA. Changes in skeletal muscle in males and females following endurance training. *Can J Physiol Pharmacol*. 2001;79(5):386–92.
119. Esbjornsson-Liljedahl M, Bodin K, Jansson E. Smaller muscle ATP reduction in women than in men by repeated bouts of sprint exercise. *J Appl Physiol*. 2002;93(3):1075–83.
120. Esbjornsson M, Rundqvist HC, Mascher H, et al. Sprint exercise enhances skeletal muscle p70S6k phosphorylation and more so in women than in men. *Acta Physiol*. 2012;205(3):411–22.
121. Larsson B, Kadi F, Lindvall B, Gerdl B. Surface electromyography and peak torque of repetitive maximum isokinetic plantar flexions in relation to aspects of muscle morphology. *J Electromyogr Kinesiol*. 2006;16(3):281–90.
122. Wust RC, Morse CI, de Haan A, et al. Sex differences in contractile properties and fatigue resistance of human skeletal muscle. *Exp Physiol*. 2008;93(7):843–50.
123. Yoon T, Doyel R, Widule C, Hunter SK. Sex differences with aging in the fatigability of dynamic contractions. *Exp Gerontol*. 2015;70:1–10.
124. Costill DL, Daniels J, Evans W, et al. Skeletal muscle enzymes and fiber composition in male and female track athletes. *J Appl Physiol*. 1976;40(2):149–54.
125. Ricoy JR, Encinas AR, Cabello A, et al. Histochemical study of the vastus lateralis muscle fibre types of athletes. *J Physiol Biochem*. 1998;54(1):41–7.
126. Wilson JM, Loenneke JP, Jo E, et al. The effects of endurance, strength, and power training on muscle fiber type shifting. *J Strength Cond Res*. 2012;26(6):1724–9.
127. Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. *J Appl Physiol*. 2000;89(1):81–8.
128. Senefeld J, Yoon T, Bement MH, Hunter SK. Fatigue and recovery from dynamic contractions in men and women differ for arm and leg muscles. *Muscle Nerve*. 2013;48(3):436–9.
129. Senefeld J, Yoon T, Hunter SK. Age differences in dynamic fatigability and variability of arm and leg muscles: associations with physical function. *Exp Gerontol*. 2017;87(Pt A):74–83.
130. Bartolomei S, Grillone G, Di Michele R, Cortesi M. A comparison between male and female athletes in relative strength and power performances. *J Funct Morphol Kinesiol*. 2021;6(1):17.
131. Russ DW, Towse TF, Wigmore DM, et al. Contrasting influences of age and sex on muscle fatigue. *Med Sci Sports Exerc*. 2008;40(2): 234–41.
132. Avin KG, Naughton MR, Ford BW, et al. Sex differences in fatigue resistance are muscle group dependent. *Med Sci Sports Exerc*. 2010; 42(10):1943–50.
133. Maughan RJ, Watson JS, Weir J. Strength and cross-sectional area of human skeletal muscle. *J Physiol*. 1983;338:37–49.
134. Lindle RS, Metter EJ, Lynch NA, et al. Age and gender comparisons of muscle strength in 654 women and men aged 20–93 yr. *J Appl Physiol*. 1997;83(5):1581–7.
135. Welle S, Tawil R, Thornton CA. Sex-related differences in gene expression in human skeletal muscle. *PLoS One*. 2008;3(1):e1385.
136. Ivey FM, Tracy BL, Lemmer JT, et al. Effects of strength training and detraining on muscle quality: age and gender comparisons. *J Gerontol A Biol Sci Med Sci*. 2000;55(3):B152–7; discussion B8–9.
137. Sundberg CW, Hunter SK, Bundle MW. Rates of performance loss and neuromuscular activity in men and women during cycling: evidence for a common metabolic basis of muscle fatigue. *J Appl Physiol*. 2017;122(1):130–41.
138. James JJ, Leach OK, Young AM, et al. The exercise power-duration relationship is equally reproducible in eumenorrheic female and male humans. *J Appl Physiol*. 2023;134(2):230–41.
139. Ravindrakumar A, Bommasamudram T, Tod D, et al. Daily variation in performance measures related to anaerobic power and capacity: a systematic review. *Chronobiol Int*. 2022;39(3):421–55.
140. Zera JN, Nagle EF, Connell E, et al. Gender differences and the influence of body composition on land and pool-based assessments of anaerobic power and capacity. *Int J Environ Res Public Health*. 2022;19(13):7902.
141. Sollie O, Losnegard T. Sex differences in physiological determinants of performance in elite adolescent, junior, and senior cross-country skiers. *Int J Sports Physiol Perform*. 2022;17(8):1304–11.
142. Mayhew JL, Salm PC. Gender differences in anaerobic power tests. *Eur J Appl Physiol Occup Physiol*. 1990;60(2):133–8.
143. Maud PJ, Shultz BB. Gender comparisons in anaerobic power and anaerobic capacity tests. *Br J Sports Med*. 1986;20(2):51–4.
144. Weber CL, Chia M, Inbar O. Gender differences in anaerobic power of the arms and legs—a scaling issue. *Med Sci Sports Exerc*. 2006; 38(1):129–37.
145. Mayhew JL, Hancock K, Rollison L, et al. Contributions of strength and body composition to the gender difference in anaerobic power. *J Sports Med Phys Fitness*. 2001;41(1):33–8.
146. Esbjornsson M, Sylven C, Holm I, Jansson E. Fast twitch fibres may predict anaerobic performance in both females and males. *Int J Sports Med*. 1993;14(05):257–63.

147. Murphy MM, Patton JF, Frederick FA. Comparative anaerobic power of men and women. *Aviat Space Environ Med.* 1986;57(7):636–41.
148. Bulbulian R, Jeong JW, Murphy M. Comparison of anaerobic components of the Wingate and Critical Power tests in males and females. *Med Sci Sports Exerc.* 1996;28(10):1336–41.
149. Perez-Gomez J, Rodriguez GV, Ara I, et al. Role of muscle mass on sprint performance: gender differences? *Eur J Appl Physiol.* 2008; 102(6):685–94.
150. Komi PV, Karlsson J. Skeletal muscle fibre types, enzyme activities and physical performance in young males and females. *Acta Physiol Scand.* 1978;103(2):210–8.
151. Jaworowski A, Porter MM, Holmback AM, et al. Enzyme activities in the tibialis anterior muscle of young moderately active men and women: relationship with body composition, muscle cross-sectional area and fibre type composition. *Acta Physiol Scand.* 2002;176(3):215–25.
152. Green HJ, Fraser IG, Ranney DA. Male and female differences in enzyme activities of energy metabolism in vastus lateralis muscle. *J Neurol Sci.* 1984;65(3):323–31.
153. Bredella MA. Sex differences in body composition. *Adv Exp Med Biol.* 2017;1043:9–27.
154. Healy ML, Gibney J, Pentecost C, et al. Endocrine profiles in 693 elite athletes in the postcompetition setting. *Clin Endocrinol.* 2014;81(2):294–305.
155. Jackson AS, Stanforth PR, Gagnon J, et al. The effect of sex, age and race on estimating percentage body fat from body mass index: The Heritage Family Study. *Int J Obes Relat Metab Disord.* 2002; 26(6):789–96.
156. White UA, Tchoukalova YD. Sex dimorphism and depot differences in adipose tissue function. *Biochim Biophys Acta.* 2014; 1842(3):377–92.
157. Gallagher D, Visser M, Sepúlveda D, et al. How useful is body mass index for comparison of body fatness across age, sex, and ethnic groups? *Am J Epidemiol.* 1996;143(3):228–39.
158. Bhasin S, Woodhouse L, Storer TW. Androgen effects on body composition. *Growth Hormon IGF Res.* 2003;13(Suppl A):S63–71. doi:10.1016/s1096-6374(03)00058-3.
159. Wells JC. Sexual dimorphism of body composition. *Best Pract Res Clin Endocrinol Metab.* 2007;21(3):415–30.
160. Fryar CD, Carroll MD, Gu Q, et al. Anthropometric reference data for children and adults: United States, 2015–2018. *Vital Health Stat* 3. 2021;36:1–44.
161. Jensen K, Johansen L, Secher NH. Influence of body mass on maximal oxygen uptake: effect of sample size. *Eur J Appl Physiol.* 2001; 84(3):201–5.
162. Ben Mansour G, Kacem A, Ishak M, et al. The effect of body composition on strength and power in male and female students. *BMC Sports Sci Med Rehabil.* 2021;13(1):150.
163. Levine BD. $\dot{V}O_{2\max}$: what do we know, and what do we still need to know? *J Physiol.* 2008;586(1):25–34.
164. Loe H, Rognmo Ø, Saltin B, Wisløff U. Aerobic capacity reference data in 3816 healthy men and women 20–90 years. *PLoS One.* 2013; 8(5):e64319.
165. Santisteban KJ, Lovering AT, Halliwill JR, Minson CT. Sex differences in $\dot{V}O_{2\max}$ and the impact on endurance-exercise performance. *Int J Environ Res Public Health.* 2022;19(9):4946.
166. Bunc V, Heller J. Energy cost of running in similarly trained men and women. *Eur J Appl Physiol Occup Physiol.* 1989;59(3):178–83.
167. Pate RR, O'Neill JR. American women in the marathon. *Sports Med.* 2007;37(4):294–8.
168. Jones AM. The physiology of the world record holder for the women's marathon. *Int J Sports Sci Coach.* 2006;1:101–16.
169. Pollock ML. Submaximal and maximal working capacity of elite distance runners. Part I: cardiorespiratory aspects. *Ann N Y Acad Sci.* 1977;301:310–22.
170. Saltin B, Astrand PO. Maximal oxygen uptake in athletes. *J Appl Physiol.* 1967;23(3):353–8.
171. Durstine JL, Pate RR, Sparling PB, et al. Lipid, lipoprotein, and iron status of elite women distance runners. *Int J Sports Med.* 1987;8(Suppl 2): 119–23.
172. Riley-Hagan M, Peshock RM, Stray-Gundersen J, et al. Left ventricular dimensions and mass using magnetic resonance imaging in female endurance athletes. *Am J Cardiol.* 1992;69(12):1067–74.
173. Joyner MJ. Physiological limits to endurance exercise performance: influence of sex. *J Physiol.* 2017;595(9):2949–54.
174. Sparling PB. A meta-analysis of studies comparing maximal oxygen uptake in men and women. *Res Q Exerc Sport.* 1980;51(3): 542–52.
175. Bassareo PP, Crisafulli A. Gender differences in hemodynamic regulation and cardiovascular adaptations to dynamic exercise. *Curr Cardiol Rev.* 2020;16(1):65–72.
176. St Pierre SR, Peirlinck M, Kuhl E. Sex matters: a comprehensive comparison of female and male hearts. *Front Physiol.* 2022;13: 831179.
177. Fu Q, Levine BD. Cardiovascular response to exercise in women. *Med Sci Sports Exerc.* 2005;37(8):1433–5.
178. Maldonado-Martin S, Mujika I, Padilla S. Physiological variables to use in the gender comparison in highly trained runners. *J Sports Med Phys Fitness.* 2004;44(1):8–14.
179. Venables MC, Achten J, Jeukendrup AE. Determinants of fat oxidation during exercise in healthy men and women: a cross-sectional study. *J Appl Physiol.* 2005;98(1):160–7.
180. Cureton K, Bishop P, Hutchinson P, et al. Sex difference in maximal oxygen uptake. Effect of equating haemoglobin concentration. *Eur J Appl Physiol Occup Physiol.* 1986;54(6):656–60.
181. Schmidt W, Prommer N. Impact of alterations in total hemoglobin mass on $\dot{V}O_{2\max}$. *Exerc Sport Sci Rev.* 2010;38(2):68–75.
182. Cheetham ME, Boobis LH, Brooks S, Williams C. Human muscle metabolism during sprint running. *J Appl Physiol.* 1986;61(1): 54–60.
183. Romijn JA, Coyle EF, Sidossis LS, et al. Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity and duration. *Am J Phys.* 1993;265(3 Pt 1):E380–91.
184. Hargreaves M, Sprietzer LL. Exercise metabolism: Fuels for the fire. In: Zierath JR, Joyner MJ, Hawley JA, editors. *The Biology of Exercise Cold.* Spring Harbor (NY): Cold Spring Harbor Laboratory Press; 2017. pp. 57–72.
185. Brooks GA, Mercier J. Balance of carbohydrate and lipid utilization during exercise: the “crossover” concept. *J Appl Physiol.* 1994;76(6): 2253–61.
186. Coggan AR, Raguso CA, Williams BD, et al. Glucose kinetics during high-intensity exercise in endurance-trained and untrained humans. *J Appl Physiol.* 1995;78(3):1203–7.
187. Tarnopolsky LJ, MacDougall JD, Atkinson SA, et al. Gender differences in substrate for endurance exercise. *J Appl Physiol.* 1990; 68(1):302–8.
188. Horton TJ, Pagliassotti MJ, Hobbs K, Hill JO. Fuel metabolism in men and women during and after long-duration exercise. *J Appl Physiol.* 1998;85(5):1823–32.
189. Cano A, Ventura L, Martinez G, et al. Analysis of sex-based differences in energy substrate utilization during moderate-intensity aerobic exercise. *Eur J Appl Physiol.* 2022;122(1):29–70.
190. Billaut F, Bishop D. Muscle fatigue in males and females during multiple-sprint exercise. *Sports Med.* 2009;39(4):257–78.
191. Russ DW, Lanza IR, Rothman D, Kent-Braun JA. Sex differences in glycolysis during brief, intense isometric contractions. *Muscle Nerve.* 2005;32(5):647–55.
192. Lamont LS, McCullough AJ, Kalhan SC. Gender differences in leucine, but not lysine, kinetics. *J Appl Physiol.* 2001;91(1):357–62.
193. Joyner MJ, Ruiz JR, Lucia A. The two-hour marathon: who and when? *J Appl Physiol.* 2011;110(1):275–7.
194. Jones AM, Burnley M, Black MI, et al. The maximal metabolic steady state: redefining the “gold standard”. *Physiol Rep.* 2019; 7(10):e14098.

195. Jones AM, Vanhatalo A, Burnley M, et al. Critical power: implications for determination of VO_{2max} and exercise tolerance. *Med Sci Sports Exerc.* 2010;42(10):1876–90.
196. Helgerud J, Ingjer F, Stromme SB. Sex differences in performance-matched marathon runners. *Eur J Appl Physiol Occup Physiol.* 1990;61(5-6):433–9.
197. Helgerud J. Maximal oxygen uptake, anaerobic threshold and running economy in women and men with similar performances level in marathons. *Eur J Appl Physiol Occup Physiol.* 1994;68(2): 155–61.
198. Joyner MJ. Physiological limiting factors and distance running: influence of gender and age on record performances. *Exerc Sport Sci Rev.* 1993;21:103–33.
199. Davies CT, Thompson MW. Aerobic performance of female marathon and male ultramarathon athletes. *Eur J Appl Physiol Occup Physiol.* 1979;41(4):233–45.
200. Hill AV. The physiological basis of athletic records. *Nature.* 1925; 116(2919):544–8.
201. Poole DC, Burnley M, Vanhatalo A, et al. Critical power: an important fatigue threshold in exercise physiology. *Med Sci Sports Exerc.* 2016;48(11):2320–34.
202. Ansdell P, Brownstein CG, Skarabot J, et al. Sex differences in fatigability and recovery relative to the intensity–duration relationship. *J Physiol.* 2019;597(23):5577–95.
203. Russ DW, Kent-Braun JA. Sex differences in human skeletal muscle fatigue are eliminated under ischemic conditions. *J Appl Physiol.* 2003;94(6):2414–22.
204. Hunter SK. Sex differences in fatigability of dynamic contractions. *Exp Physiol.* 2016;101(2):250–5.
205. Hunter SK. Sex differences and mechanisms of task-specific muscle fatigue. *Exerc Sport Sci Rev.* 2009;37(3):113–22.
206. Billaut F, Bishop DJ. Mechanical work accounts for sex differences in fatigue during repeated sprints. *Eur J Appl Physiol.* 2012;112(4): 1429–36.
207. Laurent CM, Green JM, Bishop PA, et al. Effect of gender on fatigue and recovery following maximal intensity repeated sprint performance. *J Sports Med Phys Fitness.* 2010;50(3):243–53.
208. Lewis MH, Siedler MR, Lamadrid P, et al. Sex differences may exist for performance fatigue but not recovery after single-joint upper-body and lower-body resistance exercise. *J Strength Cond Res.* 2022;36(6):1498–505.
209. Joyner MJ. Modeling: optimal marathon performance on the basis of physiological factors. *J Appl Physiol.* 1991;70(2):683–7.
210. Coyle EF, Sidossis LS, Horowitz JF, Beltz JD. Cycling efficiency is related to the percentage of type I muscle fibers. *Med Sci Sports Exerc.* 1992;24(7):782–8.
211. Coyle EF. Improved muscular efficiency displayed as Tour de France champion matures. *J Appl Physiol.* 2005;98(6):2191–6.
212. Loftin M, Sothorn M, Tuuri G, Tompkins C, et al. Gender comparison of physiologic and perceptual responses in recreational marathon runners. *Int J Sports Physiol Perform.* 2009;4(3):307–16.
213. Daniels J, Daniels N. Running economy of elite male and elite female runners. *Med Sci Sports Exerc.* 1992;24(4):483–9.
214. Mendonca GV, Matos P, Correia JM. Running economy in recreational male and female runners with similar levels of cardiovascular fitness. *J Appl Physiol.* 2020;129(3):508–15.
215. Zamparo P, Cortesi M, Gatta G. The energy cost of swimming and its determinants. *Eur J Appl Physiol.* 2020;120(1):41–66.
216. Pendergast DR, Di Prampero PE, Craig AB Jr., et al. Quantitative analysis of the front crawl in men and women. *J Appl Physiol Respir Environ Exerc Physiol.* 1977;43(3):475–9.
217. Klentrou PP, Montpetit RR. Energetics of backstroke swimming in males and females. *Med Sci Sports Exerc.* 1992;24(3):371–5.
218. Lucas-Herald AK, Bashamboo A. Gonadal development. *Endocr Dev.* 2014;27:1–16.
219. MacLaughlin DT, Donahoe PK. Sex determination and differentiation. *N Engl J Med.* 2004;350(4):367–78.
220. Lee PA, Houk CP, Ahmed SF, Hughes IA. Consensus statement on management of intersex disorders. International Consensus Conference on Intersex Pediatrics. *Pediatrics.* 2006;118(2):e488–500.
221. Lanciotti L, Cofini M, Leonardi A, et al. Up-to-date review about minipuberty and overview on hypothalamic-pituitary-gonadal axis activation in fetal and neonatal life. *Front Endocrinol (Lausanne).* 2018;9:410.
222. Kiviranta P, Kuri-Hänninen T, Saari A, et al. Transient postnatal gonadal activation and growth velocity in infancy. *Pediatrics.* 2016;138(1):e20153561.
223. Becker M, Hesse V. Minipuberty: why does it happen? *Horm Res Paediatr.* 2020;93(2):76–84.
224. Veldhuis JD, Roemmich JN, Richmond EJ, et al. Endocrine control of body composition in infancy, childhood, and puberty. *Endocr Rev.* 2005;26(1):114–46.
225. Mizuguchi S, Cunanan AJ, Suarez DG, et al. Performance comparisons of youth weightlifters as a function of age group and sex. *J Funct Morphol Kinesiol.* 2021;6(3):57.
226. Ervin RB, Fryar CD, Wang CY, et al. Strength and body weight in US children and adolescents. *Pediatrics.* 2014;134(3):e782–9.
227. Lesinski M, Schmelcher A, Herz M, et al. Maturation-, age-, and sex-specific anthropometric and physical fitness percentiles of German elite young athletes. *PLoS One.* 2020;15(8):e0237423.
228. McManus AM, Armstrong N. Physiology of elite young female athletes. *Med Sport Sci.* 2011;56:23–46.
229. Chen W, Hammond-Bennett A, Hynar A, Mason S. Health-related physical fitness and physical activity in elementary school students. *BMC Public Health.* 2018;18(1):195.
230. Martínez-Vizcaino V, Pozuelo-Carrascosa DP, García-Prieto JC, et al. Effectiveness of a school-based physical activity intervention on adiposity, fitness and blood pressure: MOVI-KIDS study. *Br J Sports Med.* 2020;54(5):279–85.
231. Hyde ET, Omura JD, Fulton JE, et al. Disparities in youth sports participation in the U.S., 2017–2018. *Am J Prev Med.* 2020;59(5): e207–10.
232. Belcher BR, Berrigan D, Dodd KW, et al. Physical activity in US youth: effect of race/ethnicity, age, gender, and weight status. *Med Sci Sports Exerc.* 2010;42(12):2211–21.
233. Gortmaker SL, Lee R, Craddock AL, et al. Disparities in youth physical activity in the United States: 2003–2006. *Med Sci Sports Exerc.* 2012;44(5):888–93.
234. Van Der Horst K, Paw MJ, Twisk JW, Van Mechelen W. A brief review on correlates of physical activity and sedentariness in youth. *Med Sci Sports Exerc.* 2007;39(8):1241–50.
235. Boiché J, Plaza M, Chalabaev A, et al. Social antecedents and consequences of gender-sport stereotypes during adolescence. *Psychol Women Q.* 2014;38(2):259–74.
236. Fühner T, Granacher U, Golle K, Kliegl R. Age and sex effects in physical fitness components of 108,295 third graders including 515 primary schools and 9 cohorts. *Sci Rep.* 2021;11(1):17566.
237. Pozuelo-Carrascosa DP, García-Hermoso A, Álvarez-Bueno C, et al. Effectiveness of school-based physical activity programmes on cardiorespiratory fitness in children: a meta-analysis of randomised controlled trials. *Br J Sports Med.* 2018;52(19):1234–40.
238. Milanese C, Sandri M, Cavedon V, Zancanaro C. The role of age, sex, anthropometry, and body composition as determinants of physical fitness in nonobese children aged 6–12. *PeerJ.* 2020; 8:e8657.
239. Atkinson MA, James J, Hunter SK. Sex differences in performance of elite youth track and field athletes. In: American College of Sports Medicine Annual Meeting 2023; 2023 May 30–June 3; Denver, CO.
240. Kaplowitz PB, Oberfield SE. Reexamination of the age limit for defining when puberty is precocious in girls in the United States: implications for evaluation and treatment. Drug and Therapeutics and Executive Committees of the Lawson Wilkins Pediatric Endocrine Society. *Pediatrics.* 1999;104(4):936–41.

241. Osinubi AA, Lewis-de Los Angeles CP, Poitevien P, Topor LS. Are Black girls exhibiting puberty earlier? Examining implications of race-based guidelines. *Pediatrics*. 2022;150(2):e2021055595.
242. Sperling M. *Pediatric Endocrinology*. 4th ed. Philadelphia (PA): Saunders/Elsevier; 2014.
243. Tonnessen E, Svendsen IS, Olsen IC, et al. Performance development in adolescent track and field athletes according to age, sex and sport discipline. *PLoS One*. 2015;10(6):e0129014.
244. Handelsman DJ. History of androgens and androgen action. *Best Pract Res Clin Endocrinol Metab*. 2022;36(4):101629.
245. Nodelovitz M. Androgen effects on bone and muscle. *Fertil Steril*. 2002;77:34–41.
246. Crewther BT, Cook C, Cardinale M, et al. Two emerging concepts for elite athletes: the short-term effects of testosterone and cortisol on the neuromuscular system and the dose–response training role of these endogenous hormones. *Sports Med*. 2011;41(2):103–23.
247. Rosner W, Auchus RJ, Azziz R, et al. Utility, limitations, and pitfalls in measuring testosterone: an Endocrine Society Position Statement. *J Clin Endocrinol Metabol*. 2007;92(2):405–13.
248. Trost LW, Mulhall JP. Challenges in testosterone measurement, data interpretation, and methodological appraisal of interventional trials. *J Sex Med*. 2016;13(7):1029–46.
249. Cardinale M, Stone MH. Is testosterone influencing explosive performance? *J Strength Cond Res*. 2006;20(1):103–7.
250. Eklund E, Berglund B, Labrie F, et al. Serum androgen profile and physical performance in women Olympic athletes. *Br J Sports Med*. 2017;51(17):1301–8.
251. Berman S, Garnier P-Y. Serum androgen levels and their relation to performance in track and field: mass spectrometry results from 2127 observations in male and female elite athletes. *Br J Sports Med*. 2017;51(17):1309–14.
252. Berman S, Hirschberg AL, Kowalski J, Eklund E. Serum androgen levels are positively correlated with athletic performance and competition results in elite female athletes. *Br J Sports Med*. 2018;52(23):1531–2.
253. Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, editors. *Williams Textbook of Endocrinology*. 13th ed. Philadelphia (PA): Elsevier; 2016.
254. Hewitt S, Korach KS, Crowley WF Jr. Molecular Biology and Physiology of Estrogen Action [Internet]. Snyder PJ, Crowley WF Jr., Martin KA, editors. *UpToDate*. Wellesley (MA): 2021 [cited 2022 Sep 26]. Available from: <https://www.uptodate.com/contents/molecular-biology-and-physiology-of-estrogen-action>.
255. Sims ST, Ware L, Capodilupo ER. Patterns of endogenous and exogenous ovarian hormone modulation on recovery metrics across the menstrual cycle. *BMJ Open Sport Exerc Med*. 2021;7(3):e001047.
256. Patel S, Homaei A, Raju AB, Meher BR. Estrogen: the necessary evil for human health, and ways to tame it. *Biomed Pharmacother*. 2018;102:403–11.
257. Hansen M. Female hormones: do they influence muscle and tendon protein metabolism? *Proc Nutr Soc*. 2018;77(1):32–41.
258. Russell N, Grossmann M. Mechanisms in endocrinology: estradiol as a male hormone. *Eur J Endocrinol*. 2019;181(1):R23–43.
259. Kong SH, Kim JH, Lee JH, et al. Dehydroepiandrosterone sulfate and free testosterone but not estradiol are related to muscle strength and bone microarchitecture in older adults. *Calcif Tissue Int*. 2019;105(3):285–93.
260. Cadejani FA, Kater CE. Basal hormones and biochemical markers as predictors of overtraining syndrome in male athletes: the EROS-BASAL study. *J Athl Train*. 2019;54(8):906–14.
261. Wiik A, Gustafsson T, Esbjörnsson M, et al. Expression of oestrogen receptor alpha and beta is higher in skeletal muscle of highly endurance-trained than of moderately active men. *Acta Physiol Scand*. 2005;184(2):105–12.
262. Janse De Jonge XAK, Thompson MW, Chuter VH, et al. Exercise performance over the menstrual cycle in temperate and hot, humid conditions. *Med Sci Sports Exerc*. 2012;44(11):2190–8.
263. McNulty KL, Elliott-Sale KJ, Dolan E, et al. The effects of menstrual cycle phase on exercise performance in eumenorrheic women: a systematic review and meta-analysis. *Sports Med*. 2020;50(10):1813–27.
264. Hirschberg AL. Challenging aspects of research on the influence of the menstrual cycle and oral contraceptives on physical performance. *Sports Med*. 2022;52(7):1453–6.
265. Hackney AC. Effects of the menstrual cycle on resting muscle glycogen content. *Horm Metab Res*. 1990;22(12):647.
266. Sims ST, Heather AK. Myths and methodologies: reducing scientific design ambiguity in studies comparing sexes and/or menstrual cycle phases. *Exp Physiol*. 2018;103(10):1309–17.
267. Oosthuyse T, Bosch AN. Oestrogen's regulation of fat metabolism during exercise and gender specific effects. *Curr Opin Pharmacol*. 2012;12(3):363–71.
268. Oosthuyse T, Bosch AN. The effect of the menstrual cycle on exercise metabolism: implications for exercise performance in eumenorrheic women. *Sports Med*. 2010;40(3):207–27.
269. D'Eon TM, Sharoff C, Chipkin SR, et al. Regulation of exercise carbohydrate metabolism by estrogen and progesterone in women. *Am J Physiol Endocrinol Metab*. 2002;283(5):E1046–55.
270. Sedlak T, Shufelt C, Iribarren C, Merz CNB. Sex hormones and the QT interval: a review. *J Womens Health*. 2012;21(9):933–41.
271. Charkoudian N, Stephens DP, Pirkle KC, et al. Influence of female reproductive hormones on local thermal control of skin blood flow. *J Appl Physiol*. 1999;87(5):1719–23.
272. Stachenfeld NS, Silva C, Keefe DL. Estrogen modifies the temperature effects of progesterone. *J Appl Physiol*. 2000;88:1643–9.
273. Kolka MA, Stephenson LA. Effect of luteal phase elevation in core temperature on forearm blood flow during exercise. *J Appl Physiol*. 1997;82:1079–83.
274. Stephenson LA, Kolka MA. Menstrual cycle phase and time of day alter reference signal controlling arm blood flow and sweating. *Am J Phys*. 1985;249:R186–R91.
275. Stephenson LA, Kolka MA. Thermoregulation in women. *Exerc Sport Sci Rev*. 1993;21:231–62.
276. Stephenson LA, Kolka MA. Esophageal temperature threshold for sweating decreases before ovulation in premenopausal women. *J Appl Physiol*. 1999;86(1):22–8.
277. Thompson B, Almarjawi A, Sculley D, Janse de Jonge X. The effect of the menstrual cycle and oral contraceptives on acute responses and chronic adaptations to resistance training: a systematic review of the literature. *Sports Med*. 2020;50(1):171–85.
278. Hofmeister S, Bodden S. Premenstrual syndrome and premenstrual dysphoric disorder. *Am Fam Physician*. 2016;94(3):236–40.
279. Lanza di Scalea T, Pearlstein T. Premenstrual dysphoric disorder. *Med Clin North Am*. 2019;103(4):613–28.
280. Czajkowska M, Drosdzol-Cop A, Gałazka I, et al. Menstrual cycle and the prevalence of premenstrual syndrome/premenstrual dysphoric disorder in adolescent athletes. *J Pediatr Adolesc Gynecol*. 2015;28(6):492–8.
281. Meignié A, Toussaint JF, Antero J. Dealing with menstrual cycle in sport: stop finding excuses to exclude women from research. *Eur J Appl Physiol*. 2022;122(11):2489–90.
282. ESHRE Capri Workshop Group. Ovarian and endometrial function during hormonal contraception. *Hum Reprod*. 2001;16(7):1527–35.
283. Elliott-Sale KJ, McNulty KL, Ansdell P, et al. The effects of oral contraceptives on exercise performance in women: a systematic review and meta-analysis. *Sports Med*. 2020;50(10):1785–812.
284. Cheng M-H, Wang S-J, Yang F-Y, et al. Menopause and physical performance—a community-based cross-sectional study. *Menopause*. 2009;16(5):892–6.
285. Bondarev D, Finni T, Kokko K, et al. Physical performance during the menopausal transition and the role of physical activity. *J Gerontol A Biol Sci Med Sci*. 2021;76(9):1587–90.
286. Sowers M, Tomey K, Jannausch M, et al. Physical functioning and menopause states. *Obstet Gynecol*. 2007;110(6):1290–6.

