The current knowledge on the effects of gender-affirming treatment on markers of performance in transgender female cyclists.

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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.

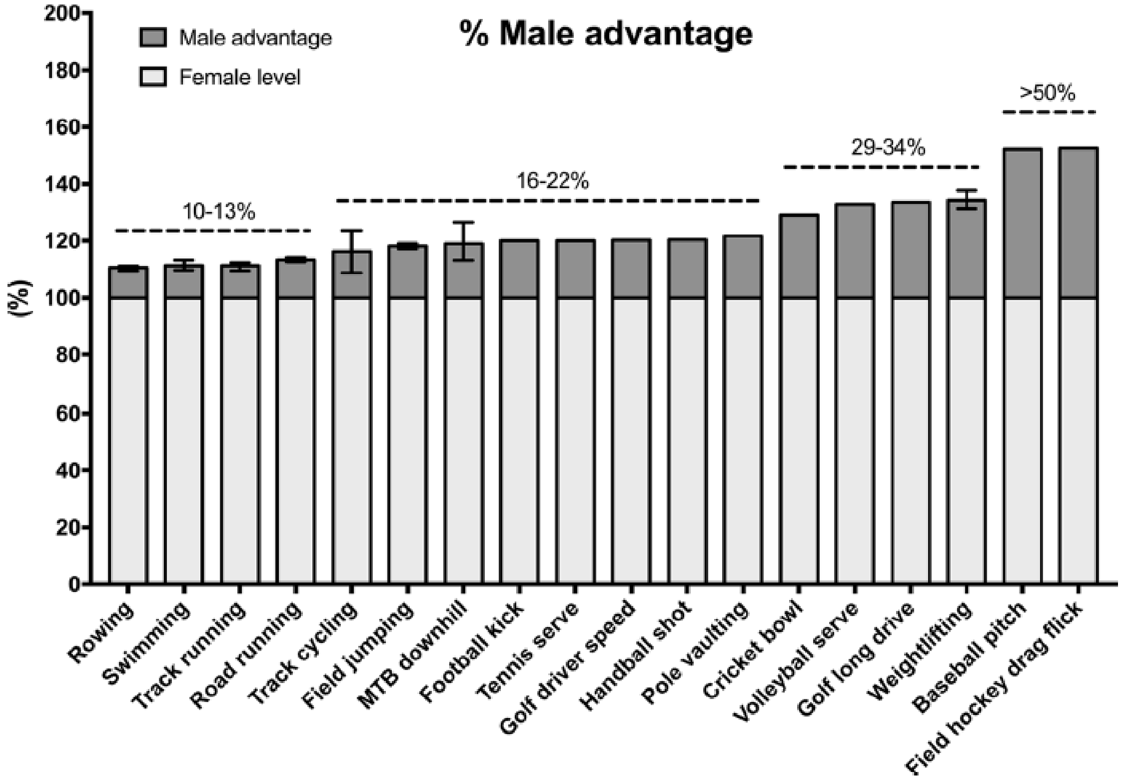


Figure 1. Male performance advantage over females across various sporting events. The female level is set to 100%. The metrics were compiled from publicly available databases (from Hilton and Lundberg, 2021).

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 ~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).

$\dot{V}O2max$ 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 $\dot{V}O_2max$ continue to be examined. The argument has been presented that $\dot{V}O_2max$ 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 $\dot{V}O_2max$, 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 $\dot{V}O_2max$ (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 (Wmax) obtained during a maximal incremental cycling test can be used as predictor of cycling performance in endurance disciplines. Changes in Wmax contribute to explain 82% of the variability in performance during a 20 km cycling time trial. This is why Wmax 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 Wmax 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 Wmax values (457 ± 46 W) than UH (Figure 2).

When expressed relative to body mass, UH presented the highest Wmax values (6.47 ± 0.33 $W \cdot kg^{-1}$), followed by TT, AT, and FT (6.41 ± 0.12, 6.35 ± 0.18 and 6.04 ± 0.29 $W \cdot kg^{-1}$, respectively). These values were significantly different between UH and FT (Figure 2). A Wmax/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 Wmax/body weight ratio values varying between mean values of 6.34 $W \cdot kg^{-1}$ (with a lowest value of 5.58 $W \cdot kg^{-1}$) (Padilla et al., 1999) and 6.79 $W \cdot kg^{-1}$ (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 Wmax 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 Wmax values, (1 kg lower body lean mass = ∼4% increase in mean Wmax during the 10-min test).

