Do Transitioned Athletes Compete at an Advantage or Disadvantage as compared with Physically Born Men and Women: A review of the Scientific Literature

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Table of Contents ***Page***

1.0 Abstract

Transitioned athletes present a unique challenge to sport governing bodies with respect to determining the eligibility of such athletes to compete against physically born men and women. The IOC Stockholm consensus on sex reassignment in sports allows transitioned men and women to compete against members of their new sex provided that sex reassignment surgery is complete, the individuals are legally recognized as a member of their new sex and proper cross-sex hormone administration has been ongoing for at least two years. The basis behind this statement is to minimize the effects of previous sex hormone exposure on athletic performance. The purpose of the current review is to examine the scientific evidence that exists to determine if transitioned athletes compete at an advantage or disadvantage as compared with physically born men and women. Men outperform women in athletic events by approximately 11-18%, potentially as a result of well known sex differences including that men are taller, have a greater maximal aerobic and anaerobic capacity, muscle mass and strength and altered substrate utilization characteristics. The observed sex differences are the result of differences in testosterone and estrogen. Testosterone increases muscle mass and strength, bone size and mineral content and haemoglobin content. Estrogen has a profound effect on substrate metabolism during exercise, increasing the reliance on lipid stores. As both testosterone and estrogen can influence performance measures it is important to ensure that transitioned athletes have sex hormone levels within the normal physiological range for their new sex. While hormone concentrations in transitioned women fall in line with those of physically born women, transitioned men spend the majority of time with supraphysiological levels of testosterone and higher estrogen as compared with physically born men. Cross-sex hormone administration to transitioned individuals results in haemoglobin and subcutaneous fat content and muscle cross-sectional areas similar to those values in physically born men and women. To date, no study has examined the effects of cross-sex hormones on any objective measures of athletic performance (maximal aerobic capacity, time trials). Additionally, no trial has been conducted in transitioned athletes as compared with physically born men and women athletes. As such, there is no concrete evidence to support or refute the position that transitioned athletes compete at an advantage or disadvantage as compared with physically born men and women athletes.

2.0 Introduction

Transitioned athletes present a unique challenge to sport governing bodies in determining the eligibility of such athletes to compete against physically born men and women. Many differences exist between men and women; however, whether these differences persist upon transition or whether they impact performance is yet to be determined. The purpose of the current review is to examine the scientific literature in an attempt to determine if enough information is currently available to address the question of whether transitioned athletes compete at an advantage/disadvantage as compared with physically born men and women. For the purpose of this review the genotypic definition of man and woman will be used. Specifically, an XY genotype will denote men and an XX genotype will denote women. Throughout the course of this report the differences between men and women, the metabolic effects of sex hormones, the hormone levels in transitioned men and women as compared with physically born men and women and future research will be discussed.

3.0 Sex Differences in Performance, Anthropometrics and Metabolism

Typically, men outperform women by 11-18% depending on the type of activity (Comben, 1996). Additionally, there is a 5-37% difference in world record times between men and women for a variety of sporting events, as summarized in Table 1. Additionally, for any given training status men have a higher maximal aerobic capacity (VO_{2peak}) relative to body weight as compared with women (26, 27). The differences in performance observed between men and women are likely the result of numerous factors that are different between the sexes. Anthropometrically, men are taller by approximately 12-15 cm (26, 27, 93), have greater muscle mass and less body fat (26, 27, 57, 93) and greater bone thickness (45, 56, 57) and bone mineral density (12, 56, 93).

Table 1: World records by sporting event for men and women as at May 18, 2008 and the percent difference in performance between men and women in each event.

Sport	Event	Men	Women	% difference*
Track and Field				
	100m	9.74s	10.49s	7.7
	400m	43.18s	47.60s	10.2
	1000m	2:11.96min	2:28.98min	12.9
	10km	27:02min	30:21min	12.3
	42km	2:04:26h	2:15:25h	8.8
	100km	6:13:33h	6:33:11h	5.3
	High jump	2.45m	2.09m	17.2
	Pole vault	6.14m	5.01m	22.6
	Long jump	8.95m	7.52m	19.0
	Javelin	98.48m	71.70m	37.4
Speed skating (short track)				
	500m	41.051s	43.216s	5.3
	1000m	1:23.815min	1:29.495min	6.8
	1500m	2:10.639min	2:16.729min	4.7

Speed skating (long track)				
	500m	34.03s	37.02s	8.8
	1000m	1:07.00min	1:13.11min	9.1
	1500m	1:42.01min	1:51.79min	9.6
	5000m	6:03.32min	6:45.61min	11.6
Swimming				
	50m freestyle	21.28s	23.97s	12.6
	100m freestyle	47.50s	52.88s	11.3
	200m freestyle	1:43.86min	1:55.52min	11.2
	400m freestyle	3:40.08min	4:01.53min	9.7

* % difference in distance for high jump, pole vault, long jump and javelin world records, and in speed for all other world records.
Data obtained from the International Association of Athletics Federations (www.iaaf.org) and the Official Site of the Olympics Movement (www.olympic.org).