287. Michael YL, Gold R, Manson JE, et al. Hormone therapy and physical function change among older women in the Women's Health Initiative: a randomized controlled trial. *Menopause*. 2010;17(2):295–302.
288. Kreukels BP, Guillamon A. Neuroimaging studies in people with gender incongruence. *Int Rev Psychiatry*. 2016;28(1):120–8.
289. Bramble MS, Lipson A, Vashist N, Vilain E. Effects of chromosomal sex and hormonal influences on shaping sex differences in brain and behavior: lessons from cases of disorders of sex development. *J Neurosci Res*. 2017;95(1-2):65–74.
290. Mueller SC, Verwilt T, Van Branteghem A, et al. The contribution of the androgen receptor (AR) in human spatial learning and memory: a study in women with complete androgen insensitivity syndrome (CAIS). *Horm Behav*. 2016;78:121–6.
291. van Hemmen J, Veltman DJ, Hoekzema E, et al. Neural activation during mental rotation in complete androgen insensitivity syndrome: the influence of sex hormones and sex chromosomes. *Cereb Cortex*. 2016;26(3):1036–45.
292. Savic I, Frisen L, Manzouri A, et al. Role of testosterone and Y chromosome genes for the masculinization of the human brain. *Hum Brain Mapp*. 2017;38(4):1801–14.
293. Collaer ML, Brook CGD, Conway GS, et al. Motor development in individuals with congenital adrenal hyperplasia: strength, targeting, and fine motor skill. *Psychoneuroendocrinology*. 2009;34(2):249–58.
294. Hines M, Fane BA, Pasterski VL, et al. Spatial abilities following prenatal androgen abnormality: targeting and mental rotations performance in individuals with congenital adrenal hyperplasia. *Psychoneuroendocrinology*. 2003;28(8):1010–26.
295. Soma KK. Testosterone and aggression: Berthold, birds and beyond. *J Neuroendocrinol*. 2006;18(7):543–51.
296. Geniole SN, Bird BM, McVittie JS, et al. Is testosterone linked to human aggression? A meta-analytic examination of the relationship between baseline, dynamic, and manipulated testosterone on human aggression. *Horm Behav*. 2020;123:104644.
297. Frisen L, Nordenström A, Falhammar H, et al. Gender role behavior, sexuality, and psychosocial adaptation in women with congenital adrenal hyperplasia due to CYP21A2 deficiency. *J Clin Endocrinol Metab*. 2009;94(9):3432–9.
298. Gandevia SC. Spinal and supraspinal factors in human muscle fatigue. *Physiol Rev*. 2001;81(4):1725–89.
299. Todd G, Gorman RB, Gandevia SC. Measurement and reproducibility of strength and voluntary activation of lower-limb muscles. *Muscle Nerve*. 2004;29(6):834–42.
300. Todd G, Taylor JL, Gandevia SC. Measurement of voluntary activation based on transcranial magnetic stimulation over the motor cortex. *J Appl Physiol*. 2016;121(3):678–86.
301. McNeil CJ, Butler JE, Taylor JL, Gandevia SC. Testing the excitability of human motoneurons. *Front Hum Neurosci*. 2013;7:152.
302. Hassanlouei H, Sundberg CW, Smith AE, et al. Physical activity modulates corticospinal excitability of the lower limb in young and old adults. *J Appl Physiol*. 2017;123(2):364–74.
303. Rozand V, Senefeld JW, Sundberg CW, et al. Differential effects of aging and physical activity on corticospinal excitability of upper and lower limb muscles. *J Neurophysiol*. 2019;122(1):241–50.
304. Yoon T, Schlinder-Delap B, Keller ML, Hunter SK. Supraspinal fatigue impedes recovery from a low-intensity sustained contraction in old adults. *J Appl Physiol*. 2012;112(5):849–58.
305. Pereira HM, Schlinder-DeLap B, Keenan KG, et al. Oscillations in neural drive and age-related reductions in force steadiness with a cognitive challenge. *J Appl Physiol*. 2019;126(4):1056–65.
306. Kowalski KL, Christie AD. Force control and motor unit firing behavior following mental fatigue in young female and male adults. *Front Integr Neurosci*. 2020;14:15.
307. Guo Y, Jones EJ, Inns TB, et al. Neuromuscular recruitment strategies of the vastus lateralis according to sex. *Acta Physiol*. 2022;235(2):e13803.
308. Brown RE, Edwards DL, Jakobi JM. Sex differences in force steadiness in three positions of the forearm. *Eur J Appl Physiol*. 2010;110(6):1251–7.
309. Vanden Noyen ML, Pereira HM, Yoon T, et al. Motor variability during sustained contractions increases with cognitive demand in older adults. *Front Aging Neurosci*. 2014;6:97.
310. Keller-Ross ML, Pereira HM, Pruse J, et al. Stressor-induced increase in muscle fatigability of young men and women is predicted by strength but not voluntary activation. *J Appl Physiol*. 2014;116(7):767–78.
311. Christou EA, Jakobi JM, Critchlow A, et al. The 1- to 2-Hz oscillations in muscle force are exacerbated by stress, especially in older adults. *J Appl Physiol*. 2004;97(1):225–35.
312. Mehta RK, Agnew MJ. Influence of mental workload on muscle endurance, fatigue, and recovery during intermittent static work. *Eur J Appl Physiol*. 2012;112(8):2891–902.
313. Storer TW, Magliano L, Woodhouse L, et al. Testosterone dose-dependently increases maximal voluntary strength and leg power, but does not affect fatigability or specific tension. *J Clin Endocrinol Metab*. 2003;88(4):1478–85.
314. Storer TW, Woodhouse L, Magliano L, et al. Changes in muscle mass, muscle strength, and power but not physical function are related to testosterone dose in healthy older men. *J Am Geriatr Soc*. 2008;56(11):1991–9.
315. Auyeung TW, Lee JS, Kwok T, et al. Testosterone but not estradiol level is positively related to muscle strength and physical performance independent of muscle mass: a cross-sectional study in 1489 older men. *Eur J Endocrinol*. 2011;164(5):811–7.
316. Rubinow KB. Estrogens and body weight regulation in men. *Adv Exp Med Biol*. 2017;1043:285–313.
317. Herbst KL, Bhasin S. Testosterone action on skeletal muscle. *Curr Opin Clin Nutr Metab Care*. 2004;7(3):271–7.
318. Finkelstein JS, Lee H, Burnett-Bowie SA, et al. Gonadal steroids and body composition, strength, and sexual function in men. *N Engl J Med*. 2013;369(11):1011–22.
319. Bhasin S, Woodhouse L, Casaburi R, et al. Testosterone dose-response relationships in healthy young men. *Am J Physiol Endocrinol Metab*. 2001;281(6):E1172–81.
320. Horwath O, Apró W, Moberg M, et al. Fiber type-specific hypertrophy and increased capillarization in skeletal muscle following testosterone administration in young women. *J Appl Physiol*. 2020;128(5):1240–50.
321. Bhasin S, Storer TW, Berman N, et al. The effects of supraphysiologic doses of testosterone on muscle size and strength in normal men. *N Engl J Med*. 1996;335(1):1–7.
322. Sinha-Hikim I, Artaza J, Woodhouse L, et al. Testosterone-induced increase in muscle size in healthy young men is associated with muscle fiber hypertrophy. *Am J Physiol Endocrinol Metab*. 2002;283(1):E154–64.
323. Huang G, Basaria S, Travison TG, et al. Testosterone dose-response relationships in hysterectomized women with or without oophorectomy: effects on sexual function, body composition, muscle performance and physical function in a randomized trial. *Menopause*. 2014;21(6):612–23.
324. Woodhouse LJ, Gupta N, Bhasin M, et al. Dose-dependent effects of testosterone on regional adipose tissue distribution in healthy young men. *J Clin Endocrinol Metab*. 2004;89(2):718–26.
325. Hirschberg AL, Elings Knutsson J, Helge T, et al. Effects of moderately increased testosterone concentration on physical performance in young women: a double blind, randomised, placebo controlled study. *Br J Sports Med*. 2020;54(10):599–604.
326. Bruusgaard JC, Johansen IB, Egner IM, et al. Myonuclei acquired by overload exercise precede hypertrophy and are not lost on detraining. *Proc Natl Acad Sci U S A*. 2010;107(34):15111–6.
327. Egner IM, Bruusgaard JC, Eftestøl E, Gundersen K. A cellular memory mechanism aids overload hypertrophy in muscle long after an episodic exposure to anabolic steroids. *J Physiol*. 2013;591(24):6221–30.

328. Luk H-Y, Levitt DE, Boyett JC, et al. Resistance exercise-induced hormonal response promotes satellite cell proliferation in untrained men but not in women. *Am J Physiol Endocrinol Metab.* 2019; 317(2):E421–e32.
329. Chao J, Rubinow KB, Kratz M, et al. Short-term estrogen withdrawal increases adiposity in healthy men. *J Clin Endocrinol Metab.* 2016;101(10):3724–31.
330. Van Pelt RE, Gavin KM, Kohrt WM. Regulation of body composition and bioenergetics by estrogens. *Endocrinol Metab Clin N Am.* 2015;44(3):663–76.
331. Enns DL, Tiidus PM. The influence of estrogen on skeletal muscle: sex matters. *Sports Med.* 2010;40(1):41–58.
332. Velders M, Diel P. How sex hormones promote skeletal muscle regeneration. *Sports Med.* 2013;43(11):1089–100.
333. Wiik A, Ekman M, Morgan G, et al. Oestrogen receptor beta is present in both muscle fibres and endothelial cells within human skeletal muscle tissue. *Histochem Cell Biol.* 2005;124(2):161–5.
334. Wiik A, Ekman M, Johansson O, et al. Expression of both oestrogen receptor alpha and beta in human skeletal muscle tissue. *Histochem Cell Biol.* 2009;131(2):181–9.
335. Faryniarz DA, Bhargava M, Lajam C, et al. Quantitation of estrogen receptors and relaxin binding in human anterior cruciate ligament fibroblasts. *In Vitro Cell Dev Biol Anim.* 2006;42(7):176–81.
336. Longo UG, Mazzola A, Carotti S, et al. The role of estrogen and progesterone receptors in the rotator cuff disease: a retrospective cohort study. *BMC Musculoskelet Disord.* 2021;22(1):891.
337. Milliken MC, Stray-Gundersen J, Peshock RM, et al. Left ventricular mass as determined by magnetic resonance imaging in male endurance athletes. *Am J Cardiol.* 1988;62(4):301–5.
338. Diaz-Canestro C, Pentz B, Sehgal A, Montero D. Sex differences in cardiorespiratory fitness are explained by blood volume and oxygen carrying capacity. *Cardiovasc Res.* 2022;118(1):334–43.
339. Howden EJ, Perhonen M, Peshock RM, et al. Females have a blunted cardiovascular response to one year of intensive supervised endurance training. *J Appl Physiol.* 2015;119(1):37–46.
340. Zavorsky GS. Evidence and possible mechanisms of altered maximum heart rate with endurance training and tapering. *Sports Med.* 2000;29(1):13–26.
341. Wheatley CM, Snyder EM, Johnson BD, Olson TP. Sex differences in cardiovascular function during submaximal exercise in humans. *Springerplus.* 2014;3:445.
342. Grandi AM, Venco A, Barzizza F, et al. Influence of age and sex on left ventricular anatomy and function in normals. *Cardiology.* 1992; 81(1):8–13.
343. Johnson BD, Zheng W, Korach KS, et al. Increased expression of the cardiac L-type calcium channel in estrogen receptor-deficient mice. *J Gen Physiol.* 1997;110(2):135–40.
344. Petre RE, Quail MP, Rossman EI, et al. Sex-based differences in myocardial contractile reserve. *Am J Physiol Regul Integr Comp Physiol.* 2007;292(2):R810–8.
345. Koenig H, Goldstone A, Lu CY. Testosterone-mediated sexual dimorphism of the rodent heart. Ventricular lysosomes, mitochondria, and cell growth are modulated by androgens. *Circ Res.* 1982;50(6): 782–7.
346. Gerche AL, Brosnan MJ. Cardiovascular effects of performance-enhancing drugs. *Circulation.* 2017;135(1):89–99.
347. Ayaz O, Howlett SE. Testosterone modulates cardiac contraction and calcium homeostasis: cellular and molecular mechanisms. *Biol Sex Differ.* 2015;6(1):9.
348. Bachman E, Trivison TG, Basaria S, et al. Testosterone induces erythrocytosis via increased erythropoietin and suppressed hepcidin: evidence for a new erythropoietin/hemoglobin set point. *J Gerontol A Biol Sci Med Sci.* 2014;69(6):725–35.
349. Cardinale DA, Horwath O, Elings-Knutsson J, et al. Enhanced skeletal muscle oxidative capacity and capillary-to-fiber ratio following moderately increased testosterone exposure in young healthy women. *Front Physiol.* 2020;11:585490.
350. Schwartz J, Katz SA, Fegley RW, Tockman MS. Sex and race differences in the development of lung function. *Am Rev Respir Dis.* 1988;138(6):1415–21.
351. Ripoll JG, Guo W, Andersen KJ, et al. Sex differences in paediatric airway anatomy. *Exp Physiol.* 2020;105(4):721–31.
352. Martin TR, Castile RG, Fredberg JJ, et al. Airway size is related to sex but not lung size in normal adults. *J Appl Physiol.* 1987;63(5): 2042–7.
353. Sheel AW, Guenette JA, Yuan R, et al. Evidence for dysanapsis using computed tomographic imaging of the airways in older ex-smokers. *J Appl Physiol.* 2009;107(5):1622–8.
354. McClaran SR, Harms CA, Pegelow DF, Dempsey JA. Smaller lungs in women affect exercise hyperpnea. *J Appl Physiol.* 1998; 84(6):1872–81.
355. Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. Changes in the normal maximal expiratory flow-volume curve with growth and aging. *Am Rev Respir Dis.* 1983;127(6):725–34.
356. Olfert IM, Balouch J, Kleinsasser A, et al. Does gender affect human pulmonary gas exchange during exercise? *J Physiol.* 2004; 557(2):529–41.
357. Guenette JA, Witt JD, McKenzie DC, et al. Respiratory mechanics during exercise in endurance-trained men and women. *J Physiol.* 2007;581(3):1309–22.
358. Cory JM, Schaeffer MR, Wilkie SS, et al. Sex differences in the intensity and qualitative dimensions of exertional dyspnea in physically active young adults. *J Appl Physiol.* 2015;119(9):998–1006.
359. Schaeffer MR, Mendonca CT, Levangie MC, et al. Physiological mechanisms of sex differences in exertional dyspnoea: role of neural respiratory motor drive. *Exp Physiol.* 2014;99(2):427–41.
360. Molgat-Seon Y, Peters CM, Sheel AW. Sex-differences in the human respiratory system and their impact on resting pulmonary function and the integrative response to exercise. *Curr Opin Physiol.* 2018;6:21–7.
361. Hart EC, Charkoudian N, Wallin BG, et al. Sex and ageing differences in resting arterial pressure regulation: the role of the β -adrenergic receptors. *J Physiol.* 2011;589(Pt 21):5285–97.
362. Ruby BC, Robergs RA, Waters DL, et al. Effects of estradiol on substrate turnover during exercise in amenorrheic females. *Med Sci Sports Exerc.* 1997;29(9):1160–9.
363. Carter S, McKenzie S, Mourtzakis M, et al. Short-term 17 β -estradiol decreases glucose R(a) but not whole body metabolism during endurance exercise. *J Appl Physiol.* 2001;90(1):139–46.
364. Tamopolsky MA, Roy BD, MacDonald JR, et al. Short-term 17 β -estradiol administration does not affect metabolism in young males. *Int J Sports Med.* 2001;22(3):175–80.
365. Braun B, Gerson L, Hagobian T, et al. No effect of short-term testosterone manipulation on exercise substrate metabolism in men. *J Appl Physiol.* 2005;99(5):1930–7.
366. Hatta H, Atomi Y, Shinohara S, et al. The effects of ovarian hormones on glucose and fatty acid oxidation during exercise in female ovariectomized rats. *Horm Metab Res.* 1988;20(10):609–11.
367. Kendrick ZV, Steffen CA, Rumsey WL, Goldberg DI. Effect of estradiol on tissue glycogen metabolism in exercised oophorectomized rats. *J Appl Physiol.* 1987;63(2):492–6.
368. Kendrick ZV, Ellis GS. Effect of estradiol on tissue glycogen metabolism and lipid availability in exercised male rats. *J Appl Physiol.* 1991;71(5):1694–9.
369. Campbell SE, Febbraio MA. Effect of ovarian hormones on mitochondrial enzyme activity in the fat oxidation pathway of skeletal muscle. *Am J Physiol Endocrinol Metab.* 2001;281(4):E803–8.
370. van Breda E, Keizer H, Kuipers H, Kranenburg G. Effect of testosterone and endurance training on glycogen metabolism in skeletal muscle of chronic hyperglycaemic female rats. *Br J Sports Med.* 2003;37(4):345–50.
371. Ramamani A, Aruldas MM, Govindarajulu P. Differential response of rat skeletal muscle glycogen metabolism to testosterone and estradiol. *Can J Physiol Pharmacol.* 1999;77(4):300–4.

372. Abildgaard J, Pedersen AT, Green CJ, et al. Menopause is associated with decreased whole body fat oxidation during exercise. *Am J Physiol Endocrinol Metab.* 2013;304(11):E1227–36.
373. Johnson LG, Kraemer RR, Kraemer GR, et al. Substrate utilization during exercise in postmenopausal women on hormone replacement therapy. *Eur J Appl Physiol.* 2002;88(3):282–7.
374. Franke WW, Berendonk B. Hormonal doping and androgenization of athletes: a secret program of the German Democratic Republic government. *Clin Chem.* 1997;43(7):1262–79.
375. Finkelstein JS, Yu EW, Burnett-Bowie SA. Gonadal steroids and body composition, strength, and sexual function in men. *N Engl J Med.* 2013;369(25):2457.
376. Houben LHP, Overkamp M, van Kraaij P, et al. Resistance exercise training increases muscle mass and strength in prostate cancer patients on androgen deprivation therapy. *Med Sci Sports Exerc.* 2023;55(4):614–24.
377. Lopez P, Newton RU, Taaffe DR, et al. Interventions for improving body composition in men with prostate cancer: a systematic review and network meta-analysis. *Med Sci Sports Exerc.* 2022;54(5):728–40.
378. Lopez P, Taaffe DR, Newton RU, Galvão DA. Resistance exercise dosage in men with prostate cancer: systematic review, meta-analysis, and meta-regression. *Med Sci Sports Exerc.* 2021;53(3):459–69.
379. Nokoff NJ, Scarbro SL, Moreau KL, et al. Body composition and markers of cardiometabolic health in transgender youth on gonadotropin-releasing hormone agonists. *Transgend Health.* 2021;6(2):111–9.
380. Klaver M, Dekker MJHJ, de Mutsert R, et al. Cross-sex hormone therapy in transgender persons affects total body weight, body fat and lean body mass: a meta-analysis. *Andrologia.* 2017;49(5).
381. Nokoff NJ, Scarbro SL, Moreau KL, et al. Body composition and markers of cardiometabolic health in transgender youth compared with cisgender youth. *J Clin Endocrinol Metab.* 2020;105(3):e704–14.
382. Gooren LJ, Bunck MC. Transsexuals and competitive sports. *Eur J Endocrinol.* 2004;151(4):425–9.
383. Scharff M, Wiepjes CM, Klaver M, et al. Change in grip strength in trans people and its association with lean body mass and bone density. *Endocr Connect.* 2019;8(7):1020–8.
384. Wiik A, Lundberg TR, Rullman E, et al. Muscle strength, size, and composition following 12 months of gender-affirming treatment in transgender individuals. *J Clin Endocrinol Metab.* 2020;105(3):dgz247.
385. Bhasin S, Hatfield DL, Hoffman JR, et al. Anabolic-androgenic steroid use in sports, health, and society. *Med Sci Sports Exerc.* 2021;53(8):1778–94.
386. Roberts TA, Smalley J, Ahrendt D. Effect of gender affirming hormones on athletic performance in transwomen and transmen: implications for sporting organisations and legislators. *Br J Sports Med.* 2021;55(11):577–83.
387. Harper J, O'Donnell E, Sorouri Khorashad B, et al. How does hormone transition in transgender women change body composition, muscle strength and haemoglobin? Systematic review with a focus on the implications for sport participation. *Br J Sports Med.* 2021;55(15):865–72.
388. Alvares LAM, Santos MR, Souza FR, et al. Cardiopulmonary capacity and muscle strength in transgender women on long-term gender-affirming hormone therapy: a cross-sectional study. *Br J Sports Med.* 2022;56(22):1292–8.
389. Harper J. Race times for transgender athletes. *J Sport Cultures Identities.* 2015;6(1):1–9.
390. Kaminsky LA, Wehrli KW, Mahon AD, et al. Evaluation of a shallow water running test for the estimation of peak aerobic power. *Med Sci Sports Exerc.* 1993;25(11):1287–92.
391. Chiccarelli E, Aden J, Ahrendt D, Smalley J. Fit transitioning: when can transgender airmen fitness test in their affirmed gender? *Mil Med.* 2022;usac320.
392. Holmér I. Energy cost of arm stroke, leg kick, and the whole stroke in competitive swimming styles. *Eur J Appl Physiol Occup Physiol.* 1974;33(2):105–18.
393. Hagmar M, Berglund B, Brismar K, Hirschberg AL. Hyperandrogenism may explain reproductive dysfunction in olympic athletes. *Med Sci Sports Exerc.* 2009;41(6):1241–8.
394. De Souza MJ, Koltun KJ, Williams NI. The role of energy availability in reproductive function in the female athlete triad and extension of its effects to men: an initial working model of a similar syndrome in male athletes. *Sports Med.* 2019;49(Suppl 2):125–37.
395. Rickenlund A, Thorén M, Carlström K, et al. Diurnal profiles of testosterone and pituitary hormones suggest different mechanisms for menstrual disturbances in endurance athletes. *J Clin Endocrinol Metab.* 2004;89(2):702–7.
396. Coste O, Paris F, Galtier F, et al. Polycystic ovary-like syndrome in adolescent competitive swimmers. *Fertil Steril.* 2011;96(4):1037–42.
397. La Vignera S, Condorelli RA, Cannarella R, et al. Sport, doping and female fertility. *Reprod Biol Endocrinol.* 2018;16(1):108.
398. Barber TM, Franks S. Obesity and polycystic ovary syndrome. *Clin Endocrinol.* 2021;95(4):531–41.
399. Lee PA, Nordenström A, Houk CP, et al. Global disorders of sex development update since 2006: perceptions, approach and care. *Horm Res Paediatr.* 2016;85(3):158–80.
400. Hughes IA, Werner R, Bunch T, Hiort O. Androgen insensitivity syndrome. *Semin Reprod Med.* 2012;30(5):432–42.
401. Okeigwe I, Kuohung W. 5-Alpha reductase deficiency: a 40-year retrospective review. *Curr Opin Endocrinol Diabetes Obes.* 2014;21(6):483–7.
402. New MI. Diagnosis and management of congenital adrenal hyperplasia. *Annu Rev Med.* 1998;49:311–28.
403. Speiser PW, Azziz R, Baskin LS, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2010;95(9):4133–60.
404. Fenichel P, Paris F, Philibert P, et al. Molecular diagnosis of 5alpha-reductase deficiency in 4 elite young female athletes through hormonal screening for hyperandrogenism. *J Clin Endocrinol Metab.* 2013;98(6):E1055–9.
405. Berman S. Androgens and athletic performance of elite female athletes. *Curr Opin Endocrinol Diabetes Obes.* 2017;24(3):246–51.
406. Cohen-Kettenis P. Psychological long-term outcome in intersex conditions. *Horm Res.* 2005;64(Suppl 2):27–30.
407. Cohen-Kettenis PT. Gender change in 46,XY persons with 5alpha-reductase-2 deficiency and 17beta-hydroxysteroid dehydrogenase-3 deficiency. *Arch Sex Behav.* 2005;34(4):399–410.
408. Kraemer WJ, Ratamess NA, Hymer WC, et al. Growth hormone(s), testosterone, insulin-like growth factors, and cortisol: roles and integration for cellular development and growth with exercise. *Front Endocrinol (Lausanne).* 2020;11:33.
409. Meinhardt UJ, Ho KK. Modulation of growth hormone action by sex steroids. *Clin Endocrinol.* 2006;65(4):413–22.
410. Gibney J, Healy ML, Sönksen PH. The growth hormone/insulin-like growth factor-I axis in exercise and sport. *Endocr Rev.* 2007;28(6):603–24.
411. Liu H, Bravata DM, Olkin I, et al. Systematic review: the effects of growth hormone on athletic performance. *Ann Intern Med.* 2008;148(10):747–58.
412. Hermansen K, Bengtsen M, Kjær M, et al. Impact of GH administration on athletic performance in healthy young adults: a systematic review and meta-analysis of placebo-controlled trials. *Growth Hormon IGF Res.* 2017;34:38–44.
413. Bimie K, Ben-Shlomo Y, Holly JM, et al. Associations of insulin and insulin-like growth factors with physical performance in old age in the Boyd Orr and Caerphilly studies. *PLoS One.* 2012;7(1):e30096.
414. Kraemer WJ, Ratamess NA, Nindl BC. Recovery responses of testosterone, growth hormone, and IGF-1 after resistance exercise. *J Appl Physiol.* 2017;122(3):549–58.
415. Gharahdaghi N, Rudrappa S, Brook MS, et al. Testosterone therapy induces molecular programming augmenting physiological adaptations to resistance exercise in older men. *J Cachexia Sarcopenia Muscle.* 2019;10(6):1276–94.