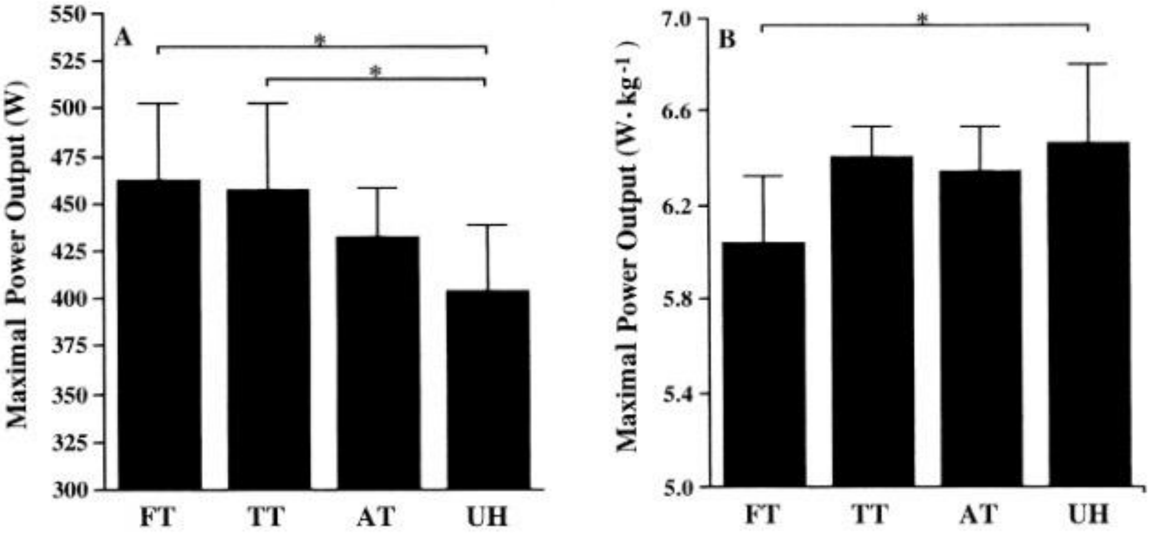


Figure 2. Maximal power output (Wmax) values 1 (Mean +/- SD) for flat terrain (FT, N = 5), time trial (TT, N = 4), all terrain (AT, N = 6), and uphill (UH, N = 9) specialists. A: absolute values; B: relative to body mass. * denotes a significant difference ($P < 0.05$) between groups. (from Padilla et 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 ~9% higher Wmax 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 Wmax 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).