Being leaner can be a performance benefit because for a given body weight more muscle mass indicates increased metabolically active tissue as well as increased capacity to generate force. Additionally, thicker/denser bones can increase stability and decrease risk of injury. Additionally, fat distribution differs between men and women with women having a more gynoid (gluteal-femoral region) fat distribution and men having a more android (abdominal region) fat distribution (11, 93), resulting in a lower centre of gravity in women. Increased body fat and body fat distribution can influence performance because increased body fat is additional weight that needs to be carried during athletic events and body fat distribution may influence performance biomechanics. Interestingly, at birth sex differences in anthropometrics already exist with boys being longer and having greater fat-free mass than girls (93).

In accordance with an increased muscle mass and muscle cross-sectional area (57), men also have increased muscle strength (57, 58). However, even when muscle cross-sectional area is accounted for, men have greater knee flexor and extensor muscle strength (57), while no sex differences in muscle strength was observed in elbow flexor and extensor muscles when determined relative to muscle cross-sectional area (57). The disproportionately higher leg muscle strength in men may be the result of a greater percentage of type II (fast twitch) muscle fibres (68, 79, 81). Type II muscle fibres, as compared with type I (slow twitch) muscle fibres, are larger allowing for greater contraction strength and power (41); whereas type I muscle fibres have a greater mitochondrial content allowing for greater muscle endurance (41). Thus, a greater proportion of type II muscle fibres would suggest a greater ability in sports requiring high force and explosive movements; whereas an individual with a greater proportion of type I fibres would be better suited for endurance events. Additionally, greater muscle mass in men also results in a higher anaerobic capacity (63, 92). However, in trained men and women, sex differences in anaerobic capacity are no longer found when relative to lean body mass (63). In untrained men and women, the sex difference in anaerobic capacity persists despite controlling for lean body mass (92). Again the sex difference in anaerobic capacity may be the result of differing muscle fibre type between men and women (68, 79, 81) and may disappear with training when muscle fibre type shifts (48, 78, 82) to meet the metabolic demands imposed on it by the athlete. A greater anaerobic capacity would allow an athlete to continue to perform at levels beyond the

anaerobic threshold (beyond the VO_{2peak}) for a greater period of time; thus allowing the athlete to perform at a higher intensity for a longer period of time.

Men and women also differ in that the Q angle (the angle of the quadriceps to the knee) is greater in women, the result of a wider pelvis (2, 39). The Q angle is a determinant of patellar tracking and is determined by measuring the angle that is formed at the knee when a line is drawn from the anterior superior iliac spine to the centre of the patella and from the centre of the patella to the centre of the tibial tuberosity (39). The greater Q angle in women results in a greater valgus orientation of the knee extensor mechanism (35), which can increase risk of knee injury (35) and may influence sport performance, specifically running efficiency (3). Indeed, elite women runners typically have narrower pelvises than age-matched controls (95). However, recently the anatomical importance of the sex difference in Q angle (~2.3^0 difference between men and women) has been questioned (39).

Lung capacity is also greater in men as compared with women. Specifically men have a greater lung volume (64, 65) and larger airways (76) as compared with height-matched women. As summarized by Harms (42), the smaller airways in women can lead to greater limitations to expiratory flow, which may result in early fatigue of the respiratory muscles (i.e. diaphragm) during heavy exercise in women. Additionally, women have lower resting lung diffusing capacity, which is the result of fewer alveoli and smaller airway diameter (46). Together these findings suggest that gas exchange, and ventilation may be limiting in women during exercise; however, a lower oxygen demand due to lower body weight may nullify the effect of these differences on exercise performance (46). However, if gas exchange is limited in women during exercise then oxygen delivery to active muscles would also be limited and would lower maximal aerobic metabolism.