416. Veldhuis JD, Anderson SM, Patrie JT, Bowers CY. Estradiol supplementation in postmenopausal women doubles rebound-like release of growth hormone (GH) triggered by sequential infusion and withdrawal of somatostatin: evidence that estrogen facilitates endogenous GH-releasing hormone drive. *J Clin Endocrinol Metab.* 2004;89(1):121–7.
417. MacInnis MJ, Gibala MJ. Physiological adaptations to interval training and the role of exercise intensity. *J Physiol.* 2017;595(9):2915–30.
418. American College of Sports Medicine. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc.* 2009;41(3):687–708.
419. Lopez P, Radaelli R, Taaffe DR, et al. Resistance training load effects on muscle hypertrophy and strength gain: systematic review and network meta-analysis. *Med Sci Sports Exerc.* 2021;53(6):1206–16.
420. Dalggaard LB, Dalgas U, Andersen JL, et al. Influence of oral contraceptive use on adaptations to resistance training. *Front Physiol.* 2019;10:824.
421. Nichols AW, Hetzler RK, Villanueva RJ, et al. Effects of combination oral contraceptives on strength development in women athletes. *J Strength Cond Res.* 2008;22(5):1625–32.
422. Wikström-Frisén L, Boraxbekk CJ, Henriksson-Larsén K. Effects on power, strength and lean body mass of menstrual/oral contraceptive cycle based resistance training. *J Sports Med Phys Fitness.* 2017;57(1–2):43–52.
423. Sung ES, Han A, Hinrichs T, et al. Effects of oral contraceptive use on muscle strength, muscle thickness, and fiber size and composition in young women undergoing 12 weeks of strength training: a cohort study. *BMC Womens Health.* 2022;22(1):150.
424. Schaumberg MA, Jenkins DG, Janse De Jonge XAK, et al. Oral contraceptive use dampens physiological adaptations to sprint interval training. *Med Sci Sports Exerc.* 2017;49(4):717–27.
425. Schaumberg MA, Stanley J, Jenkins DG, et al. Oral contraceptive use influences on-kinetic adaptations to sprint interval training in recreationally-active women. *Front Physiol.* 2020;11:629.
426. Vingren JL, Kraemer WJ, Ratamess NA, et al. Testosterone physiology in resistance exercise and training: the up-stream regulatory elements. *Sports Med.* 2010;40(12):1037–53.
427. Vajda M, Vanderka M, Buzgo G, et al. The effect of different training modalities on resting hormonal level in active young males. *J Appl Biomed.* 2021;19(2):83–90.
428. Zouhal H, Jayavel A, Parasuraman K, et al. Effects of exercise training on anabolic and catabolic hormones with advanced age: a systematic review. *Sports Med.* 2022;52(6):1353–68.
429. Hooper DR, Kraemer WJ, Focht BC, et al. Endocrinological roles for testosterone in resistance exercise responses and adaptations. *Sports Med.* 2017;47(9):1709–20.
430. Häkkinen K, Pakarinen A. Serum hormones and strength development during strength training in middle-aged and elderly males and females. *Acta Physiol Scand.* 1994;150(2):211–9.
431. Kraemer WJ, Staron RS, Hagerman FC, et al. The effects of short-term resistance training on endocrine function in men and women. *Eur J Appl Physiol Occup Physiol.* 1998;78(1):69–76.
432. Marx JO, Ratamess NA, Nindl BC, et al. Low-volume circuit versus high-volume periodized resistance training in women. *Med Sci Sports Exerc.* 2001;33(4):635–43.
433. Kojić F, Mandić D, Ilić V. Resistance training induces similar adaptations of upper and lower-body muscles between sexes. *Sci Rep.* 2021;11(1):23449.
434. Roberts BM, Nuckols G, Krieger JW. Sex differences in resistance training: a systematic review and meta-analysis. *J Strength Cond Res.* 2020;34(5):1448–60.
435. Abe T, DeHoyos DV, Pollock ML, Garzarella L. Time course for strength and muscle thickness changes following upper and lower body resistance training in men and women. *Eur J Appl Physiol.* 2000;81(3):0174–80.
436. Hagstrom AD, Marshall PW, Halaki M, Hackett DA. The effect of resistance training in women on dynamic strength and muscular hypertrophy: a systematic review with meta-analysis. *Sports Med.* 2020;50(6):1075–93.
437. Jones MD, Wewege MA, Hackett DA, et al. Sex differences in adaptations in muscle strength and size following resistance training in older adults: a systematic review and meta-analysis. *Sports Med.* 2021;51(3):503–17.
438. Bagley L, Al-Shanti N, Bradburn S, et al. Sex comparison of knee extensor size, strength, and fatigue adaptation to sprint interval training. *J Appl Sport Sci Res.* 2021;35(1):64–71.
439. Arbab-Zadeh A, Perhonen M, Howden E, et al. Cardiac remodeling in response to 1 year of intensive endurance training. *Circulation.* 2014;130(24):2152–61.
440. Levine BD, Lane LD, Buckey JC, et al. Left ventricular pressure–volume and Frank–Starling relations in endurance athletes. Implications for orthostatic tolerance and exercise performance. *Circulation.* 1991;84(3):1016–23.
441. Barnes JN, Fu Q. Sex-specific ventricular and vascular adaptations to exercise. *Adv Exp Med Biol.* 2018;1065:329–46.
442. Malhotra A, Buttrick P, Scheuer J. Effects of sex hormones on development of physiological and pathological cardiac hypertrophy in male and female rats. *Am J Phys.* 1990;259(3 Pt 2):H866–71.
443. Dalpiaz PL, Lamas AZ, Caliman IF, et al. Sex hormones promote opposite effects on ACE and ACE2 activity, hypertrophy and cardiac contractility in spontaneously hypertensive rats. *PLoS One.* 2015;10(5):e0127515.
444. Thompson PD, Franklin BA, Balady GJ, et al. Exercise and acute cardiovascular events: placing the risks into perspective. *Med Sci Sports Exerc.* 2007;39(5):886–97.
445. Roberts WO, Roberts DM, Lunos S. Marathon related cardiac arrest risk differences in men and women. *Br J Sports Med.* 2013;47(3):168–71.
446. Spina RJ, Ogawa T, Kohrt WM, et al. Differences in cardiovascular adaptations to endurance exercise training between older men and women. *J Appl Physiol.* 1993;75(2):849–55.
447. Carrick-Ranson G, Sloane NM, Howden EJ, et al. The effect of life-long endurance exercise on cardiovascular structure and exercise function in women. *J Physiol.* 2020;598(13):2589–605.
448. Green JS, Stanforth PR, Gagnon J, et al. Menopause, estrogen, and training effects on exercise hemodynamics: the HERITAGE study. *Med Sci Sports Exerc.* 2002;34(1):74–82.
449. Green JS, Crouse SF, Rohack JJ. Peak exercise hemodynamics in exercising postmenopausal women taking versus not taking supplemental estrogen. *Med Sci Sports Exerc.* 1998;30(1):158–64.
450. O'Donnell E, Kirwan LD, Goodman JM. Aerobic exercise training in healthy postmenopausal women: effects of hormone therapy. *Menopause.* 2009;16(4):770–6.
451. McCole SD, Brown MD, Moore GE, et al. Cardiovascular hemodynamics with increasing exercise intensities in postmenopausal women. *J Appl Physiol.* 1999;87(6):2334–40.
452. Tarnopolsky MA, Rennie CD, Robertshaw HA, et al. Influence of endurance exercise training and sex on intramyocellular lipid and mitochondrial ultrastructure, substrate use, and mitochondrial enzyme activity. *Am J Physiol Regul Integr Comp Physiol.* 2007;292(3):R1271–8.
453. Carter SL, Rennie C, Tarnopolsky MA. Substrate utilization during endurance exercise in men and women after endurance training. *Am J Physiol Endocrinol Metab.* 2001;280(6):E898–907.
454. Ferguson-Smith MA, Bavington LD. Natural selection for genetic variants in sport: the role of Y chromosome genes in elite female athletes with 46, XY DSD. *Sports Med.* 2014;44(12):1629–34.
455. Boczkowski K. Height of females with pure gonadal dysgenesis and normal male or female karyotype. *Hum Genet.* 1985;70(1):80–1.
456. Tukiainen T, Pirinen M, Sarin AP, et al. Chromosome X-wide association study identifies loci for fasting insulin and height and evidence for incomplete dosage compensation. *PLoS Genet.* 2014;10(2):e1004127.
457. Oakes MB, Eyvazzadeh AD, Quint E, Smith YR. Complete androgen insensitivity syndrome—a review. *J Pediatr Adolesc Gynecol.* 2008;21(6):305–10.



Review

A Scoping Review of Transgender Policies in the 15 Most Commonly Played UK Professional Sports

Michael McLarnon ¹, Jane Thornton ² , Gail Knudson ³, Nigel Jones ⁴, Danny Glover ⁵, Andrew Murray ⁶, Michael Cummings ¹ and Neil Heron ^{1,4,7,*} 

¹ Centre for Public Health, Queen's University Belfast, Belfast BT12 6BA, UK

² Schulich School of Medicine and Dentistry, Western University, London, ON N6A 3K7, Canada

³ Faculty of Medicine, University of British Columbia (UBC), Vancouver, BC V6T 1Z4, Canada

⁴ Medical Department, British Cycling, Manchester M11 4DQ, UK

⁵ Medical and Scientific Department, Ladies European Tour (Various), Denham UB9 5PG, UK

⁶ Sport and Exercise, University of Edinburgh, Edinburgh EH8 9YL, UK

⁷ School of Medicine, Keele University, Staffordshire ST5 5BG, UK

* Correspondence: n.heron@qub.ac.uk

Abstract: Introduction: There has been much debate recently on the participation of transgender and gender-diverse (TGD) athletes in sport, particularly in relation to fairness, safety and inclusion. The 2021 IOC Framework on Fairness, Inclusion and Non-discrimination acknowledges the central role that eligibility criteria play in ensuring fairness, particularly in the female category, and states that athletes should not be excluded solely on the basis of their TGD identity. Aims: To identify policies that address TGD athlete participation in the 15 major United Kingdom (UK) sporting organisations and to summarise the evidence for each of these policies. Methods: A scoping review of TGD policies from the 15 major UK sporting organisations. Results: Eleven of the governing bodies had publicly available TGD policies. Most of the sporting associations drew guidance from the official 2015 IOC Consensus Meeting on Sex Reassignment and Hyperandrogenism, particularly with regard to physiological testosterone levels. Many organisations referenced their policies as a guide for decision making but stated that they ultimately made case-by-case decisions on an athlete's eligibility. Relevant considerations not addressed in most policies included pre- versus post-pubertal athletes, justification for testosterone thresholds, the length of time out of competitive action (if any) for transitioning athletes, the irreversible advantage from male puberty (if any), the responsibility for and frequency of follow up for hormonal testing and the consequences for athletes outside set testosterone limits. Conclusions: There is a lack of consensus among the top 15 UK sporting organizations relating to elite sport participation for TGD athletes. It would be useful for sport organizations to work together to develop greater standardization/consensus for TGD athlete policies, taking into consideration fairness, safety and inclusion in each sport.

Keywords: scoping review; transgender and gender-diverse (TGD); TGD athletes; transitioning; guidelines; policies; fairness; inclusion; safety; testosterone; 2021 IOC Framework on Fairness; inclusion and non-discrimination



Citation: McLarnon, M.; Thornton, J.; Knudson, G.; Jones, N.; Glover, D.; Murray, A.; Cummings, M.; Heron, N. A Scoping Review of Transgender Policies in the 15 Most Commonly Played UK Professional Sports. *Int. J. Environ. Res. Public Health* **2023**, *20*, 3568. <https://doi.org/10.3390/ijerph20043568>

Academic Editor: Paul B. Tchounwou

Received: 17 January 2023

Accepted: 14 February 2023

Published: 17 February 2023



Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Fair, inclusive and non-discriminatory sport participation for all athletes, including transgender and gender-diverse (TGD) athletes, is currently a very topical issue within sport medicine and society in general. In 2021, the United Kingdom (UK) sport councils produced a document reviewing transgender inclusion in domestic sport (Guidance for Transgender Inclusion in Domestic Sport) [1]. This document concluded that there is no single solution to the issue, instead offering guiding principles to promote fairness, safety and inclusivity, but it recognised the presence of retained male advantage and noted that a decision should be made by sporting federations between fairness and inclusivity.

The International Olympic Committee (IOC) recently released a framework for fairness, inclusion and non-discrimination on the basis of gender identity, putting greater emphasis on inclusion, although it deferred practical guidance and decision making to individual sports based on their specific circumstances [2]. Although some regulation has existed since the 1940s [3–6], consideration of TGD athlete participation and scientific research in the area were limited until recently. This review focused on policies related to transgender athletes and did not consider policies related to intersex athletes or those with differences in sexual differentiation (DSD).

Current sporting guidelines focus predominantly on testosterone-based regulations for trans women athletes participating in women's sporting events. Researchers and policymakers cite variables that differentiate biological male and female athletic performance [7–10] produced by exposure to testosterone from the onset of male puberty, amongst other influences [5,11,12], which include height, muscle mass, pelvic and lower limb anatomy (e.g., the "Q" angle), reaction times, VO_{2max} , strength and the mechanics of movements such as running [13–23]. Observational data relating to national and world records show a record gap between the sexes of 8–12% [7,24–28].

Sport participation for all needs to be promoted, as sport provides a plethora of benefits for both mental and physical health [29,30]. Indeed, TGD athletes must be able to participate in and have access to sport, and barriers to them doing so, in whichever category is determined most appropriate for the sport, should be addressed [2]. The barriers to subsequent participation by athletes in the female category, including TGD athletes, due to fairness, safety or other issues also need to be considered as part of this discussion [2,5,12].

Aims

To understand how sporting organisations are navigating these issues, we aimed to conduct a scoping review of current guidelines from the 15 major UK sporting organisations with the highest participation numbers in order to:

1. Determine those that have an existing TGD athlete policy;
2. Review their specific guidance on eligibility (including testosterone-based regulations);
3. Summarise the policies in different sports;
4. Map the evidence gaps in the TGD policies across the different organisations.

2. Methods

A scoping review was considered the most appropriate methodological approach to address the research question. A scoping review is defined as an exploratory project that systematically maps the literature available on a topic, identifying key concepts, theories, sources of evidence and gaps in the literature [31,32]. Compared to systemic reviews, scoping reviews make it possible to investigate a less specific research question and work to inform future research [33]. This scoping review was based on the six-step methodological framework outlined by Arksey and O'Malley and informed by Levac et al. [34,35]. The Preferred Reporting Items for Systemic Review and Meta-Analysis (PRISMA) protocol was followed and the PRISMA extension for scoping reviews (PRISMA-ScR) checklist completed [31]. Throughout this review, we define transgender athletes as per the IOC; that is, "Someone who identifies with a gender that is different from the sex that they were assigned at birth. A transgender man is a man who was assigned female at birth; a transgender woman is a woman who was assigned male at birth" [2]. This review exclusively focuses on transgender athletes, without consideration for intersex athletes or athletes with differences in sex development (DSD) or related disorders.

2.1. Stage 1: Identifying the Research Question(s)

The following research objective was addressed in this report: to identify policies that address TGD athlete participation in the 15 major United Kingdom (UK) sporting organisations and to summarise the evidence for each of these policies.

To be included in this review, the sports had to be widely participated in at an amateur level within the UK. Participation levels were taken from the Sport England website via the Active Lives survey, as well as from independent reports from Harris Interactive, Statista and the Ipsos MORI sports tracker [36–40]. Polls from unofficial sources, such as major sporting magazines or online fan websites, were also reviewed, as were the Wikipedia pages for “Sport in England” and “Sport in the United Kingdom”.

2.2. Stage 2: Identifying Relevant Policies

Searches for TGD policies among the 15 major UK sports organisations were carried out from inception to December 2021 to find relevant guidelines to include in this review. This was undertaken by first identifying the sports with the highest levels of participation and then identifying the official governing bodies for each sport (both UK-wide and nationally) through simple internet searches. Following this, each organisation’s official website was searched for a transgender policy, and searches were also undertaken using search engines (Google search, Google Scholar). Where a policy was not identified or publicly available, direct inquiry with the organisation was attempted.

2.3. Stage 3: Policy Selection

TGD guidelines were accessed either via the official organisation websites or through a request addressed to a relevant representative. When separate organisations were present for the same sport in England, Scotland, Northern Ireland and Wales (for example, rugby union), the England guidelines were reviewed, as England represented the largest population of amateur athletes that would typically use such guidelines. Searches were carried out by MMcL and checked by NH, with AM reviewing any disagreements.

2.4. Stages 4 and 5: Charting the Data and Collating, Summarizing and Reporting Results

The following data were extracted for each sport: the primary governing organisation for that sport; the sports played within the remit of the organisation; the official TGD policy of the association; testosterone cut-off levels for transitioning athletes and their rationale, taking into consideration the different demands of the sports; the length of any required time out of competition during/post-gender-affirming therapy; the hormone eligibility evidence required by the governing body for sports participation; regulations around child or adolescent TGD participation; and specific case-by-case guidance for individual TGD athletes. Information was recorded using Microsoft Excel.

3. Results

Sporting Organisation Guidelines

Data analysed for each sport, relevant UK sporting organisations and sports played within the organisations are summarised in Table 1. Although individual breakdowns of gender participation are not provided by the organisations, we know that there is generally a consistently higher proportion of male athletes engaging in amateur sport [37,41]. Data taken from an analysis of the Taking Part survey provide the proportions of male/female participants in popular sports in the UK [41] and are also included within Table 1. This information was available for 8/15 of the included sports. Where available, information on the specific guidance and rules that each organisation based their policy on is included.

Table 2 summarises the contents of the sport-specific guidelines for each organisation. As many policies are adopted from the IOC’s 2021 (and, before that, 2015) position [2], this has also been included for reference.

Table 1. The most popular sports (by participation numbers) in the UK and national governing bodies.

Sport	Sporting Organisation	Sport(s) Played within the Organisation	Male (M)/Female (F) Participation Split (%)	Policy Development
Football	The Football Association (FA) (England) Scottish Football Association (SFA) Football Association of Wales Irish Football Association (IFA)	Football	Proportion of population: 12.6% M, 1.2% F Relative participation: 90.8% M, 9.2% F	The Football Association Policy on Trans People in Football based upon: • IOC 2004 statement • Sports Council Equality Group “Guidance for National Governing Bodies of Sport” on “Transsexual People and Competitive Sport” • Equality Act 2010 • Gender Recognition Act 2004 • FA Equality Manager and Medical Services team
Athletics	UK Athletics	Track and field sports; running (all types)	N/a	Policy based upon: • World Athletics Eligibility Regulations for Transgender Athletes (2019) • World Athletics Eligibility Regulations for the Female Classification (2019) Policy approved by UKA Board and owned by the Development Director
Cricket	England and Wales Cricket Board Cricket Scotland Cricket Ireland (Northern Cricket Union)	Cricket	N/a	Policy based upon: • Advice from Stonewall UK • IOC regulations • ICC regulations • Gender Recognition Act 2004 Overseen by ECB Head of Policy Development
Rowing	British Rowing	Rowing	N/a	Policy updated in 2022, based upon: • NGB Policy • IOC statement (2021)

Table 1. Cont.

Sport	Sporting Organisation	Sport(s) Played within the Organisation	Male (M)/Female (F) Participation Split (%)	Policy Development
Cycling	British Cycling	Cycling disciplines	Proportion of population: 14.4% M, 6.4% F Relative participation: 68.3% M, 31.7% F	Policy currently suspended/under review as of 06 April 2022, based upon: - Equality Act 2010 - Data Protection Act 2018 - Gender Recognition Act 2004 - IOC Consensus Meeting 2015 - The UCI Regulations on Transgender Athlete Participation March 2020
Golf	England Golf Golf Ireland (including Northern Ireland) Scottish Golf Wales Golf	Golf	Proportion of population: 8.7% M, 1.3% F Relative participation: 86% M, 14% F	Policy based upon: - Gender Recognition Act 2004 - Equality Act 2010 - Gender Recognition Panel, consisting of recognised gender specialists, as appointed by England Golf - Human Rights Act 1998
Swimming	British Swimming	Swimming	Proportion of population: 13% M, 16.5% F Relative participation: 48.9% M, 51.1% F	Policy based upon: - Sports Council Equality Group guidance - British Swimming 2011 policy on transsexual competitors (previous policy)
Tennis	Lawn Tennis Association (LTA)	Tennis	Proportion of population: 3.2% M, 2% F Relative participation: 60.9% M, 39.1% F	Policy currently under review, based upon: - Equality Act 2010 - ITF Policy (2017) Policy approved by LTA's CEO, executive team and board Authored by LTA Safe And Inclusive Tennis Team
Rugby union	Rugby Football Union (RFU) (England) Irish Rugby (IRFU) (Northern Ireland) Scottish Rugby Union (SRU) Welsh Rugby Union (WRU)	Rugby football (union rules)	N/a	Policy based upon: - Equality Act 2010 - Stonewall UK Authors acknowledged: - Professor Dr Walter Pierre Bouman - Professor John Arcelus

Table 1. Cont.

Sport	Sporting Organisation	Sport(s) Played within the Organisation	Male (M)/Female (F) Participation Split (%)	Policy Development
Rugby league	Rugby Football League (RFL) (England)	Rugby football (league rules)	N/a	N/a
Boxing	British Boxing Board of Control (BBBofC)	Boxing	N/a	No official policy
Snooker	World Professional Billiards and Snooker Association	Snooker Billiards	Proportion of population: 11.3% M, 3% F Relative participation: 77.9% M, 22.1% F	No official policy
Motor racing	Motorsport UK	All four-wheeled motorsports	N/a	No official policy
Darts	United Kingdom Darts Association	Darts	Proportion of population: 5.1% M, 1.5% F Relative participation: 76.8% M, 23.2% F	No information on policy development provided in official statement
Badminton	Badminton England Ulster Badminton (Northern Ireland) Badminton Scotland Badminton Wales	Badminton	Proportion of population: 3.4% M, 2.1% F Relative participation: 60.9% M, 39.1% F	Policy based upon: • IOC Consensus 2015 • Equality Act 2010 • Data Protection Act 1998 • General Data Protection Regulation 2018 • Gender Recognition Act 2004 Approved by CMT and the board of directors Reviewed by ethics and compliance manager

Table 2. UK sporting organizations' transgender policies for the 15 most popular sports.

Sporting Organisation	Official Transgender Statement/Policy	Adolescent/Child Participation	Testosterone Cut-Off Levels	Evidence Required	Transgender Male and Gender-Diverse Athletes on Testosterone Therapy Competition Requirements	Transgender Female and Gender-Diverse Athletes on Oestrogen Therapy Competition Requirements	Years out of Competition (e.g., during Transition)	Notes
The Football Association	The Football Association Policy on Trans People in Football (2014)	No restrictions up until the age of 16 years	Normal range for affirmed gender as per the IOC	Individual case-by-case review Complete medical record Annual verification of hormones Proof of ID	Hormone therapy results in testosterone levels within biological male range	Hormone therapy/gonadectomy resulting in blood testosterone within the biological female range	Until such time as they have been provided with written clearance by the FA	Based on the International Olympic Committee's position from May 2004. Without hormone therapy/surgery, cases are still reviewed individually
UK Athletics	UKA Eligibility for competition: Transgender and Female Classification Regulations (2021) UKA Policy and Procedures on Transsexual People in Athletics Competitions (2016)	Transgender female and gender-diverse athletes under 16, post-puberty: case-by-case review Transgender female and gender-diverse athletes, pre-pubescent: no restrictions	Normal range for affirmed gender, not specified	Serum hormonal levels Complete medical record Annual verification	Medical evidence that athlete is undergoing gender-affirming hormone therapy	Hormone therapy bringing serum testosterone within physiological biological female range or gonadectomy Can compete in male category sports if therapy has not begun	Not specified	Cases assessed on case-by-case basis following World Athletics guidance and may request support from World Athletics
England and Wales Cricket Board *	England and Wales Cricket Board Policy on Trans People Playing Cricket	Not specified	Not specified	Written clearance from the ECB Head of Policy Development	Cannot compete in any female-only competition, league or match	Written clearance from ECB Head of Policy Development	Not specified	Formed in line with guidance from the ICC, IOC and Stonewall UK (trans-rights charity). No restrictions in mixed sport

Table 2. Cont.

Sporting Organisation	Official Transgender Statement/Policy	Adolescent/Child Participation	Testosterone Cut-Off Levels	Evidence Required	Transgender Male and Gender-Diverse Athletes on Testosterone Therapy Competition Requirements	Transgender Female and Gender-Diverse Athletes on Oestrogen Therapy Competition Requirements	Years out of Competition (e.g., during Transition)	Notes
British Rowing	Trans and Non-Binary Inclusion Competition Policy and Procedures, 2022	“Due to the unique variance of physical and psychological developmental changes that take place during puberty and the medical options available to adolescents, the eligibility panel may, where appropriate, consider and approve an application without medical evidence . . . In considering an application the Panel will be mindful of the relevant criteria. It should be noted that a trans or non-binary person who has been determined eligible for the junior women’s category will, upon turning 16, be expected to comply with requirements set out [in the policy] and it is recognised that until the individual is able to access appropriate hormone treatment, they may not be eligible for the women’s category”	Not specified	Blood-measured testosterone levels	May compete as their affirmed gender in any “open” competition Need to be aware of anti-doping requirements	Must provide a signed letter stating that their consistent gender identity is “female”; this gender identity cannot be changed for a period of one year If >16 years old: testosterone level <5 nmol.L for previous 12 months and this level must be maintained during competition; medical evidence showing that the person has undergone surgery for the purpose of transitioning and therefore does not need to undergo hormone treatment; may compete as affirmed gender with evidence of serum testosterone or in male category competition if treatment has not started	Not specified. Testosterone levels for transgender females need to be <5 nmol.L for 12 months prior to competition	Adopted from the IOC position (2021). “A trans or non-binary person will no longer be eligible for the women’s category in domestic competition, if their testosterone levels rise above 5 nmol/L or if they have started female to male hormone treatment or undergone female to male gender reassignment surgery. Any trans or non-binary person who is not eligible to compete in the women’s category, will still be able to compete in the Open category.” “Submissions . . . must be made to an Expert Panel comprising two members of British Rowing’s Medical Advisory Panel, and a lawyer from one of British Rowing’s Panels.” Case-by-case decisions. “The Expert Panel may request that a trans or non-binary person whose gender identity was not female at birth, who is undergoing hormone treatment and is intending to compete in the women’s category, resubmit their declaration annually to confirm they are still undergoing treatment.” Eligibility for national teams and international competition differs from this domestic policy

Table 2. Cont.

Sporting Organisation	Official Transgender Statement/Policy	Adolescent/Child Participation	Testosterone Cut-Off Levels	Evidence Required	Transgender Male and Gender-Diverse Athletes on Testosterone Therapy Competition Requirements	Transgender Female and Gender-Diverse Athletes on Oestrogen Therapy Competition Requirements	Years out of Competition (e.g., during Transition)	Notes
British Cycling	British Cycling Transgender and Non-Binary Participation Policy (currently under review as of 6 April 2022, although data were taken from UCI guidelines updated in 2022) ¹	Not specified	<2.5 nmol/L for at least 24 months	Recreational: no evidence required Competitive: race license to compete in proposed category; approval from medical professional	No evidence required other than a signed declaration of affirmed gender	Signed declaration and hormonal evidence, with serum testosterone remaining <2.5 nmol/L throughout competitive period	12 months minimum	IOC position taken into account, as well as UCI medical policy
England Golf *	Inclusion policy with respect to transgender people entering England Golf competitions	Not specified	Not specified	Proof of status >14 days in advance of competition Legal evidence +/ – proof of hormone therapy	Evidence of legal recognition of re-assigned gender	Evidence of legal recognition of gender other than sex assigned at birth Hormone therapy for “sufficient” length of time	Female only: hormone therapy For sufficient length of time to minimise sex-related advantages	N/a
British Swimming	British Swimming Policy on Trans Competitors (under review) ²	<16, pre-pubescent: no restrictions <16, post-puberty: case-by-case review	Not specified	Evidence of pubertal stage (if < 16) Female only: hormonal levels	No hormonal or other evidence required	Hormonal therapy or verification of gonadectomy Annual re-verification of hormonal therapy	Female only: hormone therapy for sufficient length of time	Based on guidance from Sports Council Equality Group. All enquiries are presented to British Swimming’s Equality and Participation Panel. Separate guidance for contact disciplines
Lawn Tennis Association (LTA)	LTA policy and guidance on trans people playing tennis *	Not specified	Not specified Players on the performance pathway must be compliant with International Tennis Federation (ITF) policy	Proof of sex or Gender Recognition Certificate (GRC)	Not specified	Not specified	A GRC requires the person to have lived with the gender role for a minimum of 2 years	This document is currently under review in light of proposed Sport England guidance and equalities advice
Rugby Football Union (RFU) *	England Rugby Policy for the Participation of Transgender and Non-Binary Gender Players in Rugby Union (2019)	<11 age grade: no restrictions	<5 nmol/L	Written and signed gender declaration	Signed gender declaration	Signed gender declaration by the athlete Evidence of serum testosterone	Transgender female and gender-diverse athletes: testosterone <5 nmol/L for at least 12 months	No restrictions for non-contact (“tag”) rugby

Table 2. Cont.

Sporting Organisation	Official Transgender Statement/Policy	Adolescent/Child Participation	Testosterone Cut-Off Levels	Evidence Required	Transgender Male and Gender-Diverse Athletes on Testosterone Therapy Competition Requirements	Transgender Female and Gender-Diverse Athletes on Oestrogen Therapy Competition Requirements	Years out of Competition (e.g., during Transition)	Notes
Rugby Football League	RFL Transgender and Transsexual Policy	N/a	N/a	N/a	N/a	N/a	N/a	Not publicly available, published in November 2011 and referenced here: https://secure.rugby-league.com/ign_docs/Tackle%20IT%20Rugby%20League%20Factfile.pdf , accessed 1 August 2022
British Boxing Board of Control (BBBoC)	No official statement/policy	N/a	N/a	N/a	N/a	N/a	N/a	N/a
World Professional Billiards and Snooker Association	No official statement	N/a	N/a	N/a	N/a	N/a	N/a	World Women's Snooker (WWS) Transgender Policy follows IOC guidance
Motorsport UK	No official statement	N/a	N/a	N/a	N/a	N/a	N/a	N/a
United Kingdom Darts Association	United Kingdom Darts Association Transgender Policy (recently removed from website)	N/a	Not required	Official government-issued ID that indicates their gender	Documentation that gender reassignment is ongoing	Documentation that gender reassignment is ongoing, 1 year minimum	Transgender female and gender-diverse athletes: one year since transition began	N/a
Badminton England *	Badminton England Policy for Transgender Badminton Players 2019 (reviewed 2021)	N/a	<10 nmol/L	Blood-measured testosterone levels, ongoing compliance	Can compete without restriction	Not specified	Transgender female and gender-diverse athletes: hormonal suppression for minimum of 12 months; non-compliance results in 12 month suspension	Based on IOC 2015, Gender Recognition Act 2004 and Data Protection 1998
International Olympic Committee (IOC)	IOC Statement on Transgender Guidelines (November 2015)	N/a	<10 nmol/L	Blood-measured testosterone levels	Can compete without restriction	Testosterone levels must remain below 10 nmol/L for the duration of time that eligibility to compete is desired Case-by-case approval Hyperandrogenism may permit participation in male events	Gender identity declaration cannot be changed for four years Transgender female and gender-diverse athletes: hormonal suppression for minimum of 12 months; non-compliance results in 12 month suspension	To require surgical anatomical changes as a pre-condition to participation is not necessary to preserve fair competition and may violate human rights

* Largest and most representative organisation in the United Kingdom. ¹ As of 1 July 2022, international guidance from the UCI has altered their stance to reflect a lower maximum plasma testosterone of 2.5 nmol/L and extended their transition period for low testosterone from 12 to 24 months with respect to transgender female athletes [42]. ² As of 19 June 2022, swimming's world governing body, the FINA, have banned all female transgender athletes from international competitions if they are either >12 years of age or have experienced any part of male puberty beyond Tanner stage 2 [43].