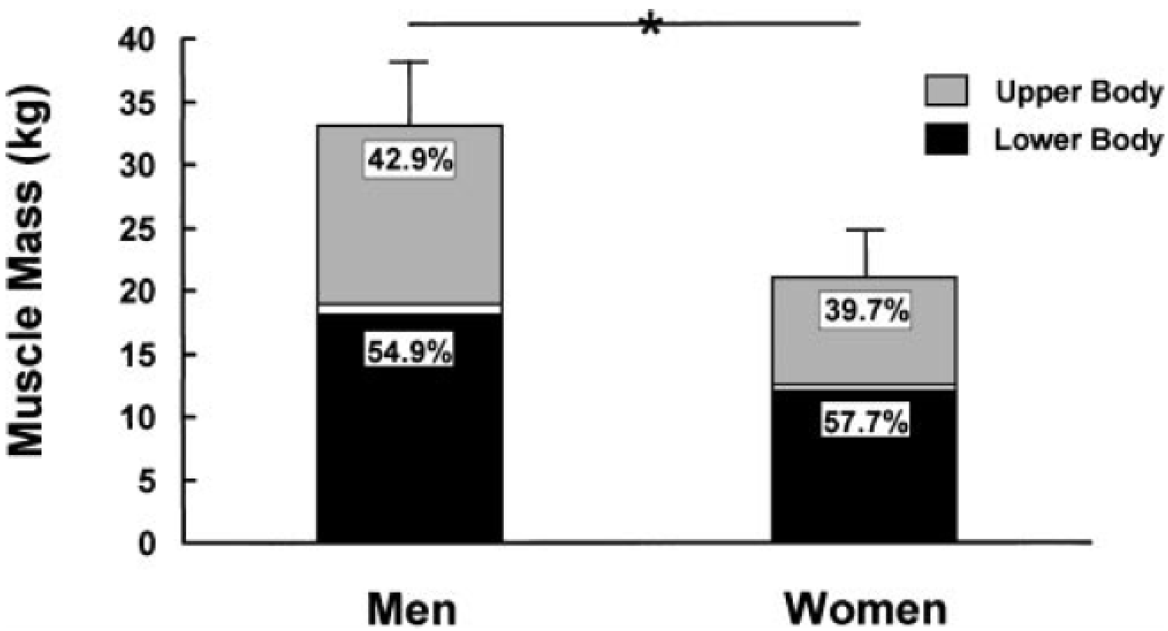


Figure 3. Skeletal muscle mass and distribution in CisMen and CisWomen.
Values are means ± SE. (from Janssen et al., 2000).

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 isomeric and isokinetic strength as well as muscle volume remained about 50% higher in TransWomen than in CisWomen ($P<0.05$).

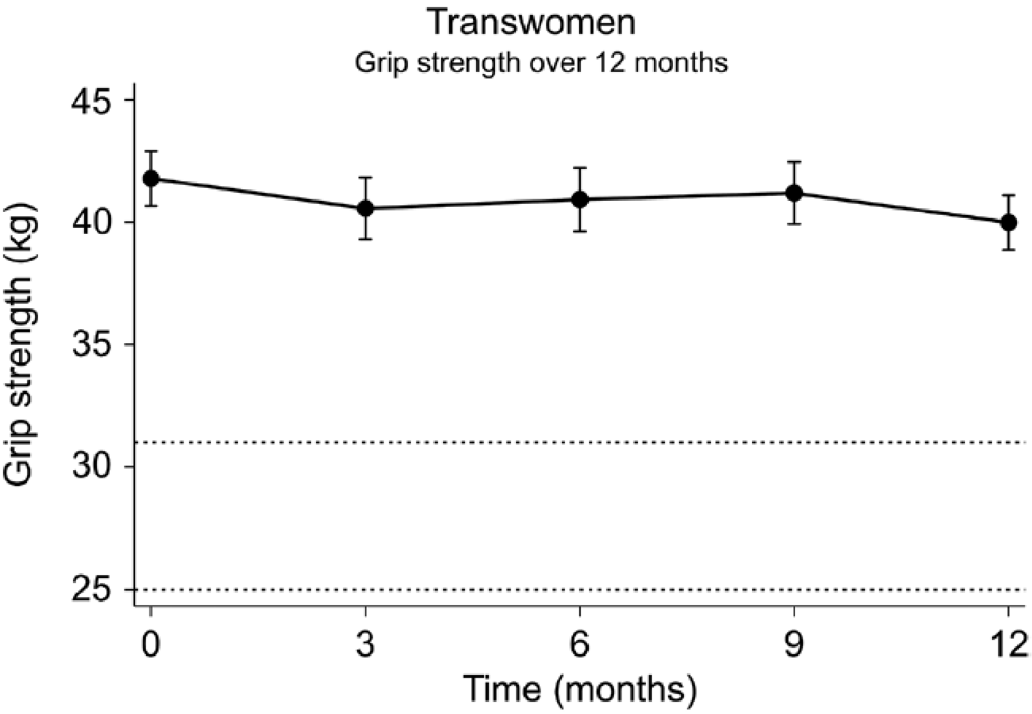


Figure 4. Change in grip strength during the first 12 months of gender-affirming hormonal treatment in TransWomen. Data are presented as means with 95% CI. The 25th and 75th percentiles of the reference populations are shown with dashed lines (25 kg and 31 kg, respectively) (From Scharff et al., 2019).

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 $\dot{V}O_2$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 erythrogenic 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.