Oxygen delivery to the muscles may also be limited in women as a result of lower haemoglobin levels (37). Haemoglobin is the oxygen carrying metalloprotein in red blood cells, allowing for delivery of oxygen from the lungs to the tissues (41). During exercise, oxygen is delivered to the active muscles via haemoglobin; thus lower haemoglobin content in women limits oxygen delivery to the active muscles and would lower maximal aerobic capacity. Importantly, there is a positive correlation between blood testosterone concentrations and haemoglobin levels (37). Additionally, absolute heart mass and volume is greater in men as compared with women (72, 73). When normalized to body surface area, to control for differences in body weight and height between men and women, sex differences in left ventricular volume, but not right ventricular volume or left and right ventricular function, disappeared (73). However, cardiac output (a function of heart rate and stroke volume) is not different between the sexes (73).

From a metabolic standpoint women rely to a greater extent on lipid stores to fuel exercise as compared with men as evidenced by a lower respiratory exchange ratio (RER) (17, 26, 34, 47, 69, 86, 88, 90). It has been consistently shown that women use less liver glycogen/glucose (lower glucose rate of appearance, rate of disappearance and metabolic clearance rate) (26, 34), have a higher rate of lipolysis (greater glycerol turnover) (17), higher plasma free fatty acid concentration (9, 66) and depending on the type of exercise performed and the menstrual cycle phase in which women are tested, lower muscle glycogen utilization (26,

86), with no difference in intramyocellular lipid (IMCL) utilization (27, 94) during endurance exercise. Additionally, skeletal muscle and myocardial glycogen depletion is lower in female, as compared with male, rats following exercise (36, 51). It has been suggested that these sex differences during exercise are due to differences in estrogen concentration/activity (15, 61). In fact, estrogen supplementation studies in animals and humans have supported the aforementioned findings of higher fat oxidation for women during endurance exercise (17, 25, 71).

While there is no difference in IMCL utilization during exercise between men and women, it has been consistently shown that women have a greater IMCL content as compared with men (26, 33, 68, 83). Increased IMCL content may influence exercise performance as it is a readily available fuel source within the muscle. Additionally, using electron microscopy it has been shown that prior to and following a period of endurance training women have a higher number of IMCL in a given area of muscle, but not a greater lipid size, as compared with men, and this greater number of IMCL contributed to the increased IMCL content in women (26). Thus, women have an increased availability of IMCL to use as a substrate source during exercise; however, IMCL utilization is not different between the sexes.

Intriguingly, while there are sex differences in IMCL storage and not IMCL utilization during exercise it appears the opposite is true with regards to muscle glycogen storage and utilization. Depending on the type of exercise performed (during running women spare muscle glycogen as compared with men (86)) or the menstrual cycle in which women are tested (in the luteal phase women spare muscle glycogen as compared with men (26)) women utilized less muscle glycogen during exercise as compared with men. However, there is no sex difference in muscle glycogen storage between the sexes (26, 53, 86, 87). Overall the increased reliance on lipid and decreased reliance on carbohydrate stores during exercise in women can influence endurance exercise performance by slowing carbohydrate depletion. The attenuated carbohydrate depletion in women allows women to exercise at a higher intensity for a longer period of time since carbohydrates are necessary to maintain exercise intensities greater than approximately 65-70% (90).

The extent to which, if any, the aforementioned sex differences influence sport performance is yet to be determined. Additionally, whether differences in hormone levels between men and women mediate these differences, with several exceptions, is also unknown.

4.0 Metabolic Effects of Testosterone and Estrogen

One of the main elements differentiating men and women is the differences in hormonal milieu. The average concentrations of testosterone and estrogen in men and mid-follicular and mid-luteal women are presented in Table 2.

Table 2: Normal hormone concentrations in physically born men and women.

	Testosterone (nmol/L)	Estrogen (pmol/L)
Men	21 $\pm$ 1	128 $\pm$ 13
Mid-follicular women	1.1 $\pm$ 0.1	184 $\pm$ 71

Mid-luteal women	1.0 ± 0.2	361 ± 107

Data are means ± standard area of the mean (SEM), where SEM is a measure of variance within the study population. Data from Devries, MC et al. *Am J Physiol Regul Integr Comp Physiol,* 2006; 291:R1120-R1128.

Aside from the obvious role sex hormones play in primary and secondary sexual characteristics, these hormones also influence numerous other metabolic systems.