Twelve of the fifteen governing bodies had an official TGD policy (even if that policy was just to state that there were no interventions required for participation), of which eleven were publicly available (with the 2011 Rugby League guideline being referenced in an alternative publication but not available despite attempts to contact the governing body directly). Of these 12, all had pre-requisites for trans women athletes (testosterone monitoring, written medical documentation or clearance before a panel (Table 2)). Five of the twelve had separate guidance for adolescent/pre-pubescent versus post-pubertal athletic participation. Seven drew guidance from the official IOC Statement on Transgender Guidelines [44], particularly in reference to physiological testosterone levels. Many (8/12) organisations included the disclaimer that they made “case-by-case” decisions on an athlete’s competitive eligibility, using their policies only as a guide for decision making. The official 2021 IOC Framework also states that all athletes are approved on a case-by-case basis in their guidance, with wordings being very similar to this policy across each sport. The additional criteria assessed in case-by-case decisions are not discussed in any policy (with the exception of badminton, for which the guidance states that the duration of hormonal therapy/transitioning would be assessed individually to ascertain adequacy). Several policies have less strict restrictions on participation at the recreational/amateur level, including athletics, tennis and cycling. For athletics, the governing body, United Kingdom Athletics (UKA), specifies that restrictions do not apply to training, friendly/fun runs or mass participation events, such as charity events; restrictions are only applied to competitions where qualifying marks, selection standards and records are set. British Cycling stipulates that there are no regulations for recreational activities, and the Lawn Tennis Association states that recreational and friendly matches are exempt. Other policies do not specifically comment on training, recreational activity within clubs or friendly matches; therefore, their stances are unclear. Only two policies (Rugby Football Union and British Rowing) mention the specific involvement of or consultation with a medical professional/medical officer in their TGD policy development. Three of the policies are currently under review.

In two of the three sports without TGD policies, it could be proposed that physical differences in competitors are unlikely to result in harm to individuals or fellow competitors or involve a significant physical competitive advantage for males (“sex-affected sports”). These sports are snooker/billiards and motorsports. The third, however, is boxing; the British Boxing Board of Control has no official TGD participation policy. Although the Rugby Football League (RFL) refers to a TGD policy published in 2011, it is not publicly available and was not made available when we emailed the RFL contact on their website.

Notably, where policies exist, a definition of transgender is often provided to outline the remit of the policy. Policies relate to transgender as opposed to intersex athletes or athletes with DSD.

4. Discussion

This is the first scoping review to summarise the TGD policies of the 15 most widely played sports in the UK, detailing the individual protocols of each sporting governing body for TGD athletes. Our review showed that 80% (12/15) of the organisations have an official TGD athlete participation policy. The policies are highly heterogeneous, with different requirements and time frames for TGD athletes to be included in a class other than that of their biological sex. The majority of policies rely heavily on the official IOC Statement on Transgender policies [2,44], stating they will refer to it when making decisions on individual athletes and generally adopting a case-by-case approach when assessing TGD athletes. Only 38% (5/13) of the guidelines have separate guidance for adolescent or child athletes. There appears to be no difference in the rigour of assessment between non-contact and contact sports and, indeed, boxing has no current TGD policy. Criteria were globally much stricter for trans female athletes wishing to participate in the female category versus trans male athletes wishing to compete in the male category. Finally, although serum testosterone levels were specified for four sports (<2.5 nmol/L for cycling, <5 nmol/L for

rugby union and rowing, and <10 nmol/L for badminton), for participation in the female events, few details are provided on what sporting organisation is responsible for the testing, the parameters around the testing and the steps taken if the athlete's testosterone level is outside these stated ranges. Three sports (athletics, cycling and tennis) have more relaxed TGD policies for sport participation at the recreational level.

4.1. Adolescent and Child Participation

Five sports (cricket, rowing, cycling, golf and tennis) had pre-puberty guidelines for TGD sport participation, with most sports stating that puberty occurred from 16 years of age onwards. However, some children, including those under 16 years of age, may identify as TGD [45], and thus sport organisations may wish to formally address this within their TGD policies. The Guidelines for Creating Policies for Transgender Children in Recreational Sports, the national policy of the United States (US), assert that no hormonally based advantage exists for sexes prior to puberty [46], although other authors contend that there is pre-pubertal difference, in keeping with the concept of “mini-puberty”, as well as genes exclusively related to the Y-chromosome [47–50]. Furthermore, the onset of puberty shows some variance among individuals, as well as the sexes, and, therefore, it is difficult to set an arbitrary age limit via which athletes could be considered pre- and post-pubertal. Puberty is, however, rare before the ages of nine and eight in males and females, respectively [51–53]. There is, therefore, a need for TGD policies in sport to address pre- and post-pubertal athletic participation.

4.2. Anthropometric Sex Differences and Impact on Sport Performance

Although physical sex differences are noted (some in athletic and some in non-athletic populations), and certain sports seem to preferentially select at the extremes of the distribution for a trait (e.g., height in basketball), it is plausible that an anthropometric advantage could exist for TGD athletes in their sport. TGD policies should investigate this further within their cohort of athletes to determine whether it is the case. Similarly, when an athlete has increased muscle mass or body size relative to peers in their gender (outside of what can be observed within the given sex), they have greater potential to inflict injuries on others, potentially compromising safety [12].

Moreover, it has been reported that muscle nuclei that have been developed during periods of testosterone therapy remain in the muscle even after drug cessation and potentially confer a lifelong muscle-building advantage [54–56]. Therefore, although it is difficult to measure the magnitude of the advantage that might be obtained in a given sport for a range of physical metrics that differ between the sexes, these performance advantages are present partly due to androgenic male puberty and are not dependent on current circulating testosterone. Thus, TGD policies should consider whether the athlete has undergone puberty and what affect this could have on their participation in their chosen sport, as well as considering circulating testosterone levels.

4.3. Testosterone Cut-off Levels and Duration of Exclusion from Sporting Participation

4.3.1. Transgender (Trans Women/Trans Female) and Gender-Diverse Athletes with Suppressed Testosterone

Our research indicated that, when specified, testosterone levels lower than 2.5 nmol/L for 24 months (cycling—UCI rules) and lower than 5 nmol/L for at least 12 months (rugby and rowing) are considered general cut-offs among UK sport organisation for trans women's participation in female sport, although badminton guidelines specify a testosterone value lower than 10 nmol/L, in keeping with the 2015 IOC guidance [44]. The UCI has recently reduced its testosterone cut-off level to 2.5 nmol/L for two years [42], and the UK national governing body policy is likely to follow. However, adult males generally have testosterone levels at least 15 times higher than females of a similar age [57], and the 95% confidence interval for circulating testosterone in healthy premenopausal adult females is 0–1.7 nmol/L [57]. Thus, sport organisation need to consider what testosterone

levels will apply to their sport and what lengths of time out of competition will apply. These findings may be particularly relevant for strength-based (requiring running and jumping) and contact sports; for example, rugby, football, boxing and martial arts. Different considerations may be needed for sports where physiological differences or potential safety concerns are not an issue and inclusivity can be prioritized.

Another important issue to consider for competitive, strength-based sport participation is non-compliance with the proposed upper limit for serum testosterone levels as measured by liquid chromatography–mass spectrometry. Only the IOC provides guidance for non-compliance with these limits [44], enforcing 12 months of exclusion following a supraphysiological result. However, little detail is provided on how this testing will be undertaken and whose responsibility it is to undertake it. The World Anti-Doping Association (WADA) has produced a physician guide for TUE applications for transgender athletes (accessed at <https://www.wada-ama.org/en/resources/therapeutic-use-exemption/tue-physician-guidelines-transgender-athletes#resource-download>, accessed on 10 January 2023) and suggests testosterone testing at least 1–2 times per year by the treating physician.

4.3.2. Transgender (Trans Men/Trans Male Athletes) and Gender-Diverse Athletes on Testosterone Therapy

Less guidance exists amongst UK sporting organisations for the participation of trans men/trans male athletes on testosterone therapy, with many groups requiring either no information (hormonal or otherwise) or simply a written declaration. The Football Association is the only organisation requesting hormonal levels and requiring them to be within the male range. Exogenous androgens are known to be performance-enhancing for all athletes and are, therefore, on the WADA's Prohibited List [58]. In hypogonadal male athletes, testosterone replacement therapy has often been found to result in testosterone levels above the upper range of normal [59], and its prevalence in mainstream sports has recently come under scrutiny for potentially conferring an advantage [60–62].

Beyond this, exogenous testosterone therapy may also confer an advantage within physiological levels [63–65], which requires further consideration. In males, testosterone levels fluctuate with the circadian rhythm and in response to disease, stress (both physical and mental), increasing age and other stimuli [66,67]. In some sports, rapid weight loss and low body fat levels are common prior to competitions (for example, in boxing) [68,69], with known effects on testosterone levels, as part of the recognised spectrum Relative Energy Deficiency in Sport (RED-S) [70–73]. Reductions in testosterone levels are observed when body fat is reduced below a certain level [74,75]. In trans male athletes receiving exogenous testosterone supplementation, such fluctuations or reductions pre-competition will not be observed, nor will diurnal fluctuations [76–79]. With dose–response effects from testosterone on strength, power, muscle size and body fat percentages within physiological ranges being demonstrable [57,65], athletes can titrate their levels to consistently remain at the upper limit of normal. Indeed, for this reason, the Nevada State Athletic Commissions (NSAC) banned testosterone replacement therapy in biological males in the Ultimate Fighting Championships (UFC) in 2014 [61,80].

4.4. Future Direction and Recommendations for TGD Sport Policies

The 2021 IOC Framework on Fairness, Inclusion and Non-discrimination promotes ten principles, primarily focusing on inclusion and non-discrimination, for sport federations to consider when organising sporting events [2]. Current considerations for the participation of transgender and gender-diverse athletes receiving gender-affirming hormone therapy (GAHT) in competitive sports are based predominantly on current serum testosterone levels. Testosterone-related performance enhancement may persist in some sports through the retention of physical advantage or muscular strength even after the normalisation of serum levels in trans women athletes [12,81]. The use of current testosterone levels has limitations, as previously discussed, and sport organisations should consider whether using current testosterone as a marker of competitive fairness fulfils their policy aims.

Further investigation into testosterone replacement in trans male athletes is required. This is of particular importance in weight-based sports, where the athlete might not be exposed to the testosterone fluctuations associated with weight changes that occur as part of the RED-S spectrum. The impact of anthropometric variables on sporting ability also likely requires further investigation. Clear policies for monitoring testosterone levels and anthropometric variables in TGD athletes should, therefore, be put in place by all sporting organisations if such policies enable TGD athletes to compete in a class other than that of their biological sex. A clear process for the management of levels lying outside of the proposed testosterone serum range should be developed, with clear guidelines on how abnormal results will be managed. Additionally, under the new 2021 IOC Framework on Fairness, Inclusion and Non-discrimination, male advantage over female athletes cannot be assumed in all sports. Studies have reported advantages in many sports in which power, strength and endurance are directly related to performance [25–28]. In some sports, further studies may be required; for example, motorsports or snooker. Sport organisations also need to specify the transitioning requirements for both pre- and post-puberty adolescent athletes, and all future transgender policies should include a pre- and post-puberty adolescent athlete section, as well as TGD policies for competitive and recreational sport. A section should also be included in all policies to define the term “transgender” for the purposes of the policy, and separate policies should be developed for intersex and DSD athletes. Additionally, when policies are finalised, consultation involving relevant stakeholders within the sport should take place and relevant external contributors should be allowed to offer input.

5. Limitations

This article provides a comprehensive overview of TGD athlete policies across UK sports and identifies areas of similarity and discrepancy. However, TGD policies outside the UK were not considered in this scoping review, although we recognise the recent TGD policy changes by the UCI [42] and Federation Internationale de Natation (FINA) [43], which will likely be reflected in UK TGD policies. Future scoping reviews could investigate and compare TGD policies from organisations outside of the UK. As different physiological requirements exist across various sports, TGD policies will likely differ between sports. It was beyond the scope of this paper to recommend TGD policies for each sport, and the paper rather aimed to highlight areas where a consistent approach to TGD athletes and sport participation is needed or could be useful. This review did not include policies related to para-athletes in UK sport; this is a topic for further investigation. TGD policy is a rapidly evolving field in sport medicine, and this scoping review therefore only provides a snapshot of sports’ current TGD policies, which are currently evolving.

6. Conclusions

This scoping review showed a lack of consistency and clear guidelines among UK sporting organisations in managing transgender and gender-diverse (TGD) athletes in competitive sports. Similar reviews investigating TGD policies outside of the UK should be considered. One area that policies for transgender athlete participation need to address is the appropriateness of using testosterone levels as a marker of performance advantage, as retained strength and anthropometric advantages are independent of current testosterone levels. Sporting federations need to develop their transgender policies with input from medical personnel, as well as the wider multi-disciplinary team and external agencies. Policies should consider the need for pre- and post-puberty guidelines, as well as guidelines for both competitive and recreational sport activities. Greater scrutiny needs to be given to trans men athletes regarding their testosterone levels, and sport-specific protocols should be established for how these testosterone levels will be monitored in transgender athletes, with clear rules for competitive sport exclusion based on them. Further studies on transitioning and transgender athletes aimed at understanding the impact of TGD athletes in their respective sports—and the potential impact of transitioning athletes on biologically female

athletes' safety, competitive opportunities and participation in sport at every level—will provide further information to help with policy making in this area. This is a challenging area for policymakers, and it is important that sport organisations are well-informed, undertake diverse considerations and consult widely in the further development and evolution of their sport's TGD policy.

Author Contributions: Conceptualization, N.H.; methodology, M.M. and N.H.; analysis, all authors (M.M., J.T., G.K., N.J., D.G., A.M., M.C., N.H.); data curation, M.M. and N.H.; writing—original draft preparation, all authors (M.M., J.T., G.K., N.J., D.G., A.M., M.C., N.H.); writing—review and editing, all authors (M.M., J.T., G.K., N.J., D.G., A.M., M.C., N.H.). All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. SCEG; TSCEG. *Guidance for Transgender Inclusion in Domestic Sport*; The Sport's Councils Equality Group: London, UK, 2021.
2. IOC Committee. *IOC Framework on Fairness, Inclusion and Non-Discrimination on the basis of Gender Identity and Sex Variations*; International Olympic Committee: Lausanne, Switzerland, 2021.
3. Dyer, K. The trend of the male–female performance differential in athletics, swimming and cycling 1948–1976. *J. Biosoc. Sci.* **1977**, *9*, 325–338.
4. Simpson, J.L.; Ljungqvist, A.; De la Chapelle, A.; Ferguson-Smith, M.A.; Genel, M.; Carlson, A.S.; Ehrhardt, A.A.; Ferris, E. Gender Verification in Competitive Sports. *Sports Med.* **1993**, *16*, 305–315. [[CrossRef](#)] [[PubMed](#)]
5. Harper, J.; O'Donnell, E.; Khorashad, B.S.; McDermott, H.; Witcomb, G.L. How does hormone transition in transgender women change body composition, muscle strength and haemoglobin? Systematic review with a focus on the implications for sport participation. *Br. J. Sport. Med.* **2021**, *55*, 865–872. [[CrossRef](#)] [[PubMed](#)]
6. Cauldwell, D.O. Psychopathia transexualis. In *The Transgender Studies Reader*; Routledge: Abingdon-on-Thames, UK, 2006; pp. 40–44.
7. Sandbakk, Ø.; Solli, G.S.; Holmberg, H.-C. Sex Differences in World-Record Performance: The Influence of Sport Discipline and Competition Duration. *Int. J. Sports Physiol. Perform.* **2018**, *13*, 2–8. [[CrossRef](#)] [[PubMed](#)]
8. Hegge, A.M.; Bucher, E.; Ettema, G.; Faude, O.; Holmberg, H.-C.; Sandbakk, Ø. Gender differences in power production, energetic capacity and efficiency of elite cross-country skiers during whole-body, upper-body, and arm poling. *Eur. J. Appl. Physiol.* **2016**, *116*, 291–300. [[CrossRef](#)] [[PubMed](#)]
9. Perez-Gomez, J.; Rodriguez, G.V.; Ara, I.; Olmedillas, H.; Chavarren, J.; González-Henriquez, J.J.; Dorado, C.; Calbet, J.A.L. Role of muscle mass on sprint performance: Gender differences? *Eur. J. Appl. Physiol.* **2008**, *102*, 685–694. [[CrossRef](#)] [[PubMed](#)]
10. Mujika, I.; Rønnestad, B.R.; Martin, D.T. Effects of Increased Muscle Strength and Muscle Mass on Endurance-Cycling Performance. *Int. J. Sports Physiol. Perform.* **2016**, *11*, 283–289. [[CrossRef](#)] [[PubMed](#)]
11. Handelsman, D.J. Sex differences in athletic performance emerge coinciding with the onset of male puberty. *Clin. Endocrinol.* **2017**, *87*, 68–72. [[CrossRef](#)]
12. Hilton, E.N.; Lundberg, T.R. Transgender Women in the Female Category of Sport: Perspectives on Testosterone Suppression and Performance Advantage. *Sports Med.* **2021**, *51*, 199–214. [[CrossRef](#)]
13. Ferber, R.; McClay Davis, I.; Williams Iii, D.S. Gender differences in lower extremity mechanics during running. *Clin. Biomech.* **2003**, *18*, 350–357. [[CrossRef](#)]
14. Jain, A.; Bansal, R.; Kumar, A.; Singh, K.D. A comparative study of visual and auditory reaction times on the basis of gender and physical activity levels of medical first year students. *Int. J. Appl. Basic Med. Res.* **2015**, *5*, 124–127. [[CrossRef](#)] [[PubMed](#)]
15. Lipps, D.B.; Galecki, A.T.; Ashton-Miller, J.A. On the Implications of a Sex Difference in the Reaction Times of Sprinters at the Beijing Olympics. *PLoS ONE* **2011**, *6*, e26141. [[CrossRef](#)] [[PubMed](#)]
16. Shultz, S.J.; Nguyen, A.-D.; Schutz, R.J. Differences in Lower Extremity Anatomical and Postural Characteristics in Males and Females between Maturation Groups. *J. Orthop. Sports Phys. Ther.* **2008**, *38*, 137–149. [[CrossRef](#)] [[PubMed](#)]
17. Tiller, N.B.; Elliott-Sale, K.J.; Knechtle, B.; Wilson, P.B.; Roberts, J.D.; Millet, G.Y. Do Sex Differences in Physiology Confer a Female Advantage in Ultra-Endurance Sport? *Sports Med.* **2021**, *51*, 895–915. [[CrossRef](#)]
18. Daniels, J.; Daniels, N. Running economy of elite male and elite female runners. *Med. Sci. Sports Exerc.* **1992**, *24*, 483–489. [[CrossRef](#)]
19. Blum, M. Estimating male and female height inequality. *Econ. Hum. Biol.* **2014**, *14*, 103–108. [[CrossRef](#)]

20. Norton, K.; Olds, T.; Olive, S.; Craig, N. Anthropometry and sports performance. In *Anthropometrica*; UNSW Press: Sydney, Australia, 1996; pp. 287–364.
21. Fuster, V.; Jerez, A.; Ortega, A. Anthropometry and strength relationship: Male-female differences. *Anthropol. Anz.* **1998**, *56*, 49–56. [CrossRef]
22. Myers, J.; Kaminsky, L.A.; Lima, R.; Christle, J.W.; Ashley, E.; Arena, R. A Reference Equation for Normal Standards for VO₂ Max: Analysis from the Fitness Registry and the Importance of Exercise National Database (FRIEND Registry). *Prog. Cardiovasc. Dis.* **2017**, *60*, 21–29. [CrossRef]
23. Bassett, D.R.; Howley, E.T. Limiting factors for maximum oxygen uptake and determinants of endurance performance. *Med. Sci. Sports Exerc.* **2000**, *32*, 70–84. [CrossRef]
24. Gooren, L.J.; Bunck, M.C. Transsexuals and competitive sports. *Eur. J. Endocrinol.* **2004**, *151*, 425–429. [CrossRef]
25. World Records. World Athletics. 2022. Available online: <https://www.worldathletics.org/records/by-category/world-records> (accessed on 10 January 2023).
26. Wikipedia. List of World Records in Track Cycling. 2022. Available online: https://en.wikipedia.org/w/index.php?title=List_of_world_records_in_track_cycling&oldid=110969387 (accessed on 10 January 2023).
27. Records. European Athletics. 2022. Available online: <https://www.european-athletics.com/historical-data/record> (accessed on 10 January 2023).
28. GBR Athletics. UK Records. 2022. Available online: <https://www.watchathletics.com/page/3278/results-british-athletics-championships-2022> (accessed on 10 January 2023).
29. Wankel, L.M.; Berger, B.G. The psychological and social benefits of sport and physical activity. *J. Leis. Res.* **1990**, *22*, 167–182. [CrossRef]
30. Coalter, F. *The Social Benefits of Sport*; SportScotland: Edinburgh, UK, 2005; Volume 17.
31. Tricco, A.C.; Lillie, E.; Zarin, W.; O'Brien, K.K.; Colquhoun, H.; Levac, D.; Moher, D.; Peters, M.D.J.; Horsley, T.; Weeks, L.; et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann. Intern. Med.* **2018**, *169*, 467–473. [CrossRef] [PubMed]
32. Peters, M.D.J.; Marnie, C.; Tricco, A.C.; Pollock, D.; Munn, Z.; Alexander, L.; McInerney, P.; Godfrey, C.M.; Khalil, H. Updated methodological guidance for the conduct of scoping reviews. *JBI Evid. Synth.* **2020**, *18*, 2119–2126. [CrossRef] [PubMed]
33. Grant, M.J.; Booth, A. A typology of reviews: An analysis of 14 review types and associated methodologies. *Health Inf. Libr. J.* **2009**, *26*, 91–108. [CrossRef] [PubMed]
34. Arksey, H.; O'Malley, L. Scoping studies: Towards a methodological framework. *Int. J. Soc. Res. Methodol.* **2005**, *8*, 19–32. [CrossRef]
35. Levac, D.; Colquhoun, H.; O'Brien, K.K. Scoping studies: Advancing the methodology. *Implement. Sci.* **2010**, *5*, 69. [CrossRef]
36. MORI IPSOS. MORI Sports Tracker—Interest in Sports. 2003. Available online: <https://www.ipsos.com/en-uk/rugby-union-britains-second-most-popular-sport> (accessed on 10 January 2023).
37. Sports England. *Active Lives Adult Survey November 2019/20 Report*; Sport England: London, UK, 2021.
38. Harris Interactive. *Sports Participation, Viewing & Fandom in the UK*; Harris Interactive: Ealing, UK, 2019.
39. Sports England. *Active Lives Adult Survey November 16/17 Report*; Sport England: London, UK, 2018.
40. Lange, D. Number of People Participating in Sport Twice a Month in England between November 2019 and November 2020, by Sport. Available online: <https://www.statista.com/statistics/975115/sport-participation-england/> (accessed on 10 January 2023).
41. Jones, H.; Millward, P.; Buraimo, B. *Adult participation in Sport: Analysis of the Taking Part Survey 2011*; UK Department for Culture, Media and Sport: London, UK, 2011.
42. Hurford, M. The UCI Announces Changes to Its Policy on Transgender Athletes: Cycling's International Governing Body Extends Transition Time and Lowers Testosterone Threshold for Competition. 2022. Available online: <https://www.bicycling.com/news/a40320907/uci-transgender-policy-2022> (accessed on 10 January 2023).
43. Fahey, C. FINA Bans Transgender Athletes from Women's Events. 2022. Available online: <https://time.com/6189147/fina-policy-transgender-athletes/> (accessed on 10 January 2023).
44. IOC Committee. *IOC Consensus Meeting on Sex Reassignment and Hyperandrogenism, November 2015*; International Olympic Committee: Lausanne, Switzerland, 2015.
45. Zucker, K.J. Epidemiology of gender dysphoria and transgender identity. *Sex Health* **2017**, *14*, 404–411. [CrossRef]
46. *Guidelines for Creating Policies for Transgender Children in Recreational Sports*; Australian Human Rights Commission: Sydney, Australia, 2009.
47. Chen, X.; McClusky, R.; Itoh, Y.; Reue, K.; Arnold, A.P. X and Y chromosome complement influence adiposity and metabolism in mice. *Endocrinology* **2013**, *154*, 1092–1104. [CrossRef]
48. Mauvais-Jarvis, F. Sex differences in metabolic homeostasis, diabetes, and obesity. *Biol. Sex Differ.* **2015**, *6*, 14. [CrossRef]
49. Copeland, K.C.; Chernausk, S. Mini-Puberty and Growth. *Pediatrics* **2016**, *138*, 1301. [CrossRef]
50. Kuiri-Hänninen, T.; Sankilampi, U.; Dunkel, L. Activation of the Hypothalamic-Pituitary-Gonadal Axis in Infancy: Minipuberty. *Horm. Res. Paediatr.* **2014**, *82*, 73–80. [CrossRef]
51. NHS. Early or Delayed Puberty. Available online: <https://www.nhs.uk/conditions/early-or-delayed-puberty/#:~:text=The%20average%20age%20for%20girls,9%20and%2014%20in%20boys> (accessed on 10 January 2023).
52. Carel, J.-C.; Léger, J. Precocious Puberty. *N. Engl. J. Med.* **2008**, *358*, 2366–2377. [CrossRef] [PubMed]