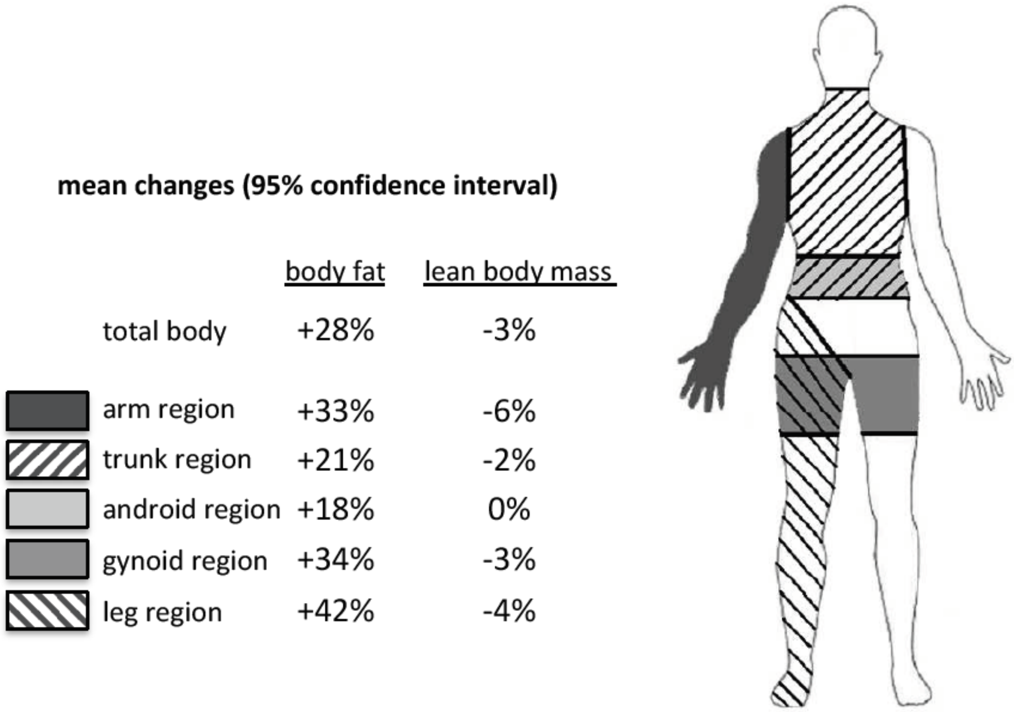
Nine studies were included in a recent systematic review, reporting the levels of Hgb or Hct in TransWomen before and after several forms of transition treatments, from a minimum of 3 to a maximum of 36 months post cross-sex hormonal treatment (Harper et al., 2021). In 8 of these studies, it was found 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.



mean changes (95% confidence interval)

		body fat	lean body mass
	total body	+28%	-3%
■	arm region	+33%	-6%
▨	trunk region	+21%	-2%
□	android region	+18%	0%
▒	gynoid region	+34%	-3%
▧	leg region	+42%	-4%

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. deceased 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).

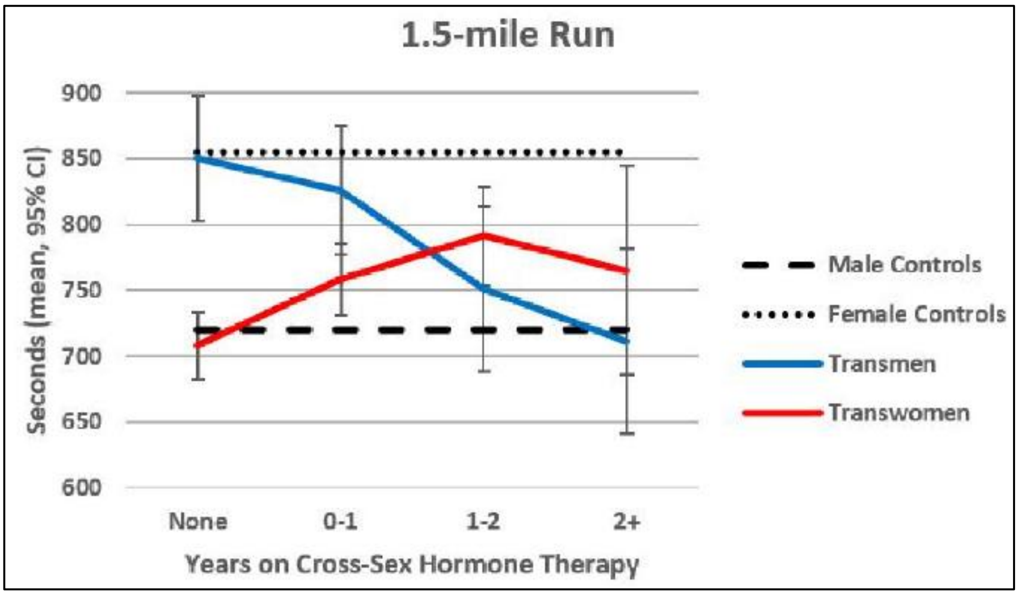


Figure 6. The effects of gender affirming treatment on the number of sit-ups performed in 1 min. Female controls = CisWomen. (From Roberts et al., 2020)

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).