4.1 Metabolic effects of testosterone

Testosterone is well known as an anabolic agent regulating muscle mass (6, 44, 75, 85) and strength (6, 31, 75, 85). In fact, testosterone supplementation can increase strength by ~5-20% and lean body mass by ~2-5 kg (43). Additionally, the effect of testosterone on muscle mass and strength are dose dependent; however, its effects to increase strength are typically only found when testosterone levels are at high end normal or supraphysiological levels (7). In fact, when given at levels that mimic normal physiological concentrations, no change in muscle strength is found, despite increases in muscle mass (80). When testosterone levels are ablated via orchidectomy in mice, there is a decrease in type I and II muscle fibre cross-sectional area and this effect is attenuated by testosterone administration (5). Specifically, slow twitch (type I) muscle fibres are the most sensitive to testosterone removal and supplementation (5). Following orchidectomy, maximal force generation decreased in mice; whereas in testosterone treated orchidectomized mice, maximal force generation was not different from control mice (5). However, while maximal force generation is enhanced following testosterone administration in orchidectomized mice, there is no difference in contraction speed (5).

Testosterone is also thought to play a role in fatigue resistance and muscle recovery. In mice, testosterone administration following orchidectomy enhanced fatigue resistance in slow twitch (type I), but not fast twitch (type II) muscle fibres (5). However, in humans, a wide range of testosterone doses did not influence muscle fatigability (85). Additionally, muscle specific tension, a measure of muscle quality, did not change in response to any testosterone dose (85). The role of testosterone on muscle recovery is not compelling. Despite higher testosterone concentrations following resistance exercise when repetitions were performed slowly, as compared with when repetitions were performed at regular speed, no difference was found in recovery of maximal strength or jump performance in humans (38).

The sex differences in bone size and mineral content and haemoglobin content are the direct result of differences in testosterone concentrations between the sexes. During puberty in boys, the anabolic effects of testosterone increase the total quantity of bone and increase calcium retention within the bone, resulting in larger, stronger bones (41). Testosterone also influences the shape of the pelvis by narrowing the pelvic inlet and lengthening it, as well as, increasing the strength of the pelvis for load-bearing (41). If no testosterone is present, the male pelvis resembles that of the female (41). Testosterone also stimulates red blood cell production, which, as described in detail above, contains haemoglobin, which carries oxygen to the working muscles. Testosterone administration to a castrated man to mimic physiological testosterone levels increases red blood cell count by 15-20% (41).

The observed sex differences in metabolism between men and women during exercise are not mediated by differences in testosterone. In fact, a recent study investigated substrate utilization during exercise in men with physiological testosterone levels, ablated testosterone and supraphysiological concentrations of testosterone and found no differences in lipid or carbohydrate oxidation during exercise (13). Thus, while testosterone does appear to regulate some of the differences between the sexes, substrate metabolism during exercise is not one of them.

4.2 Metabolic effects of estrogen

The observed sex difference in metabolism during exercise is mediated by differences in estrogen concentration between the sexes. 17-β-estradiol (E2) supplementation trials in animals (16, 60, 61), and humans (18, 25, 71, 89), have shown that short term administration of E2 can modify fuel selection during endurance exercise. In animals, E2 supplementation to oophorectomized female or male rats spared skeletal muscle, hepatic and myocardial glycogen during exhaustive and submaximal exercise, resulting in improved performance (16, 60, 61, 70). In ammenorrheic women, 100 μg/d E2 supplementation for 3 days increased free fatty acid concentration, decreased liver glucose utilization, with no effect on whole body lipolysis and no change in RER, carbohydrate or fat oxidation (71). However, there was no effect of E2 supplementation on performance during a run to exhaustion at 85% VO_{2peak} that was preceded by a 90 min run at 65% VO_{2peak} (71). E2 supplementation trials in men have yielded similar findings (18, 25, 89). Low dose E2 (100-300 μg/d) supplementation to men for 11 days, resulting in serum estradiol concentrations similar to the level seen in the follicular phase of the menstrual cycle in women, had no effect on performance or muscle glycogen utilization during a 90 min cycling bout at 60% VO_{2peak}; however, there was a trend towards higher lipid and lower carbohydrate oxidation during the exercise bout (89). When the E2 dose administered to men was increased (1-3 mg/d, 8 days) RER and carbohydrate oxidation were decreased and lipid oxidation increased (25). Additionally, high dose E2 lowered liver glucose utilization (18, 25) and resting muscle glycogen content with no effect on muscle glycogen utilization (25). Lastly, similar to the findings of Ruby *et al* (71), there was no effect of high dose E2 supplementation on whole body lipolysis in men (18). To date, only one E2 supplementation trial has found an effect of E2 on whole body substrate utilization by lowering RER and CHO oxidation and increasing lipid oxidation (25). It is possible that a dose response relationship exists with respect to E2 and RER as there was no effect of low dose E2 on RER (71, 89). However, in the study conducted by Carter *et al* (18), serum estradiol concentrations were higher than those in the Devries *et al* (25) study, and yet no effect of E2 on RER was observed. One possible explanation could be the smaller sample size used in the study by Carter *et al* (18) resulting in a type II error. Alternatively, as E2 is known to increase IMCL content and lipoprotein lipase activity in rats (22, 67, 96), and given that there is simultaneous FFA esterification and IMCL hydrolysis during exercise (40), and that increased IMCL synthesis would elevate RER, it is possible that the RER could be falsely elevated with E2. Therefore, it is possible that in the study conducted by Carter *et al* (18), that the dosing regime was so high that the effects of E2 on lipid synthesis exceeded those on lipid mobilization leading to an inability to detect an effect of E2 on lowering RER. Collectively these data suggest that E2 has a primary action on liver glycogenolysis and glucose release, while muscle glycogenolysis is not affected by short term E2 supplementation. However, as E2 lowered muscle glycogen content (25), perhaps with time an effect of E2 on muscle