53. Tanner, J. Variations in Pattern of Pubertal Changes in Girls. *Arch. Dis. Child.* **1969**, *44*, 291.
54. Egner, I.M.; Bruusgaard, J.C.; Eftestøl, E.; Gundersen, K. A cellular memory mechanism aids overload hypertrophy in muscle long after an episodic exposure to anabolic steroids. *J. Physiol.* **2013**, *591*, 6221–6230. [CrossRef] [PubMed]
55. Kadi, F.; Eriksson, A.; Holmner, S.; Thornell, L.E. Effects of anabolic steroids on the muscle cells of strength-trained athletes. *Med. Sci. Sports Exerc.* **1999**, *31*, 1528–1534. [CrossRef]
56. Hembree, W.C.; Cohen-Kettenis, P.T.; Gooren, L.; Hannema, S.E.; Meyer, W.J.; Murad, M.H.; Rosenthal, S.M.; Safer, J.D.; Tangpricha, V.; T'Sjoen, G.G. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J. Clin. Endocrinol. Metab.* **2017**, *102*, 3869–3903. [CrossRef]
57. Handelsman, D.J.; Hirschberg, A.L.; Berman, S. Circulating Testosterone as the Hormonal Basis of Sex Differences in Athletic Performance. *Endocr. Rev.* **2018**, *39*, 803–829. [CrossRef]
58. Huang, G.; Basaria, S. Do anabolic-androgenic steroids have performance-enhancing effects in female athletes? *Mol. Cell. Endocrinol.* **2018**, *464*, 56–64. [CrossRef]
59. Di Luigi, L.; Sgrò, P.; Aversa, A.; Migliaccio, S.; Bianchini, S.; Botrè, F.; Romanelli, F.; Lenzi, A. Concerns About Serum Androgens Monitoring During Testosterone Replacement Treatments in Hypogonadal Male Athletes: A Pilot Study. *J. Sex. Med.* **2012**, *9*, 873–886. [CrossRef]
60. Leddy, M.J., III. Testosterone Replacement Therapy in the Male Athlete. *Sports Med.* **2015**, 1–4. Available online: <https://journals.sagepub.com/pb-assets/cmscontent/ojs/OJS-Hormone%20Replacement%20Nov-Dec15-1471881257317.pdf> (accessed on 10 January 2023).
61. GibbsLawGroup. Testosterone Replacement Therapy Banned By Nevada Athletic Commission Decision Supported By Ultimate Fighting Championship. Available online: <https://www.classlawgroup.com/testosterone-replacement-therapy-banned-by-nevada-athletic-commission-decision-supported-by-ultimate-fighting-championship/> (accessed on 10 January 2023).
62. WADA. *Guidelines for the International Standard for Therapeutic Use Exemptions*; WADA: Montreal, QC, Canada, 2020.
63. Storer, T.W.; Magliano, L.; Woodhouse, L.; Lee, M.L.; Dzekov, C.; Dzekov, J.; Casaburi, R.; Bhasin, S. Testosterone dose-dependently increases maximal voluntary strength and leg power, but does not affect fatigability or specific tension. *J. Clin. Endocrinol. Metab.* **2003**, *88*, 1478–1485. [CrossRef] [PubMed]
64. Berman, S.; Hirschberg, A.L.; Kowalski, J.; Eklund, E. Serum androgen levels are positively correlated with athletic performance and competition results in elite female athletes. *Br. J. Sports Med.* **2018**, *52*, 1531–1532. [CrossRef] [PubMed]
65. Bhasin, S.; Woodhouse, L.; Casaburi, R.; Singh, A.B.; Bhasin, D.; Berman, N.; Chen, X.; Yarasheski, K.E.; Magliano, L.; Dzekov, C.; et al. Testosterone dose-response relationships in healthy young men. *Am. J. Physiol. Endocrinol. Metab.* **2001**, *281*, E1172–E1181. [CrossRef] [PubMed]
66. Gall, H.; Glowania, H.J.; Fischer, M. [Circadian rhythm of testosterone level in plasma. I. Physiologic 24-hour oscillations of the testosterone level in plasma]. *Andrologia* **1979**, *11*, 287–292. [CrossRef] [PubMed]
67. Daly, W.; Seegers, C.A.; Rubin, D.A.; Dobridge, J.D.; Hackney, A.C. Relationship between stress hormones and testosterone with prolonged endurance exercise. *Eur. J. Appl. Physiol.* **2005**, *93*, 375–380. [CrossRef]
68. Morton, J.P.; Robertson, C.; Sutton, L. Making the Weight: A Case Study From Professional Boxing. *Int. J. Sport Nutr. Exerc. Metab.* **2010**, *20*, 80–85. [CrossRef]
69. Hall, C.J.; Lane, A.M. Effects of rapid weight loss on mood and performance among amateur boxers. *Br. J. Sports Med.* **2001**, *35*, 390–395. [CrossRef]
70. Karila, T.; Sarkkinen, P.; Marttinen, M.; Seppälä, T.; Mero, A.; Tallroth, K. Rapid weight loss decreases serum testosterone. *Int. J. Sports Med.* **2008**, *29*, 872–877. [CrossRef]
71. Yildirim, I. Associations among dehydration, testosterone and stress hormones in terms of body weight loss before competition. *Am. J. Med. Sci.* **2015**, *350*, 103–108. [CrossRef]
72. Statuta, S.M.; Asif, I.M.; Drezner, J.A. Relative energy deficiency in sport (RED-S). *Br. J. Sports Med.* **2017**, *51*, 1570–1571. [CrossRef]
73. Elliott-Sale, K.J.; Tenforde, A.S.; Parziale, A.L.; Holtzman, B.; Ackerman, K.E. Endocrine Effects of Relative Energy Deficiency in Sport. *Int. J. Sport Nutr. Exerc. Metab.* **2018**, *28*, 335–349. [CrossRef] [PubMed]
74. Rossow, L.M.; Fukuda, D.H.; Fahs, C.A.; Loenneke, J.P.; Stout, J.R. Natural Bodybuilding Competition Preparation and Recovery: A 12-Month Case Study. *Int. J. Sports Physiol. Perform.* **2013**, *8*, 582–592. [CrossRef] [PubMed]
75. Mitchell, L.; Slater, G.; Hackett, D.; Johnson, N.; O'connor, H. Physiological implications of preparing for a natural male bodybuilding competition. *Eur. J. Sport Sci.* **2018**, *18*, 619–629. [CrossRef] [PubMed]
76. Westfield, G.; Kaiser, U.B.; Lamb, D.J.; Ramasamy, R. Short-acting testosterone: More physiologic? *Front. Endocrinol.* **2020**, *11*, 572465. [CrossRef]
77. Brambilla, D.J.; Matsumoto, A.M.; Araujo, A.B.; McKinlay, J.B. The Effect of Diurnal Variation on Clinical Measurement of Serum Testosterone and Other Sex Hormone Levels in Men. *J. Clin. Endocrinol. Metab.* **2009**, *94*, 907–913. [CrossRef]
78. Rose, R.M.; Kreuz, L.E.; Holaday, J.W.; Sulak, K.J.; Johnson, C.E. Diurnal Variation of Plasma Testosterone and Cortisol. *J. Endocrinol.* **1972**, *54*, 177–178. [CrossRef]
79. Walton, M.J.; Anderson, R.A.; Kicman, A.T.; Elton, R.A.; Ossowska, K.; Baird, D.T. A diurnal variation in testicular hormone production is maintained following gonadotrophin suppression in normal men. *Clin. Endocrinol.* **2007**, *66*, 123–129. [CrossRef]

80. USADA. What Athletes Need to Know about Wellness and Anti-Aging Clinics. 2019. Available online: <https://www.usada.org/spirit-of-sport/education/wellness-and-anti-aging-clinics/> (accessed on 10 January 2023).
81. Hilton, E.N.; Lundberg, T.R. Transgender Women in the Female Category of Sport: Is the Male Performance Advantage Removed by Testosterone Suppression? *Preprints* **2020**, 2020050226. [CrossRef]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

BMJ Open Disparities in sport participation of transgender women: a systematic and scoping review protocol

Jessica L Hamdan ¹, Andrea Goldstein Shipper ², Stephanie Roth ³,
Yaara Zisman-Ilani ^{4,5}

To cite: Hamdan JL, Shipper AG, Roth S, *et al*. Disparities in sport participation of transgender women: a systematic and scoping review protocol. *BMJ Open* 2023;**13**:e074054. doi:10.1136/bmjopen-2023-074054

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2023-074054>).

Received 25 March 2023

Accepted 27 June 2023



© Author(s) (or their employer(s)) 2023. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Kinesiology, Recreation and Sport Studies, University of Tennessee ELI, Knoxville, Tennessee, USA

²Charles Library, Temple University, Philadelphia, Pennsylvania, USA

³Helen F. Graham Cancer Center, Junior Board Cancer Resource Library, Christiana Care, Newark, Delaware, USA

⁴Department of Social and Behavioral Sciences, College of Public Health, Temple University, Philadelphia, Pennsylvania, USA

⁵Department of Clinical, Educational and Health Psychology, Division of Psychology and Language Sciences, University College London (UCL), London, UK

Correspondence to

Dr Yaara Zisman-Ilani;
yaara@temple.edu

ABSTRACT

Introduction Transgender women experience disparities in sport participation that are exacerbated by policies from sport organisations and legislation in the USA regulating the participation of transgender women in the category that best aligns with their gender identity. Both transgender and cisgender women are affected by these policies because sport organisations do not have a clear understanding of the effects of gender-affirming hormone therapy on transgender women and the unfair advantage they may have over cisgender women athletes. This article describes a review protocol to understand disparities in sport participation of transgender women.

Methods and analysis A systematic and scoping review is being conducted. Studies are included if they explore disparities in sport participation (ie, participation rates, real and/or perceived barriers to participation) of transgender women of any age. A search strategy has been developed for PubMed, EMBASE, Web of Science, Cochrane Library and CINAHL. Relevant grey literature will also be scanned. The planned search dates are July and August 2023.

Ethics and dissemination This review does not directly involve human subjects, so ethical approval is not required. Findings from the systematic review will be disseminated via publications in peer-reviewed journals and conferences.

INTRODUCTION

Transgender athletes are often subject to policies put in place by sport organisations to regulate their participation in sports even though there is **limited evidence backing these policies**.^{1–4} These policies have been developed in recent years to address potential inequalities towards cisgender women athletes, who were assigned female at birth and identify as women, by transgender women athletes, who were assigned male at birth and identify as women. Such policies include the new regulations from World Athletics, in effect as of 31 March 2023, that strictly exclude transgender women who have experienced male puberty from competing in women's World Rankings competitions.⁵ These regulations come less than a year after World Aquatics, formerly known as

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This protocol outlines a thorough search of five databases as well as grey literature.
- ⇒ This protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols guidelines.
- ⇒ The review is limited to publications in English.

the Fédération Internationale de Natation, implemented similar regulations that were released after swimmer Lia Thomas, one of 36 known transgender athletes to compete at the collegiate level in the past decade,⁶ became the first known transgender woman to win a National Collegiate Athletic Association Division I championship.⁷ Such policies from sport organisations are based on the notion that transgender women athletes are at an advantage due to being assigned male at birth.⁴ However, these policies create further suffering and discrimination for transgender women athletes, who not only struggle with daily challenges related to their transition but are also affected in their athletic careers by excluding transgender women athletes from competing and/or only allowing them to compete in a category that does not align with their gender identity.^{4,8}

Beyond elite-level sport, transgender men and women experience disparities in sport participation and participate in sports at a lower rate compared with the general population.^{8–11} In the USA, approximately 0.6% of the population ages 13 and older identify as transgender, with an even smaller proportion identifying as transgender women.¹² In the USA, there has been a rise in legislation in many states banning transgender youth from participating in sport in the category that best aligns with their gender identity.¹³ There is an association between increased suicidality and familiarity with legislation banning

transgender individuals among sexual and gender minority people.¹⁴

Gender-affirming hormone therapy (GAHT) is used by transgender individuals to better align their body with their gender identity.¹⁵ Transgender women who want to display female characteristics can take oestrogen, an antiandrogen or a combination of both.¹⁵ Oestrogen is a sex hormone that is in higher concentration in women, while antiandrogens are used to reduce testosterone levels.¹⁵ While some argue that GAHT does not remove the unfair advantage transgender women have due to being assigned male at birth,¹⁻³ others argue that there is not a clear link between testosterone levels and sport performance.¹⁶⁻¹⁸

There is an urgent need to prevent bias and discrimination for cisgender and transgender women athletes while enhancing fairness in sport. The purpose of this article is to describe a protocol of a systematic and scoping review to **understand disparities in sport participation of transgender women.** The results may help sport organisations make informed decisions to create more inclusive and fair competition.

METHODS AND ANALYSIS

Protocol and registration

Our protocol was created using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols checklist (online supplemental appendix A)¹⁹ and the Cochrane Handbook for Systematic Reviews of Interventions.²⁰

This protocol is registered on the Open Science Framework (OSF Registration DOI: <https://doi.org/10.17605/OSF.IO/GS7ZB>). No ethical approval is required.

Patient and public involvement

There was no patient or public involvement in the development of this protocol.

Eligibility criteria

This systematic and scoping review will include all literature that explores disparities in sport participation (ie, participation rates, real and/or perceived barriers to participation) of transgender women. The following inclusion criteria will be used to select eligible studies: (a) studies exploring experiences of disparities in sport participation; (b) studies including transgender women of any age; (c) all literature, including grey literature; (d) studies published in the English language. Studies not meeting these criteria, as well as systematic reviews, will be excluded. The planned start date for this review is July 2023, and the planned end date is April 2024.

Search strategy

We will search five databases: PubMed, EMBASE, Web of Science, Cochrane Library and CINAHL. The search strategy was developed by an experienced biomedical librarian for all databases and grey literature (online

supplemental appendix B) using a combination of keywords and subject headings.

We will download the results to ReadCube Papers 4.14.5 and remove all duplicates prior to screening.

Study selection

Two reviewers will conduct a pilot test by independently screening a random 10% of the titles and abstracts and will discuss the results together, with the aim of reaching a minimum of 80% level of agreement. After screening all the titles and abstracts, full-text screening will be performed by two reviewers. Throughout the screening, unresolved disagreements will be discussed with a senior reviewer acting as arbiter where necessary. All screening results will be tracked using a standardised form created in Microsoft Excel.

Data extraction and management

All eligible studies will undergo data extraction by two reviewers independently. The extracted data will be collected on a predesigned form in Microsoft Excel developed by the two reviewers. The data extraction form will include the following information: authors, title, publication year, country, study design type, participant characteristics (ie, age, race, level of education and years in sport), sample size, and results of disparities and barriers. The results will be discussed following the data extraction, and any disagreements will be resolved through discussion between the two reviewers or through the help of a third senior reviewer.

Quality assessment

We will use the Critical Appraisal Skills Programme Qualitative Checklist, which consists of 10 questions, to assess the appraisal of qualitative studies.²¹ We will use the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Cohort Studies, which includes 11 questions to assess the overall appraisal of cohort studies.²² We will use the JBI Critical Appraisal Checklist for Case Control Studies to assess the overall appraisal of case control studies using 10 questions.²³ Two reviewers will assess the risk of bias of included studies independently. The results will be discussed following the completion of the quality assessment, and any disagreements will be resolved through discussion between the two reviewers or through the help of a third reviewer. Grading of Recommendations, Assessment, Development and Evaluations will be used to assess the strength of the body of evidence for all outcomes.

Outcome measures and data synthesis

Included studies should report disparities and/or barriers of participation. Data will be grouped according to the type of literature (ie, quantitative and qualitative). Where possible, we will conduct subgroup analyses according to gender (eg, transgender women and cisgender women), sport played (eg, swimming, basketball, track and field) and level of play (eg, beginner, intermediate, advanced and elite).

ETHICS AND DISSEMINATION

This review does not directly involve human subjects, so ethical approval is not required. Findings from the work will be disseminated via publications in peer-reviewed journals and conferences. We expect findings will benefit sport organisations by helping with improved decision making to become more inclusive and increase fairness in sports. Sport organisations at all levels of competition need to identify and work to remove barriers to sport participation for transgender individuals.

Acknowledgements This protocol is conducted as part of the Temple University College of Public Health graduate-level course titled 'Systematic Reviews' EPBI 8307 during Spring 2022.

Contributors JLH drafted the first version of the manuscript and initiated the review question. YZ-I provided feedback on the manuscript, including the introduction, review question, search strategy and methodology, risk of bias assessment strategy, data extraction criteria and revisions. SR is a librarian who developed the initial search strategy, and AGS is a librarian who developed the revised search strategy.

Funding Publication of this article was funded in part by the Temple University Libraries Open Access Publishing Fund.

Disclaimer YZ-I is a member of a Patient-Centered Outcomes Research Institute (PCORI) Advisory Panel on Clinical Effectiveness and Decision Science

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Jessica L Hamdan <http://orcid.org/0009-0002-0705-3538>

Andrea Goldstein Shipper <http://orcid.org/0000-0003-2819-4276>

Stephanie Roth <http://orcid.org/0000-0001-5415-1718>

Yaara Zisman-Ilani <http://orcid.org/0000-0001-6852-2583>

REFERENCES

- Hilton EN, Lundberg TR. Correction to: transgender women in the female category of sport: perspectives on testosterone suppression and performance advantage. *Sports Med* 2021;51:2235.
- Roberts TA, Smalley J, Ahrendt D. Effect of gender affirming hormones on athletic performance in transwomen and transmen: implications for sporting organisations and legislators. *Br J Sports Med* 2021;55:577–83.
- Harper J, O'Donnell E, Sorouri Khorashad B, et al. How does hormone transition in transgender women change body composition, muscle strength and Haemoglobin? Systematic review with a focus on the implications for sport participation. *Br J Sports Med* 2021;55:865–72.
- Jones BA, Arcelus J, Bouman WP, et al. Sport and transgender people: a systematic review of the literature relating to sport participation and competitive sport policies. *Sports Med* 2017;47:701–16.
- World Athletics. World athletics council decides on Russia, Belarus and female eligibility. 2023. Available: <https://worldathletics.org/news/press-releases/council-meeting-march-2023-russia-belarus-female-eligibility> [Accessed 24 Mar 2023].
- Zeigler C, Webb K. These 36 trans athletes have competed openly in college. 2023. Available: <https://www.outsports.com/trans/2022/1/7/22850789/trans-athletes-college-ncaa-lia-thomas> [Accessed 15 May 2023].
- Futerman M. FINA restricts transgender women from competing at elite level. 2022. Available: <https://www.nytimes.com/2022/06/19/sports/fina-transgender-women-elite-swimming.html> [Accessed 24 Mar 2023].
- Jones BA, Arcelus J, Bouman WP, et al. Barriers and facilitators of physical activity and sport participation among young transgender adults who are medically transitioning. *Int J Transgend* 2017;18:227–38.
- López-Cañada E, Devis-Devis J, Valencia-Peris A, et al. Physical activity and sport in trans persons before and after gender disclosure: prevalence, frequency, and type of activities. *J Phys Act Health* 2020;17:650–6.
- Holder J, Morris J, Spreckley M. Barriers and facilitators for participation in physical activity in the transgender population: a systematic review. *Physical Activity and Health* 2022;6:136–52.
- Oliveira J, Frontini R, Jacinto M, et al. Barriers and motives for physical activity and sports practice among trans people: a systematic review. *Sustainability* 2022;14:5295.
- Herman JL, Flores AR, O'Neill KK. How many adults and youth identify as transgender in the United States? 2022. Available: <https://williamsinstitute.law.ucla.edu/publications/trans-adults-united-states/> [Accessed 15 May 2023].
- HRC Staff. ICYMI: governor lee signed tennessee's fourth anti-transgender sports ban into law; making it the state's 15th anti-LGBTQ+ law since 2015. 2023. Available: <https://www.hrc.org/press-releases/icymi-governor-lee-signed-tennessees-fourth-anti-transgender-sports-ban-into-law-making-it-the-states-15th-anti-lgbtq-law-since-2015> [Accessed 01 May 2023].
- Pharr JR, Chien L-C, Gakh M, et al. Serial mediation analysis of the association of familiarity with transgender sports bans and suicidality among sexual and gender minority adults in the United States. *Int J Environ Res Public Health* 2022;19:10641.
- Irving A, Lehault WB. Clinical pearls of gender-affirming hormone therapy in transgender patients. *Mental Health Clinician* 2017;7:164–7.
- Photopoulos J. The future of sex in elite sport. *Nature* 2021;592:S12–5.
- Anderson E, Travers A. Transgender athletes in elite sport competitions. In: Anderson E, Travers A, eds. *Transgender athletes in competitive sport*. Routledge, 2017: 156–70.
- Love A. The tenuous inclusion of transgender athletes in sport. In: Anderson E, Travers A, eds. *Transgender athletes in competitive sport*. Routledge, 2017: 194–205.
- Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
- Higgins JPT, Thomas J, Chandler J, eds. *Cochrane handbook for systematic reviews of interventions version 6.3*. Cochrane, 2022. Available: <https://training.cochrane.org/handbook>
- Critical Appraisal Skills Programme. CASP qualitative checklist. 2018. Available: https://casp-uk.net/images/checklist/documents/CASP-Qualitative-Studies-Checklist/CASP-Qualitative-Checklist-2018_fillable_form.pdf [Accessed 15 May 2023].
- Moola S, Munn Z, Tufanaru C, et al. Systematic reviews of etiology and risk, Chapter 7.1. Appendix 7.1, critical appraisal checklist for cohort studies. In: Aromataris E, Munn Z, eds. *JBIM Manual for Evidence Synthesis*. JBI, 2020.
- Moola S, Munn Z, Tufanaru C, et al. Systematic reviews of etiology and risk, Chapter 7. Appendix 7.2, critical appraisal checklist for case-control studies. In: Aromataris E, Munn Z, eds. *JBIM Manual for Evidence Synthesis*. JBI, 2020.



Comment on: “Transgender Women in the Female Category of Sport: Perspectives on Testosterone Suppression and Performance Advantage”

Blair Hamilton^{1,2,3} · Fergus Guppy⁴ · Yannis Pitsiladis^{5,6,7,8}

Accepted: 28 August 2023 / Published online: 20 September 2023
© The Author(s), under exclusive licence to Springer Nature Switzerland AG 2023

1 Introduction

The International Olympic Committee (IOC)’s Framework on Fairness, Inclusion and Non-Discrimination on the Basis of Gender Identity and Sex Variations recommends but does not mandate that sport’s governing bodies follow the ten principles [1, 2] of: (1) inclusion, (2) prevention of harm, (3) non-discrimination, (4) fairness, (5) no presumption of advantage, (6) evidenced-based approach, (7) primacy of health and bodily autonomy, (8) stakeholder-centred approach, (9) right to privacy and (10) periodic reviews. As a result of principles 5, 6 and 8, the IOC proposes that sport’s governing bodies generate high-quality sport- and population-specific research to inform the development of any eligibility criteria applying across their relevant sports, disciplines and/or events [1, 2]. Currently, there is limited research on the effects of gender affirmation therapy on sports performance in well-trained transgender athletes, which constitutes a nascent but growing field. Scientific evidence ranges from the gold standard lab-based studies on

athlete comparison groups to review articles that use a variety of methods to synthesise existing knowledge. One paper asserting policy relevance is the paper titled “Transgender Women in the Female Category of Sport, Perspectives on Testosterone Suppression and Performance Advantage” [3]. This publication by Hilton and Lundberg [3] has been prominently cited in numerous policies that exclude [4–7] and restrict [8] transgender women from the female category, with the suggestion that it offers relevant scientific evidence. Since it is up to individual international federations to decide which policy is best for their sport [1, 2], the goal of this letter is to help inform the physicians, scientists, athletes, international federations and other relevant stakeholders as to where this particular contribution to the literature falls in the hierarchy of evidence [9, 10] and to highlight concerns with the theoretical paradigms used by Hilton and Lundberg [3].

2 Hierarchy of Evidence: Narrative Reviews

Systematic reviews with accompanying meta-analyses are recognised as research designs offering high-quality evidence when conducted meticulously (Fig. 1). The goal of this type of research is to formulate an answer to a scientific issue on the basis of the synthesis of data that has been

This comment refers to the article available online at <https://doi.org/10.1007/s40279-020-01389-3>.

A response to this comment is available online at <https://doi.org/10.1007/s40279-023-01930-0>.

✉ Yannis Pitsiladis
ypitsiladis@hkbu.edu.hk
<https://www.hkbu.hk>

¹ School of Sport and Health Sciences, University of Brighton, Eastbourne, UK

² Centre for Stress and Age-Related Disease, University of Brighton, Eastbourne, UK

³ The Gender Identity Clinic Tavistock and Portman NHS Foundation Trust, London, UK

⁴ Institute of Life and Earth Sciences, Heriot-Watt University, Edinburgh, UK

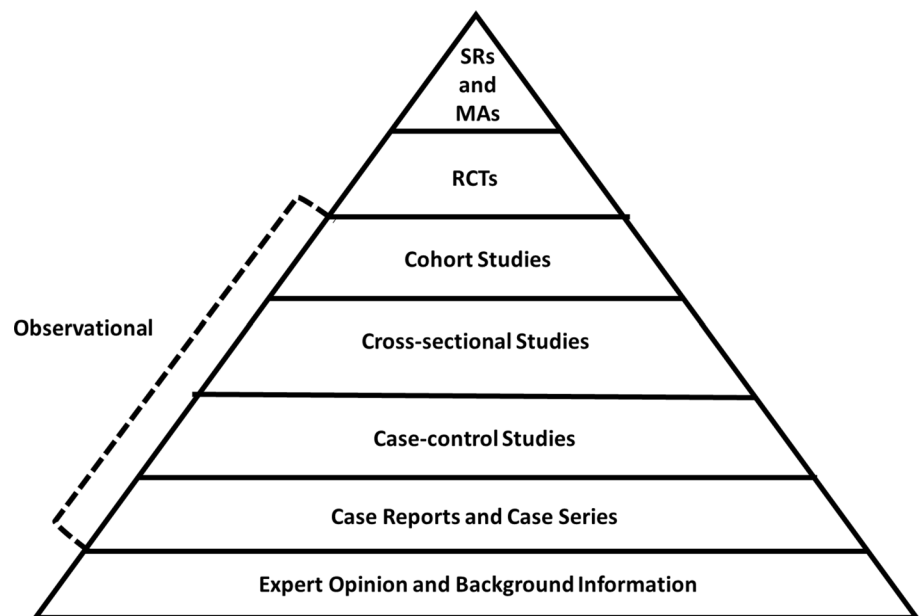
⁵ Department of Movement, Human and Health Sciences, University of Rome “Foro Italico”, Rome, Italy

⁶ European Federation of Sports Medicine Associations (EFSMA), Lausanne, Switzerland

⁷ International Federation of Sports Medicine (FIMS), Lausanne, Switzerland

⁸ Department of Sport, Physical Education and Health, Hong Kong Baptist University, Kowloon Tong, Hong Kong

Fig. 1 Strength of Evidence Pyramid in Healthcare Interventions. Adapted from a combination of Wallace et al. [9] and Evans [10]. *SR*, systematic review; *MA*, meta-analysis; *RCT*, randomized control trial



collected and analysed from a variety of different research studies. Systematic reviews and meta-analyses follow established standards, notably the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria [11]. There are crucial distinctions between systematic and narrative reviews, which try to summarise previously published research on a certain topic but generally lack systematic ways to determine research eligibility, fail to conduct exhaustive searches, are prone to study bias and lack systematic ways to quantitatively assess patterns across studies in a field/topic of research. As a result, narrative reviews may be biased in their selection by excluding relevant research or favouring the findings of particular studies.

The evidence offered by Hilton and Lundberg [3] is in the form of a narrative review and not a systematic review, albeit the search criteria are provided in the supplemental material for Sect. 4, “is the male performance advantage lost when testosterone is suppressed in transgender women?” All previous literature searched in sections “2, the biological basis for sporting performance advantages in males,” and “3, sports performance differences between males and females” do not correspond to the scope of the article, which is transgender women in the female category of sport and seeks only to fuel the underlying assumption that cisgender male study populations are an appropriate substitute for transgender women (see Sect. 3). Furthermore, the literature utilised in Sects. 2 and 3 searches does not follow PRISMA [11] guidelines or follow principle 6, recommending that evidence from the field or the laboratory “be based on data collected from a demographic group that is consistent in gender and athletic engagement [1, 2],” making it difficult for readers to judge the transparency and scientific value of the process and review. This

important distinction would allow the reader to assess the evidence presented in this article more accurately.

Given that there are currently very few transgender athletes competing in elite sports, and therefore even fewer related studies, the systematic review and meta-analysis strategy is at present impractical. Randomised control trials, the next highest-quality study design (Fig. 1), are also impractical in this area at present, leaving observational research, such as cohort studies [12–30], cross-sectional studies [28, 29, 31–38], case–control studies, case reports and case series, as the higher-ranking evidence base that could be considered by international federations (Fig. 1). Studies on the effects of gender affirming hormone treatment (GAHT) on performance-related metrics [39] will offer important insights; although results using sedentary transgender cohorts are useful, they cannot be directly extrapolated to transgender athletes. Data on transgender athletes are being generated [40, 41], but it will likely take more than 2 years to gather available observational information, which may not adequately address the question fully. Given the increasing prevalence of transgender persons in society [42, 43], systematic reviews and meta-analyses on transgender athletes may become available in the not-too-distant future. With the lack of an established systematic review approach, the evidence presented by Hilton and Lundberg [3] is limited to being characterised as low quality (Fig. 1 [9, 10]) and graded as an opinion piece with a low strength of evidence. In the interim, a comprehensive systematic evaluation on the impact of GAHT on sports performance in a sedentary transgender cohort [44] should be prioritised to guide sports organisations’ policy choices until sufficient transgender athlete data are acquired, as this is at least consistent in gender

and fulfils some of principle 6 recommended by the IOC [1, 2].

3 Underlying Assumptions

The article by Hilton and Lundberg [3] has two primary theoretical misconceptions that undermine the accuracy and therefore the usefulness of the paper, first that cisgender male study populations are an appropriate substitute for transgender women, and second, that in the examination of sports performance, absolute data have a stronger level of evidence than relative data.

A starting assumption of Hilton and Lundberg [3] is that in the absence of research on transgender women, it is appropriate to rely on data collected from cisgender men to then compare the physiological and performance characteristics of cisgender men and women, as though the two groups are equivalent contrasting with IOC principle 6 [1, 2]. Existing research suggests that transgender women do not equate to cisgender men in either physiological [27] or performance terms [30]. In terms of physiology, the work of Wiik et al. [27] demonstrated that mean transgender women's muscle volumes are already below the mean muscle volumes of cisgender men at baseline, with a similar outcome displayed in isometric torque levels. Furthermore, Van Caenegem et al. [28] showed that the lean mass was 6.8% less in pre-GAHT transgender women compared with control cisgender men (57.4 ± 8.7 kg versus 61.3 ± 6.8 kg). These results are noteworthy even though they are obtained from sedentary transgender women, and transgender women athletes may be closer to cisgender men as a starting point. However, this is unclear with physical performance measures, showing transgender women in the military had pre-GAHT upper body strength measures that were 12% lower (-6 push ups, 95% CI -20 to -12) [30] than cisgender male controls, in comparison with sedentary transgender women who had pre-GAHT strength measures 15% lower (42 ± 9 versus 49 ± 6 N/kg) than cisgender male controls [28].

With research revealing the cumulative longitudinal physiological and performance effects of GAHT in sedentary transgender women, Hilton and Lundberg [3] highlight understanding gaps which include reductions in lean body mass that range from -0.8% to -5.4% [14–16, 18, 22, 24, 27–29, 44], reduced muscle cross-sectional area ranging from -1.5% to -11.7% [12, 24, 27, 28, 44], and decreases in the O_2 -carrying protein haemoglobin, ranging from -3.4% to -14% [15, 17, 19, 44]. Overall, the assumption that transgender women and cisgender men can simply be used as equivalent groups undermines the study's assertion that it offers insights regarding the sporting capabilities of transgender women compared with cisgender women since it undertakes no such comparison.