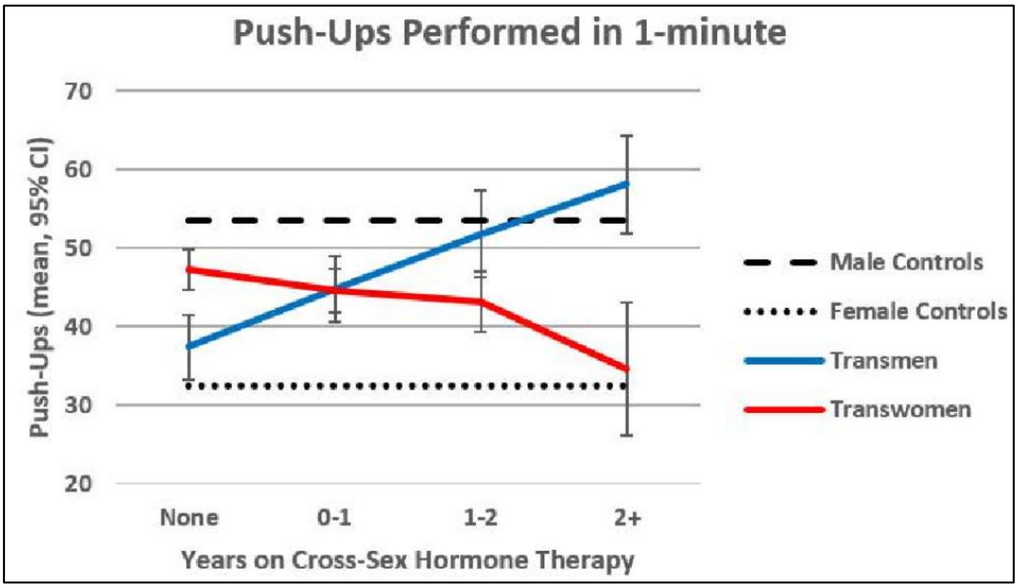


Figure 7. The effects of gender affirming treatment on the number of pus-ups performed in 1 min. Female controls = CisWomen. (From Roberts et al., 2020)

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.

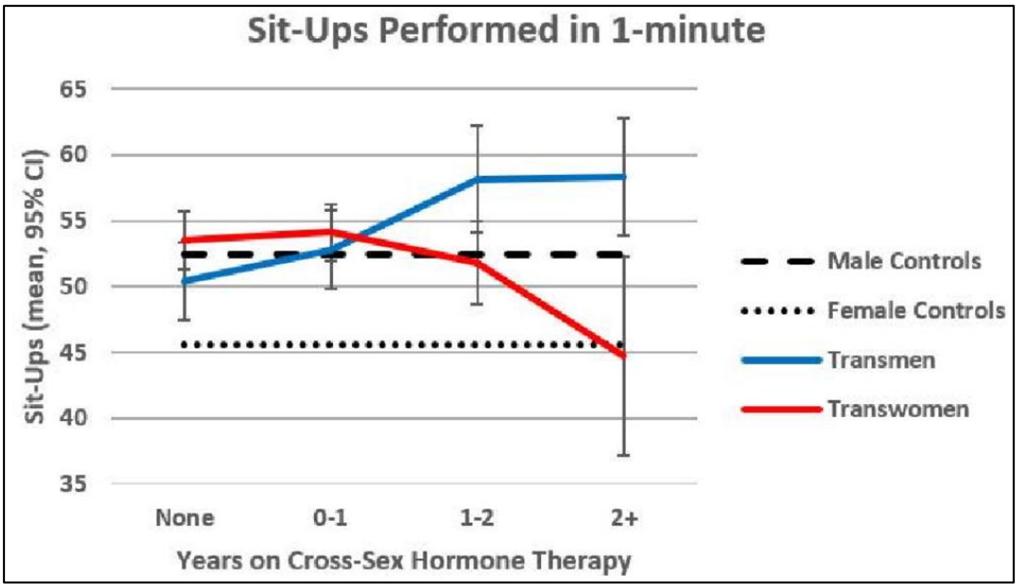


Figure 8. The effects of gender affirming treatment on the number of sit-ups performed in 1 min. Female controls = CisWomen. (From Roberts et al., 2020)

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**.

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