glycogen utilization will be seen. Additionally, these studies suggest that at the level of substrate utilization E2 has a greater impact on CHO, as opposed to lipid, metabolism.

Estrogen also acts as an anti-oxidant, attenuating exercise-induced oxidative stress and inflammation (54, 84). Acute bouts of exercise increase reactive oxygen species production in humans (1, 24, 74). Increases in reactive oxygen species production leads to oxidative stress and can result in oxidative damage in muscle and blood (1, 10, 55, 74, 97). Oxidant induced muscle damage can decrease muscle function and result in muscle soreness (24, 62) and may also result in muscle fatigue (4), decreasing performance capacity. In various cell lines, E2 inhibits reactive oxygen species generation by inhibiting NADPH oxidase enzyme activity (50, 91). Similar effects of E2 to inhibit reactive oxygen species production have been found in animal models as well (21, 32, 50, 54). However, acute increases in reactive oxygen species production during exercise stimulate gene transcription to increase antioxidant enzyme content (77). In fact, despite acute bouts of exercise increasing reactive oxygen species production, trained individuals have lower levels of oxidative stress and higher levels of antioxidant enzymes (14, 23, 59) as compared with their sedentary counterparts. These findings can be interpreted in two ways. First, if estrogen acts to attenuate reactive oxygen species production, perhaps the oxidant effect of an acute bout of exercise is lower in women, as compared with men, resulting in lower muscle damage and soreness. On the other hand, the effect of estrogen to attenuate reactive oxygen species production during exercise may result in a smaller adaptation to repeated bouts of exercise (i.e. endurance training) in women. Thus, estrogen plays an important role in the regulation of substrate metabolism during exercise as well as the oxidative stress response to exercise.

5.0 Hormone Levels in Transitioned Men and Women Compared with Physically Born Men and Women

The typical sex hormone concentrations in transitioned men and women, as well as those from physically born men and women are presented in table 3. When comparing the values, physically born women and transitioned women have very similar concentrations of both testosterone and estrogen. However, transitioned men appear to have higher estrogen and

Table 3: Testosterone and estrogen concentrations in transitioned men and women as compared with physically born men and women.

	Testosterone (nmol/L)	Estrogen (pmol/L)
Physically born men	22 ± 6	96 ± 12
Transitioned men	31 ± 11	134 ± 35
Physically born women	1.6 ± 0.6	161 ± 55
Transitioned women	1.0 ± 0.0	175 ± 37

Data are means ± SEM. Data from Elbers et al. *Am J Physiol Endocrinol Metab*, 1999; 276:E317-E325.

testosterone concentrations as compared with physically born men. This is intriguing as it suggests that transitioned men may experience performance benefits from higher levels of both testosterone (muscle strength and mass) and estrogen (increased reliance on lipid stores during