The use of relative measures is foundational to sports performance testing. From undergraduate education onwards, sports scientists in the field normalise characteristics (e.g. height or weight) when concluding how an absolute measure (e.g. of muscular strength) will translate into actual athletic ability [45–49]. Despite this, Hilton and Lundberg's [3] literature prioritise absolute rather than relative data, failing to normalise their results to either height or mass. In Table 4, Hilton and Lundberg [3] compare taller groups with shorter groups, which may account for a substantial portion of the variances in lean body mass or thigh area. Moreover, supplying reference female values generated from parallel cohorts of pre-GAHT transgender males rather than cisgender women creates a misleading impression for the reader. In Table 4, as previously discussed, sedentary transgender men are not the same as cisgender women athletes.

This issue reappears in Hilton and Lundberg's article: 50% of the reported data on muscle strength, in Table 4 [3], is sourced from the test of absolute hand grip strength, despite absolute grip strength being a function of hand size [50]. Hilton and Lundberg [3] neither provide a relative measures analysis that is most relevant in understanding sports performance and aiding in the creation of sports policy, nor discuss the lack of relative performance measures as a limitation of these data. To properly determine whether athletic performance parameters are lost or gained in transgender women and men following the initiation of GAHT, any future research on the sporting ability of transgender athletes must, in addition to the non-corrected data, normalise for height, body mass and fat-free mass as appropriate. Interestingly, the authors do report that maximal oxygen uptake is 50% greater in cisgender men than cisgender women when reported in absolute terms and 25% when reported in relative terms, indicating that half of the differences is due to body mass alone.

Had Hilton and Lundberg [3] made their data available, as recommended by open science guidelines [51, 52] and the European Commission Research and Innovation Strategy 2020–2024 [53], the analyses might have been re-run by others in science to corroborate the authors' findings and strengthen their analyses. Therefore, due to the priority of absolute data and the lack of open scientific methods, the analyses can only be characterised as limited.

4 Concluding Remarks

Hilton and Lundberg [3] are being widely cited by international federations to inform policy, yet as discussed here, the arguments and underlying assumptions presented in this paper are supported by the lowest level of evidence (Fig. 1) and do not align with the principles of the IOC Framework [1, 2], specifically principles 5, 6 and 8. It is unsurprising,

therefore, that legal challenges have already been made as a result of the policies that this literature has provided as the evidence base [54, 55], which will serve to undermine the efforts and have negative repercussions for international federations, such as harming the confidence of its athletes, sponsors and the general public. To ensure both the integrity of the policy process and competition, international federations should reflect on the strength of the evidence in the studies they consider and utilise the highest-quality evidence available to make their decisions. Due to the growing number of transgender people in society, sub-elite transgender athletic data will be available imminently; however, due to the low participation rates of transgender athletes in elite sport and the growing number of exclusionary or limiting policies on their participation in elite sport, performance data on elite transgender athletes will likely not be readily available in the near future. Performance metrics are the most informative data, and research is currently underway using both sedentary [39, 56] and transgender [40, 41] athlete cohorts. While awaiting these data, international federations should not rush into making decisions informed by poor scientific evidence and should therefore prioritise following the ten principles of IOC framework [1, 2].

Declarations

Author contributions The idea, material preparation, literature review, reporting and critical revision of the work were performed by Blair Hamilton, Fergus Guppy and Yannis Pitsiladis. Blair Hamilton wrote the first draft of the manuscript. Fergus Guppy and Yannis Pitsiladis critically revised subsequent versions of the manuscript until all authors were able to approve the final manuscript.

Funding The writing of this manuscript was not funded.

Conflict of Interest Yannis Pitsiladis is a member of the IOC Medical and Scientific Commission, which has recently published articles and framework documents on the topic. Blair Hamilton and Fergus Guppy have recently published articles on the topic on behalf of International Federation of Sports Medicine (FIMS). All authors declare that they have no further conflict of interest or competing interests.

Ethics approval No ethics approval was required for this manuscript.

References

1. International Olympic Committee. Framework on fairness, inclusion and non-discrimination on the basis of gender identity and sex variations. 2021 [cited 2021 November, 29th]; Available from: <https://stillmed.olympics.com/media/Documents/News/2021/11/IOC-Framework-Fairness-Inclusion-Non-discrimination-2021.pdf>
2. Martowicz M, Budgett R, Pape M, Mascagni K, Engebretsen L, Dienstbach-Wech L, et al. Position statement: IOC framework on fairness, inclusion and non-discrimination on the basis of gender identity and sex variations. *Br J Sports Med*. 2023;57(1):26–32.
3. Hilton EN, Lundberg TR. Transgender women in the female category of sport: perspectives on testosterone suppression and performance advantage. *Sports Med*. 2020;51(1):199–214.
4. World Rugby. World Rugby Transgender Guideline. 2020 October 9th 2020 [cited 2021 November, 29th]; Available from: <https://playerwelfare.worldrugby.org/?documentid=231>
5. FINA. Policy on eligibility for the men's and women's competition categories. 2022 [cited F 3 and 4; Available from: <https://resources.fina.org/fina/document/2022/06/19/525de003-51f4-47d3-8d5a-716dac5f77c7/FINA-INCLUSION-POLICY-AND-APPENDICES-FINAL-.pdf>
6. British Triathlon. Transgender policy effective January 1st, 2023. FRG029 2022 [cited; Available from: <https://www.britishtriathlon.org/britain/documents/about/edi/transgender-policy-effective-from-01-jan-2023.pdf>
7. Sports Council Equality Group. SCEG Project for Review and Redraft of Guidance for Transgender Inclusion in Domestic Sport. 2020 [cited 20201 December, 6th]; Available from: <https://equalityinsport.org/resources/index.html>
8. Union Cycliste Internationale. Chapter V Eligibility Regulations for Transgender Athletes. Part 13 Medical Rules 2022 [cited Article 13.5.013; Available from: https://assets.ctfassets.net/76117gh5x5an/Et9v6Fyux9fWPDpKRGpY9/96949e5f7bbc8e34d536731c504ac96f/Modification_Transgender_Regulation_22_Juin_2022_ENG.pdf
9. Wallace SS, Barak G, Truong G, Parker MW. Hierarchy of evidence within the medical literature. *Hosp Pediatr*. 2022;12(8):745–50.
10. Evans D. Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions. *J Clin Nurs*. 2003;12(1):77–84.
11. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, The PRISMA, et al. statement: an updated guideline for reporting systematic reviews. *BMJ*. 2020;2021:372.
12. Elbers J, Asscheman H, Seidell J, Gooren LJ. Effects of sex steroid hormones on regional fat depots as assessed by magnetic resonance imaging in transsexuals. *Am J Physiol Endocrinol Metab*. 1999;276(2):E317–25.
13. Gooren LJ, Bunck MC. Transsexuals and competitive sports. *Eur J Endocrinol*. 2004;151(4):425–30.
14. Mueller A, Zollver H, Kronawitter D, Oppelt P, Claassen T, Hoffmann I, et al. Body composition and bone mineral density in male-to-female transsexuals during cross-sex hormone therapy using gonadotrophin-releasing hormone agonist. *Exp Clin Endocrinol Diabetes*. 2011;119(02):95–100.
15. Wierckx K, Van Caenegem E, Schreiner T, Haraldsen I, Fisher A, Toye K, et al. Cross-sex hormone therapy in trans persons is safe and effective at short-time follow-up: results from the European network for the investigation of gender incongruence. *J Sex Med*. 2014;11(8):1999–2011.
16. Gava G, Cerpolini S, Martelli V, Battista G, Seracchioli R, Meriggiola MC. Cyproterone acetate vs leuprolide acetate in combination with transdermal oestradiol in transwomen: a comparison of safety and effectiveness. *Clin Endocrinol*. 2016;85(2):239–46.
17. Auer MK, Cecil A, Roepke Y, Bultynck C, Pas C, Fuss J, et al. 12-months metabolic changes among gender dysphoric individuals under cross-sex hormone treatment: a targeted metabolomics study. *Sci Rep*. 2016;6(1):1–10.
18. Auer MK, Ebert T, Pietzner M, Defreyne J, Fuss J, Stalla GK, et al. Effects of sex hormone treatment on the metabolic syndrome in transgender individuals: focus on metabolic cytokines. *J Clin Endocrinol Metab*. 2018;103(2):790–802.
19. Jarin J, Pine-Twaddell E, Trotman G, Stevens J, Conard LA, Tefera E, et al. Cross-sex hormones and metabolic parameters in adolescents with gender dysphoria. *Pediatrics*. 2017;139:5.

20. Defreyne J, Vantomme B, Van Caenegem E, Wierckx K, De Blok C, Klaver M, et al. Prospective evaluation of hematocrit in gender-affirming hormone treatment: results from European Network for the Investigation of Gender Incongruence. *Andrology*. 2018;6(3):446–54.
21. Vita R, Settineri S, Liotta M, Benvenga S, Trimarchi F. Changes in hormonal and metabolic parameters in transgender subjects on cross-sex hormone therapy: a cohort study. *Maturitas*. 2018;107:92–6.
22. Klaver M, De Blok C, Wiepjes C, Nota NM, Dekker MJ, de Mutsert R, et al. Changes in regional body fat, lean body mass and body shape in trans persons using cross-sex hormonal therapy: results from a multicenter prospective study. *Eur J Endocrinol*. 2018;178(2):163–71.
23. Olson-Kennedy J, Okonta V, Clark LF, Belzer M. Physiologic response to gender-affirming hormones among transgender youth. *J Adolesc Health*. 2018;62(4):397–401.
24. Tack LJ, Craen M, Lapauw B, Goemaere S, Toye K, Kaufman J-M, et al. Proandrogenic and antiandrogenic progestins in transgender youth: differential effects on body composition and bone metabolism. *J Clin Endocrinol Metab*. 2018;103(6):2147–56.
25. Tack LJ, Heyse R, Craen M, Dhondt K, Bossche HV, Laridaen J, et al. Consecutive cyproterone acetate and estradiol treatment in late-pubertal transgender female adolescents. *Journal of Sexual Medicine*. 2017;14(5):747–57.
26. Scharff M, Wiepjes CM, Klaver M, Schreiner T, T'Sjoen G, den Heijer M. Change in grip strength in trans people and its association with lean body mass and bone density. *Endocr Connect*. 2019;8(7):1020–8.
27. Wiik A, Lundberg T, Rullman E, Andersson D, Holmberg M, Mandić M, et al. Muscle strength, size, and composition following 12 months of gender-affirming treatment in transgender individuals. *J Clin Endocrinol Metab*. 2020;105:3.
28. Van Caenegem E, Wierckx K, Taes Y, Schreiner T, Vandewalle S, Toye K, et al. Preservation of volumetric bone density and geometry in trans women during cross-sex hormonal therapy: a prospective observational study. *Osteoporos Int*. 2015;26(1):35–47.
29. Haraldsen I, Haug E, Falch J, Egeland T, Opjordsmoen S. Cross-sex pattern of bone mineral density in early onset gender identity disorder. *Horm Behav*. 2007;52(3):334–43.
30. Roberts TA, Smalley J, Ahrendt D. Effect of gender affirming hormones on athletic performance in transwomen and transmen: implications for sporting organisations and legislators. *Br J Sports Med*. 2020;55(11):557–83.
31. SoRelle JA, Jiao R, Gao E, Veazey J, Frame I, Quinn AM, et al. Impact of hormone therapy on laboratory values in transgender patients. *Clin Chem*. 2019;65(1):170–9.
32. Greene DN, McPherson GW, Rongitsch J, Imborek KL, Schmidt RL, Humble RM, et al. Hematology reference intervals for transgender adults on stable hormone therapy. *Clin Chim Acta*. 2019;492:84–90.
33. Roberts TK, Kraft CS, French D, Ji W, Wu AH, Tangpricha V, et al. Interpreting laboratory results in transgender patients on hormone therapy. *Am J Med*. 2014;127(2):159–62.
34. Lapauw B, Taes Y, Simoens S, Van Caenegem E, Weyers S, Goemaere S, et al. Body composition, volumetric and areal bone parameters in male-to-female transsexual persons. *Bone*. 2008;43(6):1016–21.
35. Jain J, Kwan D, Forcier M. Medroxyprogesterone acetate in gender-affirming therapy for transwomen: results from a retrospective study. *J Clin Endocrinol Metab*. 2019;104(11):5148–56.
36. Alvares LA, Santos MR, Souza FR, Santos LM, Mendonça BB, Alves MJNN, et al. First evidence of cardiopulmonary adaptation to physical effort in transgender women after long-term hormone therapy: a cross-sectional study. *J Endocr Soc*. 2021;5(1):790–1.
37. Alvares LA, Santos MR, Souza FR, Santos LM, Ramos HA, Mendonça BB, et al. Muscle strength in transgender women after long-term hormone therapy: a cross-sectional study. *J Endocr Soc*. 2021;5(1):792.
38. Alvares LAM, Santos MR, Souza FR, Santos LM, de Mendonça BB, Costa EMF, et al. Cardiopulmonary capacity and muscle strength in transgender women on long-term gender-affirming hormone therapy: a cross-sectional study. *Br J Sports Med*. 2022;56(22):1292–8.
39. Jones PR, Voisin S, Nolan BJ, Landen S, Jacques M, Newell B, et al. Uncovering the effects of gender affirming hormone therapy on skeletal muscle and epigenetics: protocol for a prospective matched cohort study in transgender individuals (the GAME study). *BMJ Open*. 2022;12(5):e060869.
40. Hamilton BR, Lima G, Barrett J, Seal L, Kolliari-Turner A, Guppy F, et al. The effects of gender affirming treatment on the sporting performance and muscle memory of transgender athletes. A Protocol for The Tavistock Transgender Athlete Study. *SportRxiv*. 2021;1:1.
41. Hamilton B, Comeras-Chueca C, Bush P, Seal L, Guppy F, Pitsiladis Y. Sporting performance of athletes of the gender spectrum: a cross-sectional comparison study protocol. *SportRxiv*. 2022;1:1.
42. Aitken M, Steensma TD, Blanchard R, VanderLaan DP, Wood H, Fuentes A, et al. Evidence for an altered sex ratio in clinic-referred adolescents with gender dysphoria. *J Sex Med*. 2015;12(3):756–63.
43. De Vries A, Kreukels B, T'sjoen G, Ålgars M, Mattila A. Increase of referrals to gender identity clinics: a European trend. *Transgend Healthcare Europe Book Abstracts*. 2015;2:10.
44. Harper J, O'Donnell E, Sorouri Khorashad B, McDermott H, Witcomb GL. How does hormone transition in transgender women change body composition, muscle strength and haemoglobin? Systematic review with a focus on the implications for sport participation. *Br J Sports Med*. 2021;55(15):865–72.
45. Schneiker KT, Fyfe JJ, Teo SYM, Bishop DJ. Comparative effects of contrast training and progressive resistance training on strength and power-related measures in subelite Australian rules football players. *J Strength Condit Res*. 2023;2:2.
46. Letter RT, Dwyer DB, Drinkwater EJ, Feros SA. The physical qualities of elite Australian pace bowlers: typical characteristics and longitudinal changes in men and women. *Int J Sports Physiol Perform*. 2022;17(12):1691–7.
47. Folhes O, Reis VM, Marques DL, Neiva HP, Marques MC. Maximum isometric and dynamic strength of mixed martial arts athletes according to weight class and competitive level. *Int J Environ Res Public Health*. 2022;19:14.
48. Andersen E, Lockie RG, Dawes JJ. Relationship of absolute and relative lower-body strength to predictors of athletic performance in collegiate women soccer players. *Sports*. 2018;6(4):106.
49. Suchomel TJ, Nimphius S, Stone MH. The importance of muscular strength in athletic performance. *Sports Med*. 2016;46:1419–49.
50. Alahmari K, Kakaraparthi V, Reddy R, Silvian PS, Ahmad I, Rengaramanujam K. Percentage difference of hand dimensions and their correlation with hand grip and pinch strength among school-children in Saudi Arabia. *Niger J Clin Pract*. 2019;22(10):1356.
51. van der Zee T, Reich J. Open education science. *AERA Open*. 2018;4(3):2332858418787466.
52. Crüwell S, van Doorn J, Etz A, Makel MC, Moshontz H, Niebaum J, et al. 7 easy steps to open science: an annotated reading list. 2018.
53. European Commission. The EU's Open Science Policy. Open Science 2023 [cited 2023 April 27th]; Available from: https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/our-digital-future/open-science_en
54. Tomas F. RFU hit by legal action over transgender women ban. 2022 [cited; Available from: <https://www.telegraph.co.uk/>

- [rugby-union/2022/09/03/exclusive-rfu-hit-legal-action-transgender-women-ban/](https://www.rugby-union/2022/09/03/exclusive-rfu-hit-legal-action-transgender-women-ban/)
55. American Civil Liberties Union. Soule et al., V. CT Association of Schools et al., 2022 November 23, 2022 [cited; Available from: <https://www.aclu.org/cases/soule-et-al-v-ct-association-schools-et-al>]
56. Lehmann Christensen L, Glintborg D, Taulbjerg Kristensen T, Diederichsen A, T'Sjoen G, Frystyk J, et al. Masculinising testosterone treatment and effects on preclinical cardiovascular disease, muscle strength and power, aggression, physical fitness and respiratory function in transgender men: protocol for a 10-year, prospective, observational cohort study in Denmark at the Body Identity Clinic (BIC). *BMJ Open*. 2020;10(12): e045714.



OPEN ACCESS

EDITED BY

Giuseppe D'Antona,
University of Pavia, Italy

REVIEWED BY

Domenico Martone,
Parthenope University of Naples, Italy
Lindsay Pieper,
University of Lynchburg, United States

*CORRESPONDENCE

D. J. Oberlin
✉ douglas.oberlin@lehman.cuny.edu

RECEIVED 17 May 2023

ACCEPTED 10 October 2023

PUBLISHED 27 October 2023

CITATION

Oberlin DJ (2023) Sex differences and athletic performance. Where do trans individuals fit into sports and athletics based on current research? *Front. Sports Act. Living* 5:1224476. doi: 10.3389/fspor.2023.1224476

COPYRIGHT

© 2023 Oberlin. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](#). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Sex differences and athletic performance. Where do trans individuals fit into sports and athletics based on current research?

D. J. Oberlin*

Department of Exercise Sciences and Recreation, City University of New York, Lehman College, Bronx, NY, United States

There are well known sex differences in parameters of physical fitness/performance due to changes occurring during sexual development. Thus, many sport and athletic events have regulations separating male and female participants. However, the inclusion or exclusion of transgender individuals in athletics has recently received outsized attention despite relatively few cases of transgender athletes. When determining which athletic gender category trans individuals should be permitted to compete in, it is important to understand the level of physical fitness/performance these individuals possess relative to their cisgender counterparts. Unfortunately, there are few studies investigating this topic, and several complications that confound this research. The current review seeks to discuss sex and gender as concepts, review sex differences in fitness/performance and how they develop, and then, consider how current evidence suggests that trans individuals compare to cis individuals. Finally, this review seeks to offer considerations for whether trans individuals should be excluded from sports and athletics, and how future research should proceed to better understand this marginalized population.

KEYWORDS

transgender, sports, gender, genderqueer, performance

1. Introduction

While transgender individuals have likely always existed, they have recently received an outsized level of attention and scrutiny from governments and other regulatory bodies (1–5). This scrutiny spans multiple issues, one of which has been participation in sports and athletics (1, 2, 6, 7). Concerns have been raised for whether trans individuals should be allowed to compete in sports with cisgender individuals, suggesting they should not compete in the category that aligns with their gender identity or that they should participate in a separate category entirely (1, 3–6, 8–11). Addressing these concerns requires consideration of several concepts: sex and gender, how sports and athletics currently regulate participation by sex and gender, potential human right violations or discrimination coming from exclusionary approaches, what sex differences exist in athletics and how these develop and affect athletic performance, and whether trans individuals' participation in sports inherently leads to risks of either inequity or injury. This is not a systematic review, and makes no claim to “solve” this matter. The purpose of the current review is to better describe the modern landscape of how and why gender is used as criteria for inclusion/exclusion from sport and athletics, and to drive further

considerations of how or whether transgender individuals should be excluded from these events. To achieve this, pubmed and google scholar were used to search for terms including: “trans”, “gender”, “transgender”, “sports”, “performance”, “exercise”, “athletics”. Articles were included if they met the following criteria: (1) original research rather than review, (2) research compared transgender individuals on gender affirming hormone therapy to cisgender individuals rather than comparing cis men and cis women, and (3) some measures of fitness or performance were measured. This was done to find articles that investigated transgender performance, accounting for hormonal differences, and comparing these with cisgender counterparts. Articles were excluded if no more than one trans individual was compared to cisgender individuals. These criteria were used for the following reasons. (1) Transgender individuals on gender affirming hormone therapy should not be equated to their pre-transition cisgender counterparts. Gender affirming hormone therapy can alter physiologic parameters (12–16). Thus, transgender individuals must be directly measured rather than assuming cisgender sex differences are analogous to cisgender and transgender differences. (2) To avoid assuming that a single transgender individual can be generalized to an entire population. While case studies can be informative, selecting an exceptional trans athlete or a sedentary trans individual and assuming they represent an entire community would likely lead to misleading conclusions.

2. Sex and gender

2.1. Distinguishing sex and gender

Before discussing gender as a criterion for sports participation, the concepts of sex and gender should be clearly understood. Although often used synonymously, sex and gender are two different terms used to describe related concepts. Sex is a biological concept having to do with chromosomes, genitalia, gonads, and hormones (17–19). While related to sex, gender has to do with behaviors, societal roles/expectations, and attributes which are valued or discouraged within a social group (19–21). These related concepts can be conflated, as biological sex and bodily appearance influences how members within a society interact with one another (20, 22). The various interactions among members of a community pressure individuals within the community to behave in a particular manner or display certain characteristics based on their perceived sex (20, 22). To a casual observer, the differences between sex and gender may seem trivial, however they address individual qualities which have wide variations even within what may be considered a single group. Thus, to further a discussion of transgender individuals in sport and athletics, the concepts of sex and gender must first be understood, although they may be impossible to entirely disentangle.

Prior to understanding chromosomes, sex was determined to be male or female based on the genitalia possessed by an individual and their secondary sex characteristics (23–25).

However, by the early 20th century, scientists were beginning to understand that chromosomes shared between mother and father would determine something about the sex of the offspring, but it would still be decades before a greater understanding of the variety of possible outcomes could be better understood (26–29). Currently, chromosomes, gonads, hormones, and genitals (and to a lesser extent secondary sex characteristics) have all been used to describe the concept of biological sex in humans (18). While chromosomal varieties can certainly result in XY males and XX females, it is also possible for individuals to be born with sex chromosome aneuploidy leading to variations such as XXX, XXY, XYY, XXXX, XXYY, XXXY, XXXXY, or even XXXXX (30–34). Differences in sex chromosomes have also led to discoveries of sex chromosome dose effects leading to variations in gene regulation as well as in body size and other phenotypic differences (33, 34). Besides variations in chromosomes, there are other possible anatomical deviations from what is typically considered male or female, such as males with ambiguous external genitalia, a uterus, and fallopian tubes to females who also carry a Y chromosome, have ambiguous external genitalia, and possess both ovaries and testis (18, 35). Hormonal concentrations, particularly of testosterone, are also used to distinguish male from female (18, 36). Both males and females have some concentration of both testosterone and estrogen, and these concentrations vary among individuals (37–39). However, testosterone is frequently used as a marker to distinguish male from female as males have 15–20× more testosterone than females (36–38, 40). Despite this, there are also wide variations within cisgender men and women which do not make them more or less male or female (36–38). Hence, even a biological concept of sex, whether based on chromosomes, anatomy, hormones, or other criteria, does not fit neatly into two rigid categories (17, 18).

Gender is a more complicated topic than biological sex, because gender, according to the World Health Organization, “refers to the characteristics of women, men, girls and boys that are socially constructed” (20–22). Due to being social constructs, the various characteristics and genders can change over time, and/or across various cultures (21, 22). Because of its societal nature, the treatment of individuals not adhering to gender norms have faced varying degrees of penalty depending upon the time period, geographic regions, and culture and politics (3, 21, 41). Attempting to review all permutations of all characteristics which are associated with gender is beyond the scope of this review. However, any individuals having characteristics, traits, or gender identities not aligned with the societal norms for their biological sex may be considered some degree of gender non-conforming and may be subjected to similar castigation as transgender individuals.

The term transgender is relatively modern and predated by terms such as transvestite or transsexual prior to the 20th century (42). However in the 1960s, the term transgenderism became more common as it was noted that sexuality was not necessarily related to being transgender (43). While transgender may not perfectly capture the range of possible gender identities, it expresses the idea of sex and gender being unaligned (17, 44).

Thus, cisgender was coined to describe an individual whose sex and gender are the same (44). Discussion of cis and trans gender individuals, and their rights in society may seem to be a modern issue, however, these discussions date back, at least, to the 19th century (45). Historical studies from these times document individuals who may be considered transgender by modern understanding (45–47). Some historians and activists argue that examples of people assuming unconventional gender roles or breaking with gender norms have existed throughout history (46, 47). However, it is nearly impossible to determine the gender identities of historical figures, as these individuals likely had no concept of gender identity in the modern context; additionally, there were harsh consequences for those who deviated from societal gender norms at various points in history (45–47). Thus, the current review will only focus on modern issues of gender identity as they relate to participation in sports and athletics.

2.2. Sports and gender classifications

When discussing sex, gender, and participation in sports and athletics, the main point of contention seems to be who should or should not be allowed to participate. The International Olympic Charter states that “The practice of sport is a human right. Every individual must have the possibility of practicing sport, without discrimination of any kind...” (48). If taken on its face, this Olympic principle indicates that trans individuals should have no restrictions on access to sports and athletics, and that discrimination violates that human right. The International Olympic Committee follows this principle in their most recent framework on fairness, however leaves the final decision on inclusion of transgender individuals to the various international federations on the basis of fairness and safety (49). This departure from the IOC consensus meeting on sex reassignment and hyperandrogenism acknowledged that one set of regulations did not account for the variability in different sport and athletic requirements, thus international federations would be best placed to make final determinations (49–51). The IOC stressed the importance of an evidence-based approach to assessing under what circumstances trans individuals should be restricted from participation (49, 50). Many of the international federations do choose to restrict participation in their respective athletic events on the basis of either trans status or, based on the blood concentration of hormones for trans individuals (8, 11, 52). It is common for sport/athletic federations to cite certain scientific facts and studies to justify their provisions (8, 11, 52). However, while it is true that some average differences can be measured between cis and trans individuals, these can vary across different studies and different physiologic traits (15, 53–56). While the sport/athletic federations provisions focus on mean differences between cis and trans individuals, they tend to ignore differences amongst a cis only population that lead to advantages, disadvantages, or confer no advantage in athletics and sport performance (11, 38, 40, 57–59). The total number of cis individuals that are naturally advantaged or disadvantaged would likely exceed the total number of transgender individuals wishing

to compete based on their low proportion of the total population (60). Hence, the exclusion of the transgender individuals from sports and athletics based solely on concerns of inequity or injury risk, may be a solution in search of a problem.

3. Physiologic sex differences and their effects on performance among cisgender individuals

To discuss differences in exercise and performance among cis and trans gender individuals, there must first be an understanding of biologic sex differences, and the concern over what traits are lost or retained following an individual's transition. These differences arise from a combination of developmental, morphological, and hormonal differences between males and females (61). Some of these differences occur as a result of growth and development in puberty, while others are a result of persistent endogenous hormone concentrations (62–66).

3.1. General differences from development through adulthood in cisgender individuals

Sex differences are not as pronounced among younger males and females but emerge among adult males and females (63–66). Prior to puberty, young males and females have similar aerobic capacity, strength, body composition, and overall athletic performance (63, 65, 66). However, studies do find slight advantages in anaerobic and strength performance, such as running and throwing, among young males compared to females, while young females have similarly slight advantages in flexibility (67, 68). It is uncertain to what extent this is a result of physiologic differences, rates of maturation, or sociologic differences, as young males are more likely to spend time engaged in physical activity compared to young females which may also lead to differences in performance (69, 70).

The magnitude of sex differences increases as individuals mature (65). Adolescent and adult males and females show average differences in aerobic capacity, body composition, and strength (61). These are interrelated but will be addressed individually. As children grow and move through puberty, both sexes have increases in body size, although to a greater extent among males, leading to greater male average mass and height (62, 71). During puberty, differences in body composition become apparent, with males having lower average body fat, and higher average muscle mass compared to age matched females (64, 72, 73). This difference in body composition leads to increasing strength and aerobic capacity to a greater extent among males than females (64, 74). Due to a greater proportion of lean mass to total body mass, males on average are able to produce greater force for their body size (75–77). This can lead to advantages in sports where strength and power are valued (56, 78). Despite average differences, it is worth noting that overlap exists between the normal upper and lower ranges of males and females (62). The differences in size and composition of the

body do not only relate to strength and power, but also to aerobic focused athletics.

Prepubertal males and females have similar aerobic capacities relative to body mass (63, 79). However, post-pubertal males show greater aerobic capacity compared to females due to changes such as increased hemoglobin and leaner body composition (64, 73, 74, 80, 81). The average sex differences in body composition favors higher relative aerobic capacity among males whose greater muscle mass and lower fat mass allows for greater uptake of oxygen per kilogram of total body mass during physical activity (79, 82, 83). Additionally, males will surpass females in left ventricular end diastolic volume and ventricular wall thickness, allowing greater cardiac output at similar heart rates (84). This is aided by the greater average hematocrit/hemoglobin among males compared to females (85–87). From birth to the onset of puberty, hematocrit/hemoglobin values are generally similar, but during maturation, males have a greater increase in hematocrit/hemoglobin compared to age matched females, although there is still overlap in normal ranges between these groups (85, 87). The combination of greater proportion of lean mass, heart size, hemoglobin leading to greater aerobic capacity leads to generally faster race times in many aerobically focused events (88–91).

Despite these sex differences that develop during puberty, there are still large areas of overlap in performance, the degree of which is dependent upon the physical demands of the activity (56, 78, 92, 93). An example can be seen in **Figure 1**, showing the overlap in finish times of the San Francisco Marathon runners 12 years and older (94). The overlap in performance is due to variability in body sizes, individual training and preparation, genetics, proper diet and hydration status, and likely other variables. It is also worth noting that across the history of marathons, including the data from the San Francisco Marathon, fewer total women have participated (94). As more women become involved in sport and improve in training, the gap in performance may narrow further (95). However, males, on average, seem to enjoy an advantage in

many athletic competitions, due largely to the effects of testosterone playing out during pubertal development and through adulthood (36, 56, 66).

3.2. Hormonal differences in cisgender individuals from puberty and beyond

Many of the sex differences that become apparent during development are a result of hormonal differences that occur during puberty and persist beyond (66). In general, males will have higher testosterone concentrations than females, but lower estrogen concentrations relative to females (36, 37, 39, 96). However, the average difference in estrogen concentrations between males and females is less pronounced than the difference in testosterone (36, 37, 39, 96). Thus, it is important to understand how these different sex hormones contribute to physiologic factors associated with physical performance. Testosterone is known as an anabolic and androgenic hormone while estrogen is more commonly associated with soft tissue and bone health (36, 97, 98). Therefore, these will be discussed beyond the roles they play in development during puberty, to the characteristics they maintain in adults.

The effects of estrogen on performance have been studied predominantly in female athletes. How, or if, estrogen affects performance is not entirely understood due to changes in hormonal concentrations through the menstrual cycle, alterations of estrogen and progesterone resulting from oral contraceptive use, and changes in hormonal concentrations occurring around menopause (37, 99–101). Despite these limitations, several investigations have examined how performance may be influenced at different phases of the menstrual cycle (102, 103). While estrogen is associated with changes in cardiovascular function, respiratory function, thermoregulation, and substrate metabolism, the impact of the estrogen variations across the menstrual cycle have not shown consistent advantages or

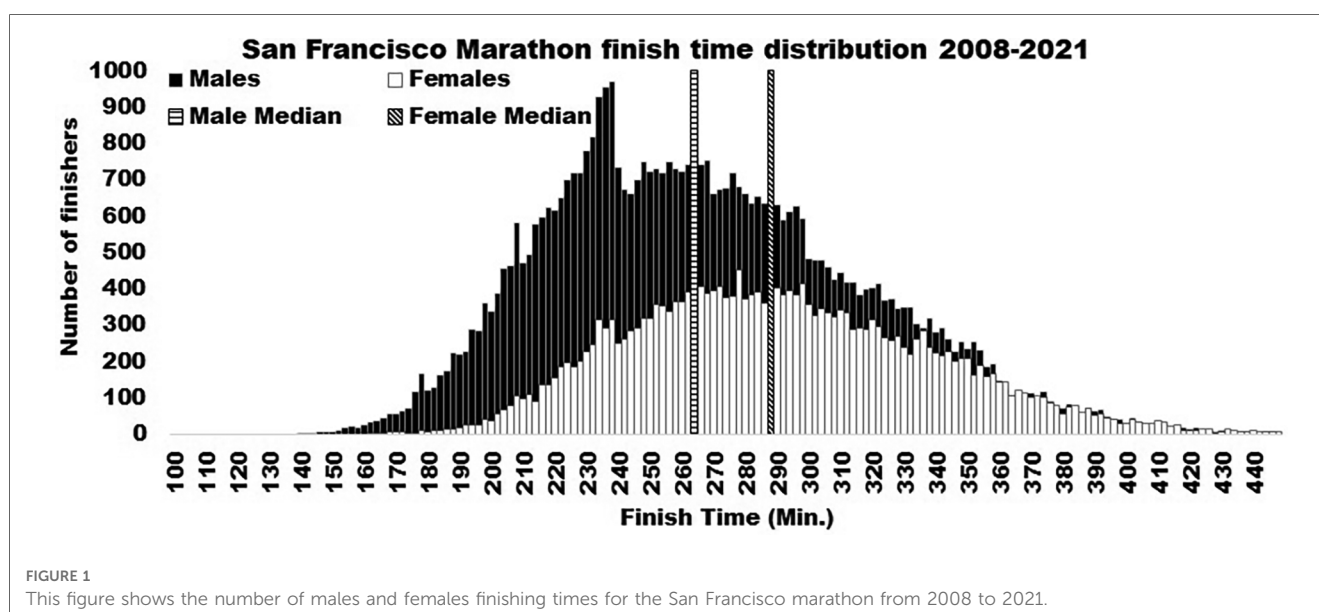


FIGURE 1

This figure shows the number of males and females finishing times for the San Francisco marathon from 2008 to 2021.

disadvantages in sports performance (92, 104). However, there are changes in estrogen before, during, and after athletic competitions in both males and females, thus future research may find that these changes are influencing performance (37, 96).

By contrast, testosterone, and its influence on athletic performance, has been intensely studied in both males and females. This is in part due to the abuse of testosterone, and/or closely related compounds, as ergogenic aids (105–107). The difference in testosterone concentration between sexes are wider than those seen with estrogen and are unlikely to overlap between sex groups with males having as much as 20× the testosterone of females (36–38, 40). However, there is interindividual variation within sexes, with some males or females having as much as double the testosterone of their peers (36–38, 40). Despite the difference in hormone concentration between sexes, testosterone promotes muscle growth and strength in both males and females (106, 108–111). Even within a single group, such as cis men or cis women, serum testosterone concentrations seem to relate to enhanced muscle mass, strength, aerobic endurance, and possibly psychological advantages (108, 112–114). Although, the degree to which this influences performance is questionable and affected by the total difference in hormone concentrations and in sport specific demands (114–116). This issue can become contentious due to the variability in endogenous testosterone levels among athletes, even within a single cisgender category (113, 117). For example, there may be 2–3× more or less testosterone within either elite male or female athletes and still be within normal ranges (59, 66). On the other hand, cis men with naturally occurring hyperandrogenism are not limited in their ability to compete while a cis woman with hyperandrogenism would be (118–120). This is despite the fact that this, as well as many other genetic/biologic factors, are beyond the control of the individual athletes (118, 121).

4. Cis and trans gender performance differences

Thus, there are clearly average differences in performance between males and females, despite an overlap in the average distribution (depending on the sport, age, and skill level). However, transgender individuals, particularly those who have undergone gender affirming hormone therapy and/or gender affirming surgical procedures, have physiologic and potentially morphologic differences from their pre-transition cisgender counterparts (16, 53, 54, 122). Therefore, it is not sufficient to examine sex differences among cis men and women and apply these directly to trans men and women, nor is it sufficient to examine pre to post transition without some cisgender comparisons. Unfortunately, there is a dearth of research on cis and trans gender differences. This lack of data are due to several factors: (1) trans individuals make up only 0.5% of the general population, and likely smaller proportion of highly trained athletes, making this population difficult to recruit and study, (2) highly trained individuals should not be compared to recreationally trained or untrained individuals and few highly

trained trans individuals are able to be recruited within a single athletic discipline for a study (3) being trans does not necessitate gender affirming hormone therapy or surgeries, allowing various physiologic and morphologic possibilities amongst the trans community (50). Despite these limitations, attempts have been made to compare cis and trans gender individuals on many parameters of athletic performance, or proxies for these parameters (such as hand-grip strength) (12, 53–55, 122, 123).

In general, studies find that trans individuals, following gender affirming hormone therapy, become more similar to their gender identity (post-transition) cisgender counterparts, or are somewhere between the expected male and female averages (53–55, 122). Certain aspects of pre-transition-sex seem to be less malleable, such as total height and limb length (53, 122). However, there are changes in aerobic capacity, body composition, and muscular strength and endurance (12, 16, 53, 54, 122). Although these parameters may take months or years to complete this transition (12, 53, 54). The time to transition is relevant as (1) earlier in the process of transition, trans individuals may still retain traits more similar to their pre-transition gender, and (2) the effects of transitioning become confounded with the effects of aging and changes in training status (54, 55, 124–126). Due to all the potential pitfalls, a single definitive study of this topic is impossible, however, those which have been attempted can be used to glean better understanding of whether trans individuals' participation in sports and athletics is likely to lead to increased inequity or injury in sports and athletics.

Using a large sample among transgender exercise studies, Roberts et al. showed how the performance of both trans men and trans women on military physical fitness assessments changed over two years of gender affirming hormone therapy (54). Roberts et al. assessed number of push-ups and sit-ups performed as a field assessment of muscular strength and endurance (54). In addition, a 1.5-mile run was used as a field assessment of aerobic capacity (54). It was notable that neither trans men nor trans women aligned perfectly with their cisgender counterparts prior to gender affirming hormone therapy, with trans men performing more pushups and sit-ups (37.4 ± 2.03 and 50.4 ± 1.47) than cis women (32.6 ± 2.12 and 45.6 ± 1.51), and trans women performing fewer pushups than cis men (47.3 ± 1.34 vs. 53.5 ± 1.35) (54). Despite this, these groups were otherwise similar (54). Following two years of gender affirming hormone therapy, trans men showed no differences in pushups or 1.5 mile run time from cis men (56.1 ± 3.05 and 711 ± 34.91 sec. vs. 51.5 ± 4.31 and 720 ± 35.71 sec.), however they surpassed cis men for number of sit-ups performed (58.3 ± 2.20 vs. 52.4 ± 2.27) (54). For trans women following gender affirming hormone therapy, there were no differences in sit-ups or push-ups performed from cis women (44.8 ± 3.79 and 34.6 ± 4.21 vs. 45.7 ± 3.85 and 32.5 ± 4.31). However, post gender affirming hormone therapy, trans women still surpassed cis women for their 1.5 mile run time (765 ± 39.83 s. vs. 855 ± 40.56 s.), but performed significantly slower than cis men (720 ± 40.56 s.) unlike their pre hormone therapy assessment (54).

This study by Roberts et al. has also been used to support restricting trans individuals from participation in sport and athletic competitions (127, 128). As described above, following 2 years of gender affirming hormone therapy, trans women completed their 1.5 mile run slower than cis men, but still faster than cis women, raising potential concerns (54, 127). Fortunately, some of the original research team from the Roberts et al. study continued to follow-up for four years (129). However, the new analysis did not necessarily use the same participants as Roberts et al., having higher sample sizes for earlier years and lower sample sizes as they moved to year four. The follow-up study by Chiccarelli et al. noted that equivalence testing [the Two One-Sided Test (TOST)] should be used in addition to standard hypothesis testing to compare transgender individuals with their cisgender counterparts. The study also made comparisons of trans individuals' own pre-transition and post-transition performance as percentiles for men or women (129). Using these approaches, the researchers showed that trans women performance on the 1.5 mile run was not statistically different from cis women times following two years of gender affirming hormone therapy and remained equivalent to cis women out to year four (874 ± 133 s vs. 876 ± 111 s.) (129). Furthermore, the TOST analysis showed that the trans women's female percentile scores were equivalent to their pre-transition male percentile scores (129). These findings are similar to a study by Harper et al. which showed similar age adjusted running scores pre and post transition (55). However, Chiccarelli et al. they did find that the pushup test for trans women did not decline enough to be equivalent to their pre-transition percentile ranking, and the number of push-ups performed were still greater than those performed by cis women (35.3 ± 7 vs. 30 ± 10) (129). Trans men also continually performed more like cis men and significantly better than cis women over the four years, and it is worth noting that by year four of follow-up, trans men were out performing cis men on both pushups and sit-ups (129). Based on these data, trans men and trans women continually performed more similarly to their affirmed cisgender performance averages, and approach their own pre-transition percentile scores over the four years of gender affirming hormone therapy (129). Although these findings seem to indicate that trans individuals may eventually reach equivalence with their cisgender counterparts, it should also be noted that the participant pool diminished over the four years of follow-up, increasing the risk of self-selection bias and increasing risk of potential error (14, 129).

A study by Jenkins et al. were able to account for more granular fitness parameters among trans women than those used by Roberts et al. and Chiccarelli et al., however this came at the cost of a small total sample of trans women of various ages and physical activity levels (53). To best account for these differences, trans individuals were matched with cis men and women of matched age and activity levels. All the trans women had been using gender affirming hormone therapy for at least two years allowing the researchers to compare many of their fitness attributes to cis men and women. Trans women indeed retained body mass and height significantly greater than cis women, and similar to cis men (53). However, their body composition ($25.17 \pm 8.57\%$ body

fat) was between that of cis men ($17.12 \pm 5.22\%$) and cis women ($32.98 \pm 9.06\%$), and not statistically different from either (53). Trans women were also shown to have higher grip-strength than cis women (93.0 ± 14.0 kg vs. 63.9 ± 9.5 kg) with no difference from cis men (112.7 ± 23.2 kg) (35). These findings do align with other studies that find strength and muscle mass do not adapt as quickly to gender affirming hormone therapy as cardiorespiratory parameters (14, 16, 54, 127, 129). However, on more performance related tests of: vertical jump height, pushups, and maximal aerobic capacity, trans women performed similarly to, or less than, cis women (33.98 ± 4.34 cm, 17.83 ± 5.46 , and 29.43 ± 9.41 ml/kg/min compared to 34.24 ± 7.84 cm, 19.67 ± 11.64 , and 30.43 ± 9.15 ml/kg/min), and significantly less than cis men (47.34 ± 6.43 cm, 48.0 ± 5.37 , and 41.15 ± 13.77 ml/kg/min) (53). With such a small sample, this should not be overly interpreted, although it does seem to align with findings from Roberts et al. and Chiccarelli et al.

A slightly larger study by Alvares et al. also examined body compositional differences between cis men and women, and trans women (12). The study by Alvares et al., unlike data from Jenkins et al., showed a significantly higher percent body fat among trans women compared to cis men ($29.5 \pm 1.47\%$ vs. $20.2 \pm 1.52\%$), with no differences between trans women and cis women (32.9 ± 1.58) (12). Despite no differences in percent body fat, trans women still showed greater lean mass than cis women (30.7 ± 0.85 kg lean mass vs. 21.9 ± 0.67 kg lean mass) (12). Unlike the study by Jenkins et al., Alvares et al. measured a much smaller difference in grip strength between cis women and trans women (29.7 ± 1.0 kg vs. 35.2 ± 1.39 kg), with both being significantly lower than cis men (48.4 ± 1.79 kg) (12). Both studies seem to agree that relative aerobic capacity of trans women is decreased to levels similar to those of cis women (33.5 ± 1.21 ml/kg/min vs. 35.7 ± 1.30 ml/kg/min (12, 53). Alvares goes further and quantifies hemoglobin levels showing that trans women have similar hemoglobin to cis women (14.0 ± 0.15 g/dl vs. 13.8 ± 0.17 g/dl) and less than cis men (15.3 ± 0.29 g/dl) (12). These same findings for hemoglobin changes have been shown in other gender affirming hormone therapy treatments, and the subsequent changes in running performance are even shown among trans athletes (13, 55, 130).

Unfortunately, few studies are able to examine trans athletes due to the small population. A study by Harper et al. examined runners' race times across transition from men to women to determine how transitioning affected their performance (55). The study followed nine athletes over an average of 7 ± 1.9 years of transition (range of years of transition = 1–29). Harper found that there was a decrease in performance measured by race times (55). To account for the aging effect on running performance, Harper et al. used age grading, comparing run times to a standard run time accounting for race distance and sex. The age grades were on average, unchanged following transition (68.7% vs. 68.5%), suggesting that athletes as trans women did not enjoy an advantage compared to their pre-transition abilities. In other words, as trans women, they were performing at a similar competitive level, compared to other cis women, as they had as cis men compared to other cis men (55).

While data are still scarce, the limited information available does not suggest that trans men and trans women have much, if any, athletic advantage post-transition. Indeed, in most cases they perform more similarly to those matching their gender identity, or somewhere between cis men and women (12, 15, 53–55). If these individuals are performing somewhere between cis men and women on some performance parameters, does it pose a meaningful risk of inequity in sport or risk of athletic injuries, or are concerns for these problems misplacing blame to cover discrimination?

5. Misplacing blame

As reviewed above, there are in fact sex differences on average performance values between males and females. However, too often, these differences are used as evidence to restrict trans individuals from sports and athletics (11, 52). The average differences observed between males and females are cited as problems leading to inequality and elevated risk in sports and athletics despite evidence that trans individuals do not match their pre-transition cisgender counterparts (11, 131). However, if these average differences lead to inequity or injury, restricting trans individuals from these sports and athletics may not be the best solution. This can be approached similar to a public health issue, assessing what important factors influence outcomes, and what effect would come from altering individual factors (i.e., the population attributable risk). For example, Transgender Guidelines by World Rugby state concern for the larger average mass of males relative to females, and how this influences the force of impact (i.e., mass $\times$ acceleration) (11). However, when looking at a sample distribution of players, >300 males sampled fall below the 2nd percentile of average male body mass and >300 females sampled are above the 98th percentile of average female body mass (11). If being too large or too small were a critical concern for rugby injuries, more injuries may be prevented by restricting those >600 players who fell far outside the average player mass than banning trans athletes. If average body mass values and their standard deviations for elite rugby

players were used to generate a normal distribution of mass, there would still be areas of overlap among females and males. This can be seen in **Figure 2** in which distributions were calculated from data reported by Ramos-Álvarez et al. using the following equation: $f(x; \mu, \sigma) = \frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$ (57). Injury in sport is a serious problem, however a ban on trans individuals does not solve this problem because there is already normal variation among cisgender individuals (53, 54). Using average pre-transition body sizes reported by Roberts et al., an estimation of the body mass distributions among cis and transgender men and women were estimated (assuming a normal distribution) showing large areas of overlap, even before gender affirming hormone therapy, as shown in **Figure 3** (54). Perhaps in this case, if injuries are a primary concern, rugby should have weight classes similar to other sports where body mass is an important parameter rather than a ban on trans athletes.

Another example of misplaced blame would be concerns that trans women have too much testosterone or that trans men are gaining an unfairly advantage by taking testosterone (8, 11, 56, 127). Herein lies the myth that cis men, not on gender affirming hormone therapy, will claim to be a trans women to win at female sporting events. However, trans individuals use gender affirming hormone therapy to better match their gender identity, not to gain unfair sporting advantages (132). While it is true that certain morphological changes that occur during puberty may be irreversible, trans individuals on gender affirming hormone therapy clearly do not retain the same physiologic parameters as their pre-transition counterparts (12, 15, 16, 54–56, 129). It is unclear to what extent, or for how long, any hormone mediated advantages may persist once a trans individual begins regular gender affirming hormone therapy (12, 15, 53, 56, 129). It has been shown that parameters affecting aerobic performance transition more quickly than those affecting strength performance (16, 127, 129). However, excluding trans individuals does not prevent cases of athletes having hormonal advantages. The World Anti-Doping Agency (WADA) found 93 of the 4,422 athletes tested (2.1%) to have “adverse analytical finding” for steroid use (105). WADA does not report how many of those athletes were cis or trans, however, as transgender individuals are

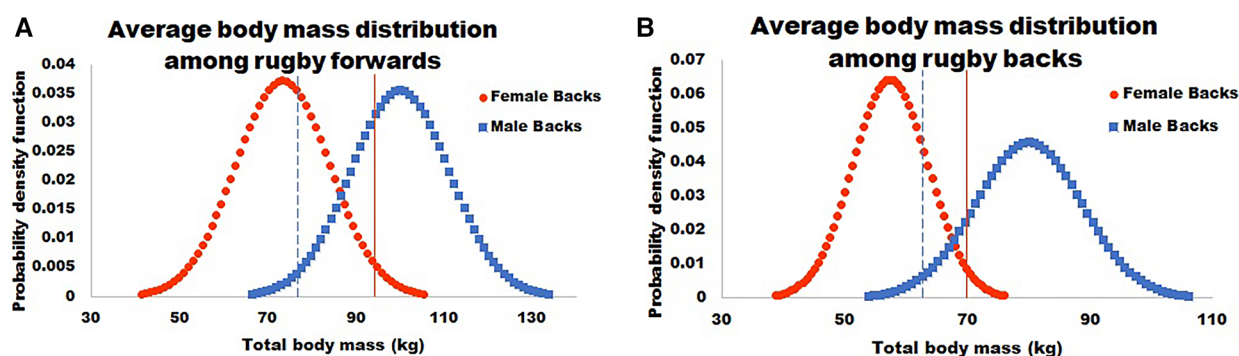


FIGURE 2

This figure shows the average body mass distribution among male (squares) and female (circles) rugby players. It also notes 2 standard deviations to the high end for females (solid line) and to the low end for males (dashed line). Data calculated based on values reported in Ramos-Álvarez et al. 2021 (12).

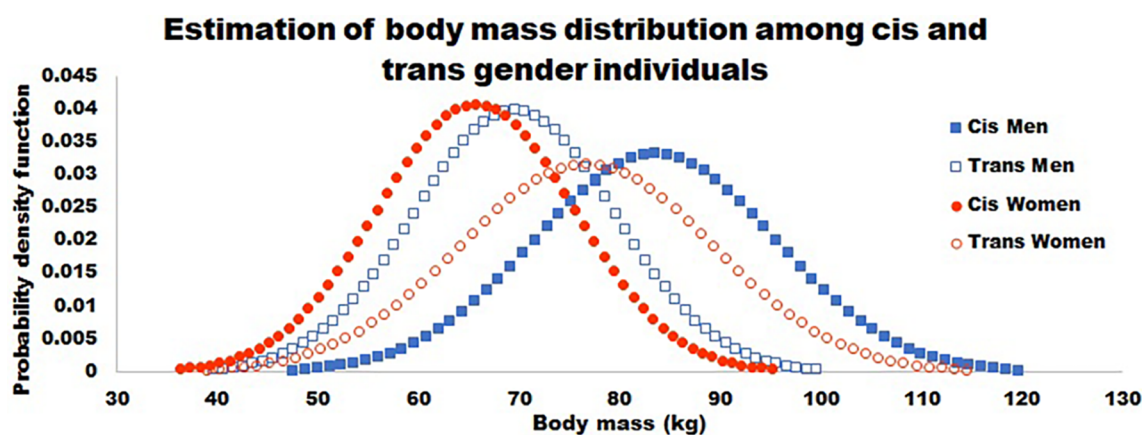


FIGURE 3

This figure shows an estimation of body mass distributions before gender affirming hormone therapy based on values reported by Roberts et al. 2020. Men and women are shown in squares and circles respectively, with cis and trans being denoted by closed or open symbols. As Roberts showed, there are not differences between the cisgender individuals and those who transitioned from that gender. However, there are large areas of overlap estimated among these populations even before gender affirming treatments.

underrepresented in athletics, it is likely that these are cis athletes (60). Besides use of exogenous hormones, cisgender individuals naturally vary in their hormonal profiles (40, 59, 66, 133). Thus, restricting trans individuals is unlikely to prevent issues of ergogenic hormonal advantages in sports.

Finally, it is well known that within sports and athletics, competitive advantage is in large part influenced by genetic predisposition (121, 134, 135). It is accepted that some individuals are born with natural advantages, however, the suggestion that trans individuals may enjoy some advantage in certain cases is regarded as unacceptable. Yet there does not seem to be a domination of sports by trans athletes if their advantage is so great. When examining issues that allegedly arise by trans athletes' participation in sports and athletics, the solutions are more driven by a political/cultural divide rather than an honest attempt to actually mitigate inequities or risk of injuries that are occurring (1, 136).

assessments do not account for training and skill at sports/athletics which may influence success as much as physiologic potential. Finally, there is the problem of neither sex nor gender being true binaries. This makes it nearly impossible to make comparisons among these individuals when classified into superimposed categories. As an example, even individuals who are cisgender, may have differences in sexual development, or have sexual aneuploidy, but would be simply classified based on their gender identity unless they were outed. Trans individuals, on the other hand, may have had various surgical procedures or take different gender affirming hormone therapy to better match assumed sex standards. All of these factors would need to be accounted for to truly understand what extent these individuals vary in sport and athletic performance. Future studies will be essential to gain a more comprehensive understanding of this population, and conclude whether and to what extent sex differences are retained post-transition.

6. Limitations and future directions

There are several limitations and future directions in this topic area. Many others have also noted that there is a need to study individuals who are both trans and elite athletes. Currently, the limited knowledge of athletic performance among trans men and women are limited to individuals who are either moderately active, recreationally trained, or military trained individuals (53–55, 129). Due to trans individuals making up such a small proportion of the total population, and their disproportionate rates of discrimination, recruitment of highly trained trans individuals is one of the greatest difficulties in this area of research (2, 7). In addition to difficulty in recruitment, the performance difference between males and females across different sports are not uniform (56, 92, 137). Individual components of fitness or task proficiency do not always translate to sport and athletic performance. Thus, fitness

7. Conclusion

Individuals should not have to make a choice between being their authentic selves or being athletes (138). While trans athletes competing in various sports and athletic events raises interesting considerations of how certain morphologic and physiologic factors affect performance, these questions are not exclusive to trans individuals. There are wide variations within cisgender populations, even when excluding individuals with differences in sexual development (121, 139). It is expected that about 2.3% of a normally distributed population is likely to fall above two standard deviations from a population mean. These exceptional individuals may be those who are gifted and excel at some sport or athletic performance (121, 135, 140). In contrast only 0.5%–0.6% of the population identify as trans (60). There is no concern for restricting individuals who are exceptionally large or

small, those who are genetically gifted, or those with differing hormone concentrations or muscle mass, so long as their gender and biologic sex align (120, 121). The disproportionate focus on the relatively small portion of the population who are trans seems based on the belief that cis men, who cannot succeed in sports among other cis men, would choose to misidentify as trans women to gain an advantage in sports against cis women. However, there are no legitimate cases of this occurring. An individual's sex does not determine their success or failure at any athletic event despite the high level of competition. This can be demonstrated when looking at not average outcomes, but the level of overlap among outcomes. The exclusion of trans individuals also insults the skill and athleticism of both cis and trans athletes. While sex differences do develop following puberty, many of the sex differences are reduced, if not erased, over time by gender affirming hormone therapy. Finally, if it is found that trans individuals have advantages in certain athletic events or sports; in those cases, there will still be a question of whether this should be considered unfair, or accepted as another instance of naturally occurring variability seen in athletes already participating in these events.