exercise). Traditionally, testosterone is administered to transitioned men once every 14 days, resulting in supraphysiological testosterone concentrations that remain elevated for at least 5-9 days after testosterone administration (8) and then drop to subnormal levels during the last few days before the next scheduled injection (52). However, recently a long-acting testosterone, testosterone undecanoate, dosing regime has been developed. This dosing regime requires female-to-male transitioned individuals to undergo two initial injections separated by 6 weeks, followed by one injection every 12 weeks thereafter (52). Thus, using this regime transitioned men only require 4 doses per year. This dosing regime is advantageous because the testosterone concentrations that result immediately following injection are within the physiological range and remained stable between doses (52). Additionally, at the end of one year of dosing with testosterone undecanoate, testosterone levels in transitioned men were mid-range of normal physiological values for physically born men (52). As testosterone has a multitude of performance-enhancing effects (see above), transitioned men who wish to compete at the elite level should strive to minimize the large variation in testosterone concentrations (peaks and troughs) that result with traditional testosterone injection regimes and should utilize the testosterone undecanoate regime, as described above. The reasons for this recommendation are two-fold. First, as described above, traditional testosterone dosing regimes result in supraphysiological testosterone levels for at least 5-9 days following testosterone injection. As transitioned men undergo testosterone dosing every 14 days, they spend a large proportion of time with supraphysiological testosterone concentrations, which may enhance athletic performance, resulting in an unfair advantage as compared with physically born men. Second, as drug testing is common practice in elite sport, the traditional dosing regime may result in a failed drug-test as testosterone levels are elevated for at least 36-64% of the time during the two week period after a single testosterone dose. Using the new long-acting testosterone ensures that transitioned men are not competing at an unfair advantage, as compared with physically born men and prevents the transitioned male athlete from failing a drug test as testosterone levels do not reach supraphysiological levels using this dosing method.

5.1 Acceptable limits for testosterone and estrogen in sport and how this pertains to transitioned athletes

The Canadian Centre for Ethics in Sport is the regulating body in Canadian Sport for doping infractions (19). There is no acceptable level of synthetic or exogenous testosterone or estrogen in competing athletes (19). Thus, transitioned athletes taking cross-sex hormones would be required to complete a Therapeutic Use Exemption (TUE) to permit the use of synthetic testosterone or estrogen (i.e. testosterone undecanoate, ethinyl estradiol) (19). If a TUE has not been obtained by a transitioned athlete and exogenous sources of testosterone or estrogen are found within the athlete's sample, a doping infraction would be charged against the athlete (19). In this case, the transitioned athlete would be able to present his/her case to the review board to explain why the endogenous hormone was found (19).

6.0 Effects of Cross-sex Hormones on Parameters that may Influence Performance

Data on the effects of cross-sex hormone administration on factors that may influence performance are sparse.

6.1 Testosterone administration to transitioned men

Testosterone administration to transitioned men increased haemoglobin and hematocrit content within one year of hormone supplementation (37, 52), with no further increase beyond one year (37), thus perhaps increasing oxygen delivery to the muscle during exercise. Importantly, there was no difference in haemoglobin levels between transitioned men and physically born men (37). Testosterone administration to transitioned men also increased muscle cross-sectional area; however, muscle cross-sectional area was still smaller than that of transitioned women prior to testosterone deprivation (i.e. physically born men) (28, 29, 37). However, of note, while average muscle cross-sectional area was greater in physically born men, there was a large range in muscle cross-sectional area within both groups of men (37). Further examination of the data shows that at the average muscle cross-sectional area was only greater in physically born men because they had a larger minimum muscle cross-sectional area, as compared with transitioned men (37). At the high end of the spectrum, muscle cross-sectional area was not different between transitioned and physically born men (37). These findings suggest that since an athletic population would have greater muscle mass and the maximal muscle cross-sectional area did not differ between transitioned and physically born men, differences in muscle mass between physically born and transitioned men may not be an issue when comparing athletic performance. However, as the above-mentioned study was not conducted in athletes, this hypothesis warrants further investigation.

Testosterone administration to transitioned men also decreased fat content at the triceps, biceps, suprailiac and paraumbilical regions, with no change at the subscapular region (28). Specifically, there was an overall decrease in subcutaneous fat content with testosterone administration (28, 29), despite an increase in body weight (28). The decrease in body fat content was the greatest in the gynoid region resulting in a decrease in the waist-to-hip ratio (28). Additionally, the lower subcutaneous fat content following testosterone treatment was the result of smaller fat cell size (30). However, subcutaneous fat content was still greater in transitioned men as compared with physically born men (28). On the other hand testosterone administration increased visceral fat content within 1 year of treatment (28, 29), which was further increased at 3 years of treatment (29). There was also an increased basal, but not stimulated, lipolytic activity in abdominal, but not gluteal, adipocytes following 1 year of testosterone supplementation (30).