References

- Sharrow EA. Sports, transgender rights and the bodily politics of cisgender supremacy. *Laws*. (2021) 10(3):63. doi: 10.3390/laws10030063
- Mapping Transgender Equality in the United States. 2017, Movement Advancement Project (MAP).
- Rad MS, Shackelford C, Lee KA, Jassin K, Ginges J. Folk theories of gender and anti-transgender attitudes: gender differences and policy preferences. *PLOS ONE*. (2020) 14(12):e0226967. doi: 10.1371/journal.pone.0226967
- Krishnakumar P. This record-breaking year for anti-transgender legislation would affect minors the most, in CNN Politics. 2021.
- Nakajima K. Bills targeting trans youth are growing more common — and radically reshaping lives. In: Jin CH, editors. *NPR*. Washington DC: National Public Radio, Inc. (2022).
- West-Sell SA, Van Ness JM, Ciccolella ME. Law, policy, and physiology as determinants of fairness for transgender athletes. *Prof Exerc Physiol*. (2019) 22(2):1–10. https://www.asep.org/index.php/download_file/view/1231/178/
- James SE, Herman JL, Rankin S, Keisling M, Mottet L, Anafi M. 2015 U.S. Transgender Survey. 2016, National Center for Transgender Equality: Washington, DC.
- World Athletics. World Athletics Eligibility Regulations for Transgender Athletes. 2023, World Athletics: The Principality of Monaco.
- Alfonseca K. Young transgender athletes grappling with anti-trans sports legislation, in ABC News. 2021.
- Natanson H. Va. Bill would bar trans student-athletes from teams matching gender identities. In: Vozzella L, editors. *The Washington Post*. Washington, D.C.: Washington Post Company's new media subsidiary, Washington post. Newsweek Interactive (2022). Available from: <https://www.washingtonpost.com/dc-md-va/2022/11/15/virginia-bill-transgender-athletes-gender-identity/>
- World Rugby. World rugby transgender guideline. Report, 2020.
- Alvares LAM, Santos MR, Souza FR, Santos LM, de Mendonça BB, Frade Costa EM, et al. Cardiopulmonary capacity and muscle strength in transgender women on long-term gender-affirming hormone therapy: a cross-sectional study. *Br J Sports Med*. (2022) 56(22):1292–8. doi: 10.1136/bjsports-2021-105400
- Antun A, Zhang Q, Bhasin S, Bradlyn A, Dana Flanders W, Getahun D, et al. Longitudinal changes in hematologic parameters among transgender people receiving hormone therapy. *J Endocr Soc*. (2020) 4(11):1–11. doi: 10.1210/endo/bvaa119
- Cheung AS, Zwickl S, Miller K, Nolan BJ, Wong AFQ, Jones P, et al. The impact of gender affirming hormone therapy on physical performance. *J Clin Endocrinol Metab*. (2023):dgad414. doi: 10.1210/clinem/dgad414. [Epub ahead of print]
- Harper J, O'Donnell E, Khorashad BS, McDermott H, Witcomb GL. How does hormone transition in transgender women change body composition, muscle strength and haemoglobin? Systematic review with a focus on the implications for sport participation. *Br J Sports Med*. (2021) 55(15):865–72. doi: 10.1136/bjsports-2020-103106
- Wiik A, Lundberg TR, Rullman E, Andersson DP, Holmberg M, Mandić M, et al. Muscle strength, size, and composition following 12 months of gender-affirming treatment in transgender individuals. *J Clin Endocrinol Metab*. (2020) 105(3):e805–13. doi: 10.1210/clinem/dgz247
- Karkazis K. The misuses of “biological sex”. *Lancet*. (2019) 394(10212):1898–9. doi: 10.1016/S0140-6736(19)32764-3
- Ainsworth C. Sex redefined. *Nature*. (2015) 518(7539):288–91. doi: 10.1038/518288a
- Mauvais-Jarvis F, Merz NB, Barnes PJ, Brinton RD, Carrero J-J, DeMeo DL, et al. Sex and gender: modifiers of health, disease, and medicine. *Lancet*. (2020) 396(10250):565–82. doi: 10.1016/S0140-6736(20)31561-0
- 5050, G.H. Glossary. 2022 2023; Available at: <https://globalhealth5050.org/glossary/>
- Shannon G, Jansen M, Williams K, Cáceres C, Motta A, Odhiambo A, et al. Gender equality in science, medicine, and global health: where are we at and why does it matter? *Lancet*. (2019) 393(10171):560–9. doi: 10.1016/S0140-6736(18)33135-0
- World Health Organization, A.K. Gender and health. 2023; Available at: https://www.who.int/health-topics/gender#tab=tab_1 (Cited February 6, 2023).
- Darwin C. *The descent of man, and selection in relation to sex*. New York: Hurst (1870). 705.
- Havelock E. *Man and woman a study of human secondary and tertiary sexual characters*. 8th ed., rev. London: W. Heinemann ltd (1934). 469.
- Kellogg JH. Plain facts about sexual life. 1877, Battle Creek, Michigan: Office of the Health reformer. 356.
- Pike FH. A critical and statistical study of the determination of sex, particularly in human offspring. *Am Nat*. (1907) 41(485):303–22. doi: 10.1086/278772
- Hance RT. The determination of sex. *Sci Mon*. (1927) 24(1):25–30. <https://www.jstor.org/stable/7794>
- Crow EW, Crow JF. 100 Years ago: walter sutton and the chromosome theory of heredity. *Genetics*. (2002) 160(1):1–4. doi: 10.1093/genetics/160.1.1
- McClung CE. The accessory chromosome—sex determinant? *Biol Bull*. (1902) 3(1–2):43–84. doi: 10.2307/1535527
- Jacobs PA, Baikie AG, Court Brown WM, Macgregor TN, Maclean N, Harnden DG. Evidence for the existence of the human “super female”. *Obstet Gynecol Surv*. (1960) 15(3):440. doi: 10.1097/00006254-196006000-00052
- Ford CE, Jones KW, Polani PE, De Almeida JC, Briggs JH. A sex-chromosome anomaly in a case of gonadal dysgenesis (Turner's syndrome). 1959.

Author contributions

DO performed the research and writing for this work.

Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

32. Jacobs PA, Strong JA. A case of human intersexuality having a possible XXY sex-determining mechanism. *Nature*. (1959) 183:302–3. doi: 10.1038/183302a0
33. Raznahan A, Parikshak NN, Chandran V, Blumenthal JD, Clasen LS, Alexander-Bloch AF, et al. Sex-chromosome dosage effects on gene expression in humans. *Proc Natl Acad Sci USA*. (2018) 115(28):7398–403. doi: 10.1073/pnas.1802889115
34. Ottesen AM, Akslaede L, Garn I, Tartaglia N, Tassone F, Gravholt CH, et al. Increased number of sex chromosomes affects height in a nonlinear fashion: a study of 305 patients with sex chromosome aneuploidy. *Am J Med Genet Part A*. (2010) 152(5):1206–12. doi: 10.1002/ajmg.a.33334
35. Sherwani AY, Shah AQ, Wani AM, Bashir AC, Bashir AK, Sofi FA, et al. Hysterectomy in a male? A rare case report. *Int J Surg Case Rep*. (2014) 5(12):1285–7. doi: 10.1016/j.ijscr.2014.10.020
36. Clark RV, Wald JA, Swerdloff RS, Wang C, Wu FCW, Bowers LD, et al. Large divergence in testosterone concentrations between men and women: frame of reference for elite athletes in sex-specific competition in sports, a narrative review. *Clin Endocrinol (Oxf)*. (2019) 90(1):15–22. doi: 10.1111/cen.13840
37. Ginsburg GS, O'Toole M, Rimm E, Douglas PS, Rifai N. Gender differences in exercise-induced changes in sex hormone levels and lipid peroxidation in athletes participating in the Hawaii ironman triathlon: ginsburg-gender and exercise-induced lipid peroxidation. *Clin Chim Acta*. (2001) 305(1):131–9. doi: 10.1016/S0009-8981(00)00427-7
38. Crewther BT, Cook CJ. A longitudinal analysis of salivary testosterone concentrations and competitiveness in elite and non-elite women athletes. *Physiol Behav*. (2018) 188:157–61. doi: 10.1016/j.physbeh.2018.02.012
39. Ho KY, Evans WS, Blizzard RM, Veldhuis JD, Merriam GR, Samojlik E, et al. Effects of sex and age on the 24-hour profile of growth hormone secretion in man: importance of endogenous estradiol concentrations. *J Clin Endocrinol Metab*. (1987) 64(1):51–8. doi: 10.1210/jcem-64-1-51
40. Cook CJ, Beaven CM. Salivary testosterone is related to self-selected training load in elite female athletes. *Physiol Behav*. (2013) 116–117:8–12. doi: 10.1016/j.physbeh.2013.03.013
41. Castro-Peraza ME, García-Acosta JM, Delgado N, Perdomo-Hernández AM, Sosa-Alvarez MI, Llabrés-Solé R, et al. Gender identity: the human right of depathologization. *Int J Environ Res Public Health*. (2019) 16(6):978. doi: 10.3390/ijerph16060978
42. S O. Transgenderism: facts and fictions. *Indian J Psychiatry*. (2009) 51(1):73–5. doi: 10.4103/0019-5545.44917
43. Oliven JF. *Sexual hygiene and pathology: A manual for the physician and the professions*. 2nd edn. Lippincott (1965). 621 p.
44. Aultman B. Cisgender. *TSQ: Transgender Stud Q*. (2014) 1(1–2):61–2. doi: 10.1215/23289252-2399614
45. Beemyn G. A presence in the past: a transgender historiography. *J Women's Hist*. (2013) 25(4):113–21. doi: 10.1353/jowh.2013.0062
46. Reis E. Teaching transgender history, identity, and politics. *Radic Hist Rev*. (2004) 88(1):166–77. doi: 10.1215/01636545-2004-88-166
47. DeVun L, Tortorici Z. Trans, time, and history. *Transgender Stud Q*. (2018) 5(4):518–39. doi: 10.1215/23289252-7090003
48. Committee IO. *Olympic Charter*. Lausanne, Switzerland: International Olympic Committee (2021). 112.
49. Committee IO. *IOC Framework on Fairness, Inclusion and Non-Discrimination on the Basis of Gender Identity and Sex Variations 2021*. p. 6.
50. Martowicz M, Budgett R, Pape M, Mascagni K, Engebretsen L, Dienstbach-Wech L, et al. Position statement: IOC framework on fairness, inclusion and non-discrimination on the basis of gender identity and sex variations. *Br J Sports Med*. (2023) 57(1):26. doi: 10.1136/bjsports-2022-106386
51. International Olympic Committee. *IOC Consensus meeting on sex reassignment and hyperandrogenism*. Lausanne, Switzerland: International Olympic Committee (2015). 015–1.
52. World Aquatics. *Policy on eligibility for the men's and women's competition categories*. Lausanne, Switzerland: Fédération internationale de natation (FINA) (2022).
53. Jenkins CL, Ouellette K, Thompson B, Mullin EM, Leinung M. Performance in transgender females versus cisgender males and females. *J Exerc Physiol Online*. (2020) 23(6):62–76. https://www.asep.org/asep/asep/JEPonlineDECEMBER2020_Christine%20Jenkins.pdf
54. Roberts TA, Smalley J, Ahrendt D. Effect of gender affirming hormones on athletic performance in transwomen and transmen: implications for sporting organisations and legislators. *Br J Sports Med*. (2020) 55(11):577–83. doi: 10.1136/bjsports-2020-102329
55. Harper J. Race times for transgender athletes. *J Sport Cult Identities*. (2015) 6(1):1–9. doi: 10.18848/2381-6678/CGP/v06i01/54079
56. Hilton EN, Lundberg TR. Transgender Women in The Female Category of Sport: Is the Male Performance Advantage Removed by Testosterone Suppression? 2020: Preprints.
57. Ramos-Álvarez JJ, Montoya JJ, Solís-Mencia C, Miguel-Tobal F, López-Tapia P, Sánchez-Oliver AJ, et al. Anthropometric profile assessed by bioimpedance and anthropometry measures of male and female rugby players competing in the spanish national league. *Appl Sci*. (2021) 11(24):11759. doi: 10.3390/app112411759
58. Rønnestad BR, Nygaard H, Raastad T. Physiological elevation of endogenous hormones results in superior strength training adaptation. *Eur J Appl Physiol*. (2011) 111(9):2249–59. doi: 10.1007/s00421-011-1860-0
59. Balthazar CH, Garcia MC, Spadari-Bratfisch RC. Salivary concentrations of cortisol and testosterone and prediction of performance in a professional triathlon competition. *Stress*. (2012) 15(5):495–502. doi: 10.3109/10253890.2011.642033
60. Herman JLF, Andrew R, O'Neill KK. How Many Adults and youth Identify as Transgender in the United States? 2022, Williams Institute, UCLA School of Law.
61. Ansdell P, Thomas K, Hicks KM, Hunter SK, Howatson G, Goodall S. Physiological sex differences affect the integrative response to exercise: acute and chronic implications. *Exp Physiol*. (2020) 105(12):2007–21. doi: 10.1113/EP088548
62. Kuczmarski RJ. CDC growth charts for the United States: Methods and development. 2002, National Center for Health Statistics (2000).
63. Winsley RJ, Fulford J, Roberts AC, Welsman JR, Armstrong N. Sex difference in peak oxygen uptake in prepubertal children. *J Sci Med Sport*. (2009) 12(6):647–51. doi: 10.1016/j.jsams.2008.05.006
64. Wells JC. Sexual dimorphism of body composition. *Best Pract Res Clin Endocrinol Metab*. (2007) 21(3):415–30. doi: 10.1016/j.beem.2007.04.007
65. Handelsman DJ. Sex differences in athletic performance emerge coinciding with the onset of male puberty. *Clin Endocrinol (Oxf)*. (2017) 87(1):68–72. doi: 10.1111/cen.13350
66. Handelsman DJ, Hirschberg AL, Bermon S. Circulating testosterone as the hormonal basis of sex differences in athletic performance. *Endocr Rev*. (2018) 39(5):803–29. doi: 10.1210/er.2018-00020
67. Marta CC, Marinho DA, Barbosa TM, Izquierdo M, Marques MC. Physical fitness differences between prepubescent boys and girls. *J Strength Cond Res*. (2012) 26(7):1756–66. doi: 10.1519/JSC.0b013e31825bb4aa
68. Luz LGO, Cumming SP, Duarte JP, Valente-dos-Santos J, Almeida MJ, Machado-Rodrigues A, et al. Independent and combined effects of sex and biological maturation on motor coordination and performance in prepubertal children. *Percept Mot Skills*. (2016) 122(2):610–35. doi: 10.1177/0031512516637733
69. Trost SG, Pate RR, Sallis JF, Freedson PS, Taylor WC, Dowda M, et al. Age and gender differences in objectively measured physical activity in youth. *Med Sci Sports Exerc*. (2002) 34(2):350–5. doi: 10.1097/00005768-200202000-00025
70. Sallis JF. Epidemiology of physical activity and fitness in children and adolescents. *Crit Rev Food Sci Nutr*. (1993) 33(4–5):403–8. doi: 10.1080/10408399309527639
71. Cassola VF, Milian FM, Kramer R, de Oliveira Lira CAB, Khoury HJ. Standing adult human phantoms based on 10th, 50th and 90th mass and height percentiles of male and female caucasian populations. *Phys Med Biol*. (2011) 56(13):3749. doi: 10.1088/0031-9155/56/13/002
72. Taylor RW, Grant AM, Williams SM, Goulding A. Sex differences in regional body fat distribution from pre- to postpuberty. *Obesity*. (2010) 18(7):1410–6. doi: 10.1038/oby.2009.399
73. Veldhuis JD, Roemmich JN, Richmond EJ, Rogol AD, Lovejoy JC, Sheffield-Moore M, et al. Endocrine control of body composition in infancy, childhood, and puberty. *Endocr Rev*. (2005) 26(1):114–46. doi: 10.1210/er.2003-0038
74. Bredella MA. Sex differences in body composition. In: Mauvais-Jarvis F, editors. *Sex and gender factors affecting metabolic homeostasis, diabetes and obesity*. Cham: Springer (2017). doi: 10.1007/978-3-319-70178-3_2
75. Bishop P, Cureton K, Collins M. Sex difference in muscular strength in equally-trained men and women. *Ergonomics*. (1987) 30(4):675–87. doi: 10.1080/00140138708969760
76. Landen S, Hiam D, Voisin S, Jacques M, Lamon S, Eynon N. Physiological and molecular sex differences in human skeletal muscle in response to exercise training. *J Physiol (Lond)*. (2023) 601(3):419–34. doi: 10.1111/JP279499
77. Monteiro E, Fernandes A, Bigio L, Palma A, dos Santos LG, Cavanaugh MT, et al. Male relative muscle strength exceeds females for bench press and back squat. *J Exerc Physiol*. (2016) 19:79–85. http://www.asep.org/asep/asep/JEPonlineOCTOBER2016_Monteiro_Bigio.pdf
78. Huebner M, Perperoglou A. Sex differences and impact of body mass on performance from childhood to senior athletes in Olympic weightlifting. *PLOS ONE*. (2020) 15(9):e0238369. doi: 10.1371/journal.pone.0238369
79. Armstrong N, Welsman JR. Assessment and interpretation of aerobic fitness in children and adolescents. *Exerc Sport Sci Rev*. (1994) 22(1):435–76. doi: 10.1249/00003677-199401000-00016
80. Krabbe S, Christensen T, Worm J, Christiansen C, Transbøl I. Relationship between haemoglobin and serum testosterone in normal children and adolescents and in boys with delayed puberty. *Acta Paediatrica*. (1978) 67(5):655–8. doi: 10.1111/j.1651-2227.1978.tb17818.x

81. Thomsen K, Riis B, Krabbe S, Christiansen C. Testosterone regulates the haemoglobin concentration in male puberty. *Acta Paediatrica*. (1986) 75(5):793–6. doi: 10.1111/j.1651-2227.1986.tb10292.x
82. Goran M, Fields DA, Hunter GR, Herd SL, Weinsier RL. Total body fat does not influence maximal aerobic capacity. *Int J Obes*. (2000) 24(7):841–8. doi: 10.1038/sj.ijo.0801241
83. Demirkan E, Can S, Arslan E. The relationship between body composition and aerobic fitness in boys and girls distance runners. *Int J Sports Sci*. (2016) 6(2):62–5. doi: 10.5923/j.sports.20160602.07
84. de Simone G, Devereux RB, Daniels SR, Meyer RA. Gender differences in left ventricular growth. *Hypertension*. (1995) 26(6):979–83. doi: 10.1161/01.HYP.26.6.979
85. Castro OL, Haddy TB, Rana SR. Age- and sex-related blood cell values in healthy black Americans. *Public Health Rep*. (1987) 102(2):232. PMID: 3104982; PMCID: PMC1477821.
86. Murphy WG. The sex difference in haemoglobin levels in adults—mechanisms, causes, and consequences. *Blood Rev*. (2014) 28(2):41–7. doi: 10.1016/j.blre.2013.12.003
87. Gligoroska JP, Gontarev S, Dejanova B, Todorovska L, Stojmanova DS, Manchevska S. Red blood cell variables in children and adolescents regarding the age and sex. *Iran J Public Health*. (2019) 48(4):704–12. PMCID: PMC6500523; PMID: 31110981
88. Lepers R. Sex difference in triathlon performance. *Front Physiol*. (2019) 10:973. doi: 10.3389/fphys.2019.00973
89. Senefeld JW, Clayburn AJ, Baker SE, Carter RE, Johnson PW, Joyner MJ. Sex differences in youth elite swimming. *PLOS ONE*. (2019) 14(11):e0225724. doi: 10.1371/journal.pone.0225724
90. Nikolaidis PT, Rosemann T, Knechtle B. Sex differences in the age of peak marathon race time. *Chin. J. Physiol*. (2018) 61:85–91. doi: 10.4077/CJP.2018.BAG535
91. Andersson EP, Govus A, Shannon OM, McGawley K. Sex differences in performance and pacing strategies during sprint skiing. *Front Physiol*. (2019) 10:295. doi: 10.3389/fphys.2019.00295
92. Tiller NB, Elliott-Sale KJ, Knechtle B, Wilson PB, Roberts JD, Millet GY. Do sex differences in physiology confer a female advantage in ultra-endurance sport? *Sports Med*. (2021) 51(5):895–915. doi: 10.1007/s40279-020-01417-2
93. Knechtle B, Dalamitros AA, Barbosa TM, Sousa CV, Rosemann T, Nikolaidis PT. Sex differences in swimming disciplines—can women outperform men in swimming? *Int J Environ Res Public Health*. (2020) 17(10):3651. doi: 10.3390/ijerph17103651
94. Das D. San Francisco Marathon 2008–2021: Open Data and Statistics. 2021. Available at: <https://debarghyadas.com/writes/sanfrancisco-marathon-data/> (Cited September 26, 2021).
95. Joyner MJ. Physiological limits to endurance exercise performance: influence of sex. *J Physiol (Lond)*. (2017) 595(9):2949–54. doi: 10.1113/jp272268
96. Sato K, Iemitsu M, Katayama K, Ishida K, Kanao Y, Saito M. Responses of sex steroid hormones to different intensities of exercise in endurance athletes. *Exp Physiol*. (2016) 101(1):168–75. doi: 10.1113/EP085361
97. Ohlsson C, Vandenput L. The role of estrogens for male bone health. *Eur J Endocrinol*. (2009) 160(6):883–9. doi: 10.1530/EJE-09-0118
98. Chidi-Ogbolu N, Baar K. Effect of estrogen on musculoskeletal performance and injury risk. *Front Physiol*. (2019) 9:1–11. doi: 10.3389/fphys.2018.01834
99. Lebrun CM. Effect of the different phases of the menstrual cycle and oral contraceptives on athletic performance. *Sports Med*. (1993) 16(6):400–30. doi: 10.2165/00007256-199316060-00005
100. Bruinvels G, Burden RJ, McGregor AJ, Ackerman KE, Dooley M, Richards T, et al. Sport, exercise and the menstrual cycle: where is the research? *British Journal of Sports Medicine*. (2017) 51(6):487–88. doi: 10.1136/bjsports-2016-096279
101. Fischetto G, Sax A. The menstrual cycle and sport performance. *New Stud Athl*. (2013) 28(3/4):57–69. doi: 10.1016/j.csm.2005.01.003
102. Carmichael MA, Thomson RL, Moran LJ, Wycherley TP. The impact of menstrual cycle phase on athletes' performance: a narrative review. *Int J Environ Res Public Health*. (2021) 18(4):1667. doi: 10.3390/ijerph18041667
103. Constantini NW, Dubnov G, Lebrun CM. The menstrual cycle and sport performance. *Clin Sports Med*. (2005) 24(2):e51–82. doi: 10.1016/j.csm.2005.01.003
104. Meignié A, Duclos M, Carling C, Orhant E, Provost P, Toussaint J-F, et al. The effects of menstrual cycle phase on elite athlete performance: a critical and systematic review. *Front Physiol*. (2021) 12:1–10. doi: 10.3389/fphys.2021.654585
105. Agency WA-D. Anti-Doping testing figures report. Montréal (Québec), Canada: Anti-Doping Agency (2023) p. 311. Available from: https://www.wada-ama.org/sites/default/files/2023-01/2021_anti-doping_testing_figures_en.pdf
106. Bhasin S, Hatfield DL, Hoffman JR, Kraemer WJ, Labotz M, Phillips SM, et al. Anabolic-androgenic steroid use in sports, health, and society. *Med Sci Sports Exerc*. (2021) 53(8):1778–94. doi: 10.1249/MSS.0000000000002670
107. Parkinson AB, Evans NA. Anabolic androgenic steroids: a survey of 500 users. *Med Sci Sports Exerc*. (2006) 38(4):644–51. doi: 10.1249/01.mss.0000210194.56834.5d
108. Huang G, Basaria S. Do anabolic-androgenic steroids have performance-enhancing effects in female athletes? *Mol Cell Endocrinol*. (2018) 464:56–64. doi: 10.1016/j.mce.2017.07.010
109. Huo S, Scialli AR, McGarvey S, Hill E, Tügetimur B, Hogenmiller A, et al. Treatment of men for “low testosterone”: a systematic review. *PLOS ONE*. (2016) 11(9):e0162480. doi: 10.1371/journal.pone.0162480
110. Elashoff JD, Jacknow AD, Shain SG, Braunstein GD. Effects of anabolic-androgenic steroids on muscular strength. *Ann Intern Med*. (1991) 115(5):387–93. doi: 10.7326/0003-4819-115-5-387
111. Falquetto H, Júnior JLR, Silvério MNO, Farias JCH, Schoenfeld BJ, Manfredi LH. Can conditions of skeletal muscle loss be improved by combining exercise with anabolic-androgenic steroids? A systematic review and meta-analysis of testosterone-based interventions. *Rev Endocr Metab Disord*. (2021) 22(2):161–78. doi: 10.1007/s11154-021-09634-4
112. Friedl KE. Effects of testosterone and related androgens on athletic performance in men. IN: Kraemer WJ, Rogol AD, editors. *The Endocrine System in Sports and Exercise*. (2005). p. 525–43. doi: 10.1002/9780470757826.ch35
113. Berman S. Androgens and athletic performance of elite female athletes. *Curr Opin Endocrinol Diabetes Obes*. (2017) 24(3):246–51. doi: 10.1097/MED.0000000000000335
114. Hirschberg AL, Knutsson JE, Helge T, Godhe M, Ekblom M, Berman S, et al. Effects of moderately increased testosterone concentration on physical performance in young women: a double blind, randomised, placebo controlled study. *Br J Sports Med*. (2020) 54(10):599. doi: 10.1136/bjsports-2018-100525
115. Pielke R, Tucker R, Boye E. Scientific integrity and the IAAF testosterone regulations. *Int Sports Law J*. (2019) 19(1):18–26. doi: 10.1007/s40318-019-00143-w
116. Ahmetov II, Stepanova AA, Biktairova EM, Semenova EA, Shchuplova IS, Bets LV, et al. Is testosterone responsible for athletic success in female athletes? *bioRxiv*. 2019; p. 557348. doi: 10.23736/S0022-4707.20.10171-3
117. Berman S, Garnier PY, Hirschberg AL, Robinson N, Giraud S, Nicoli R, et al. Serum androgen levels in elite female athletes. *J Clin Endocrinol Metab*. (2014) 99(11):4328–35. doi: 10.1210/jc.2014-1391
118. Cooper J. Testosterone: ‘the best discriminating factor’. *Philosophies*. (2019) 4(3):36. doi: 10.3390/philosophies4030036
119. Sönksen PH, Dawn Bavington L, Boehning T, Cowan D, Guha N, Holt R, et al. Hyperandrogenism controversy in elite women's sport: an examination and critique of recent evidence. *Br J Sports Med*. (2018) 52(23):1481. doi: 10.1136/bjsports-2017-098446
120. Hirschberg AL. Female hyperandrogenism and elite sport. *Endocr Connect*. (2020) 9(4):R81–r92. doi: 10.1530/EC-19-0537
121. Kelly A, Côté J, Jeffreys M, Turnidge J, editors. *Birth advantages and relative age effects in sport: Exploring organizational structures and creating appropriate Settings*. (1st ed). New York, NY: Routledge (2021). <https://doi.org/10.4324/9781003163572>
122. Gooren LJ, Bunck MC. Transsexuals and competitive sports. *Eur J Endocrinol*. (2004) 151(4):425–9. doi: 10.1530/eje.0.1510425
123. Hamilton BR, Lima G, Barrett J, Seal L, Kolliari-Turner A, Guppy FM, et al. The Effects of Gender Affirming Treatment on the Sporting Performance and Muscle Memory of Transgender Athletes. A Protocol for The Tavistock Transgender Athlete Study. 2021. doi: 10.31236/osf.io/4rc2b
124. Deschenes MR. Effects of aging on muscle fibre type and size. *Sports Med*. (2004) 34(12):809–24. doi: 10.2165/00007256-200434120-00002
125. Thompson LV. Effects of age and training on skeletal muscle physiology and performance. *Phys Ther*. (1994) 74(1):71–81. doi: 10.1093/ptj/74.1.71
126. Shvartz E, Reibold RC. Aerobic fitness norms for males and females aged 6 to 75 years: a review. *Aviat Space Environ Med*. (1990) 61(1):3–11. PMID: 2405832
127. Heather AK. Transwoman elite athletes: their extra percentage relative to female physiology. *Int J Environ Res Public Health*. (2022) 19(15):9103. doi: 10.3390/ijerph19159103
128. Imbrišević M. Patriarchy in disguise: burke on pike and world rugby. *Sport Ethics Philos*. (2022) 1(1):1–31. doi: 10.1080/17511321.2022.2114534
129. Chiccarelli E, Aden J, Ahrendt D, Smalley J. Fit transitioning: when can transgender airmen fitness test in their affirmed gender? *Mil Med*. (2023) 188(7–8):e1588–95. doi: 10.1093/milmed/usac320
130. Jacobite JW, Gooren LJ, Schulte HM. Long-Acting intramuscular testosterone undecanoate for treatment of female-to-male transgender individuals. *J Sex Med*. (2007) 4(5):1479–84. doi: 10.1111/j.1743-6109.2007.00556.x
131. Pigozzi F, Bigard X, Steinacker J, Wolfrath B, Badtiev V, Schneider C, et al. Joint position statement of the international federation of sports medicine (FIMS) and European federation of sports medicine associations (EFSMA) on the IOC framework on fairness, inclusion and non-discrimination based on gender identity and sex variations. *BMJ Open Sport Exerc Med*. (2022) 8(1):e001273. doi: 10.1136/bmjsem-2021-001273

132. D'hoore L, T'Sjoen G. Gender-affirming hormone therapy: an updated literature review with an eye on the future. *J Intern Med.* (2022) 291(5):574–92. doi: 10.1111/joim.13441
133. Riachy R, McKinney K, Tuvdendorj DR. Various factors may modulate the effect of exercise on testosterone levels in men. *J Funct Morphol Kinesiol.* (2020) 5(4):81. doi: 10.3390/jfmk5040081
134. Antero J, Saulière G, Marck A, Toussaint J-F. A medal in the olympics runs in the family: a cohort study of performance heritability in the games history. *Front Physiol.* (2018) 9:1313. doi: 10.3389/fphys.2018.01313
135. Sanchis-Gomar F, Pareja-Galeano H, Rodriguez-Marroyo JA, de Koning JJ, Lucia A, Foster C. Olympic Genes on the podium? *Int J Sports Physiol Perform.* (2016) 11(7):973–4. doi: 10.1123/ijspp.2016-0421
136. Parker K, Horowitz JM, Brown A. *U.S. Adults have Complex views on gender identity and transgender issues.* Washington, DC, USA: Pew Research Center (2022).
137. Besson T, Macchi R, Rossi J, Morio CYM, Kunimasa Y, Nicol C, et al. Sex differences in endurance running. *Sports Med.* (2022) 52(6):1235–57. doi: 10.1007/s40279-022-01651-w
138. Semerjian TZ, Cohen JH. FTM Means female to me": transgender athletes performing gender. *Women Sport Phys Act J.* (2006) 15(2):28. doi: 10.1123/wspaj.15.2.28
139. Wolfarth B, Bray MS, Hagberg JM, Pérusse L, Rauramaa R, Rivera MA, et al. The human gene map for performance and health-related fitness phenotypes: the 2004 update. *Med Sci Sports Exerc.* (2005) 37(6):881–903. doi: 10.1249/01.mss.0000168663.55604.1d
140. Rankinen T, Pérusse L, Rauramaa R, Rivera MA, Wolfarth B, Bouchard C. The human gene map for performance and health-related fitness phenotypes: the 2003 update. *Med Sci Sports Exerc.* (2004) 36(9):1451–69. doi: 10.1249/01.MSS.0000139902.42385.5F