6.2 Estrogen administration to transitioned women

Estrogen and anti-androgen administration to transitioned women decreased haemoglobin content in transitioned women and these levels were comparable to values in physically born women (37). Again these changes were observed in transitioned women within one year of cross-sex hormone administration and no further change in haemoglobin content was found after three years of hormone administration (37). To date no study has investigated the effect of estrogen administration on hematocrit content in transitioned women. Estrogen and anti-androgen supplementation to transitioned women decreased muscle cross-sectional area (28, 37); however, muscle cross-sectional area was still greater than that of transitioned men prior to testosterone administration (i.e. physically born women). Importantly, although the average muscle cross-sectional area was greater in transitioned women, there was a dramatic range in muscle cross-sectional area within both groups (37). Specifically, while at the low end of the

spectrum, physically born women had smaller muscle cross-sectional area; at the high end of the spectrum muscle cross-sectional area was equal between transitioned women and physically born women (37). This finding is of importance as individuals (both transitioned and physically born women) taking part in sport would likely have greater muscle mass than the average population, thus as difference did not exist at the upper end of the muscle cross-sectional area spectrum, differences in muscle cross-sectional area may not exist between transitioned women and physically born women athletes. However, as the aforementioned trial did not compare muscle cross-sectional area in transitioned and physically born women athletes, this premise remains unsubstantiated.

Estrogen and anti-androgen administration also alters body fat content and distribution (28, 30). Specifically, in transitioned women estrogen supplementation increased both subcutaneous (28, 30) and visceral fat (28) content, resulting in an overall increase in percent body fat. Additionally, the increase in subcutaneous fat was most prominent in the gynoid region (66% vs 57% increase); however, the waist-to-hip ratio did not change in transitioned women (28). Additionally, total subcutaneous fat content still appeared to be lower in transitioned women following one year of estrogen treatment as compared with physically born women (28). Looking at individual anatomical locations, estrogen and anti-androgen administration increased percent body fat at the triceps, biceps, subscapula, suprailiac and para-umbilical regions (28). Estrogen and anti-androgen supplementation also increased individual adipocyte size and decreased basal lipolytic activity of gluteal and abdominal fat cells (30). However, similar to the effect of testosterone supplementation to transitioned men, estrogen and anti-androgen supplementation to transitioned women did not alter rates of stimulated lipolysis (30).

Despite women generally being lighter than men (26, 27), total body weight increased in response to estrogen and anti-androgen supplementation in transitioned women, despite a decrease in muscle mass (28). Thus, for sporting events where an athlete would have to carry their own body weight (i.e. running) an increase in body weight following estrogen and anti-androgen treatment may be detrimental to performance. However, again, to date no study has been conducted investigating the effect of estrogen supplementation on body weight in transitioned women athletes. As athletes are very active and proper nutrition plays an important role in athletic performance, it is likely that body weight would decrease in this subset of transitioned women. Additionally, the body weight decrease would likely be due to the effect of estrogen to decrease muscle mass, while body fat stores would not increase as dramatically as that found in non-athletic transitioned women. However, this theory needs to be tested.

To date no study has been conducted investigating the long term effects of estrogen supplementation on carbohydrate or lipid metabolism during endurance exercise. However, as described in detail above (see “metabolic effects of estrogen), E2 supplementation to men can spare liver glucose/glycogen utilization (17, 25), resulting in lower carbohydrate and higher lipid oxidation during a bout of endurance exercise (25). However, these E2 supplementation trials have used dosing periods of 72h to 11 days (18, 25, 71, 89), thus their applicability to metabolism during exercise in transitioned women needs further investigation.

6.3 Based on the evidence presented above, would either transitioned men or women compete at an advantage against physically born men and women?

Based on the evidence above, to date there is really no concrete evidence to support or refute that transitioned men or women would compete at an advantage as compared with physically born men and women. Testosterone administration to transitioned men resulted in haemoglobin levels similar to those in physically born men (37). Additionally, at the upper level, muscle cross-sectional area was not different between physically born and transitioned men (37). In fact, the only sex difference that persisted following one year of testosterone administration was a higher amount of subcutaneous fat in transitioned men, as compared with physically born men (28). Thus, if this factor was an important determinant of performance it may result in a performance detriment when transitioned men competed against physically born men. However, importantly as discussed in the sex difference section above, absolute muscle mass is not necessarily indicative of muscle quality (57), as evidenced by the finding that when absolute muscle mass is controlled for, men still have greater leg muscle strength (57). Estrogen and anti-androgen treatment to transitioned women resulted in haemoglobin levels similar to those found in physically born women (37). Anthropometrically, at the higher end muscle cross-sectional area was equal between transitioned and physically born women (37); whereas subcutaneous fat content remained lower and total body weight higher in transitioned women, as compared with physically born women (28). Importantly, none of the studies that have been conducted to date have specifically looked at performance variables in transitioned versus physically born men and women. The only study written to address the issue of transitioned individuals in competitive sport (37) did so using a retrospective design in a non-athletic population. Additionally, no study has recorded whether height has changed in response to cross-sex hormone administration. Thus, based on the currently available information there is not enough evidence to support or refute a claim that transitioned athletes compete at an unfair advantage or disadvantage as compared with physically born men and women.

6.4 How do the findings to date compare with the IOC Stockholm Consensus?

In 2003 the International Olympic Committee (IOC) Medical Commissioner convened a group of individuals to issue recommendations on sex reassignment in sports (49). The group issued the following recommendations (49):

1) Individuals undergoing sex reassignment of male to female (and vice versa) prior to puberty should be regarded as girls and women (and vice versa) and no restrictions should be made with regards to participation in sport.
2) Individuals undergoing sex reassignment of male to female (and vice versa) after puberty are eligible for participation in sport in their new sex category provided the following conditions are met:
    a. Sex-reassignment surgery has been completed, including external genitalia changes and gonadectomy
    b. The athlete is legally recognized as a member of their new sex
    c. Cross-sex hormone therapy appropriate for the new sex has been administered in a verifiable manner and for a sufficient length of time to minimize sex-related advantages in sport competition.

d. In the opinion of the review board, competition against one's new sex should commence no sooner than 2 years after gonadectomy.

However, the data presented above suggests that fewer than 2 years may be required to minimize the effects of sex hormone exposure prior to transition on sport performance. Testosterone administration to transitioned men increased haemoglobin content and muscle cross-sectional area within one year with no further change after three years (37). Estrogen administration to transitioned women decreased haemoglobin content within one year with no further decrease after three years (37). Additionally, estrogen supplementation decreased muscle cross-sectional area within one year with only a slight further decrease after three years (37). Thus, these preliminary findings suggest that one year of cross-sex hormone supplementation may be sufficient to minimize the effects of prior hormone exposure on performance in transitioned men and women. However, again these results are taken from average transitioned individuals, not transitioned athletes, thus the applicability of these results to an athletic population is yet to be determined.

7.0 Perspectives

7.1 Is there a performance advantage or disadvantage?

To date there are limited data with regards to the effects cross-sex hormone administration have on factors that influence performance. No study has been conducted in transitioned athletes and no study has performed any objective performance testing (i.e. VO_{2peak}, time trial performance or strength). We do know the effects of testosterone and estrogen administration on body composition and muscle mass; however, these factors themselves do not necessarily dictate performance. Until specific research is conducted comparing performance measures in transitioned and physically born men and women no conclusive statement can be made with regards to competitive advantage/disadvantage. One factor that does stand out with regards to fair play in sporting competition is the finding that depending on the type of testosterone that is used by transitioned men, supraphysiological concentrations of testosterone persist for 5-9 days following injection. As dosing periods using traditional injection regimes are every 14 days, transitioned men spend the majority of their time with an elevated testosterone level (8). As testosterone is a known anabolic agent increasing muscle mass and improving strength (6, 31, 75, 85), care must be taken to ensure that testosterone levels in transitioned men match those of physically born men. One recommendation that can be made is the use of testosterone undecanoate in transitioned men wanting to compete in sporting events, as this dosing regime produces long-term stable testosterone levels (52). However, again, further research is likely needed before this recommendation can be conclusive.

8.0 Conclusions

Overall there is a paucity of data regarding the effect of transitioning on athletic performance. What performance data does exist was not taken from transitioned athletes; thus its applicability within an athletic population is uncertain. To date no study has conducted any sort of exercise test to assess athletic performance. The only study to have addressed transitioned athletes in competitive sport used a retrospective study design and considered muscle mass and

haemoglobin content to be predictors of athletic prowess. Undoubtedly these factors do influence performance; however, in athletics the whole is greater than its parts and as such, performance during athletic events needs to be assessed. While to date the data available does not appear to suggest that transitioned athletes would compete at an advantage or disadvantage as compared with physically born men and women, there is not enough data available to fully substantiate this claim. Much more research needs to be conducted before a consensus can be made. However, due to the low prevalence of transitioned individuals in the population, conducting these studies will be challenging. Due to these complications we may never truly know whether transitioned athletes compete at an advantage or disadvantage as compared with physically born men and women.

9.0 References

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