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 properly 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 sex steroids (testosterone or estradiol), or surgical sex reassignment. The objective of "gender affirming hormone treatments" (GAHT) is to induce secondary sex characteristics to align the body with the gender identity. In TransWomen, GAHT comprise mainly estradiol therapy typically associated with testosterone blockers such as GnRH agonists, spironolactone or cyproterone acetate.

Some Transgender athletes would like to participate in competitive sport, and the division of athletes into male and female categories requires determining the conditions under which these athletes can compete in their new gender category. The current debate over including Transgender athletes in sports competitions is centered on biological and physiological 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. Sex differences in athletic performance

The performance disparities between male and female athletes vary across sports (Figure 1). These differences in athletic performance appear after puberty and are thought to be most likely due to increased circulating testosterone levels in "male" athletes whose sex was assigned at birth compared to "female" athletes. After puberty, males are faster, jump higher, are more powerful than females, and have greater endurance and anthropometric advantages.

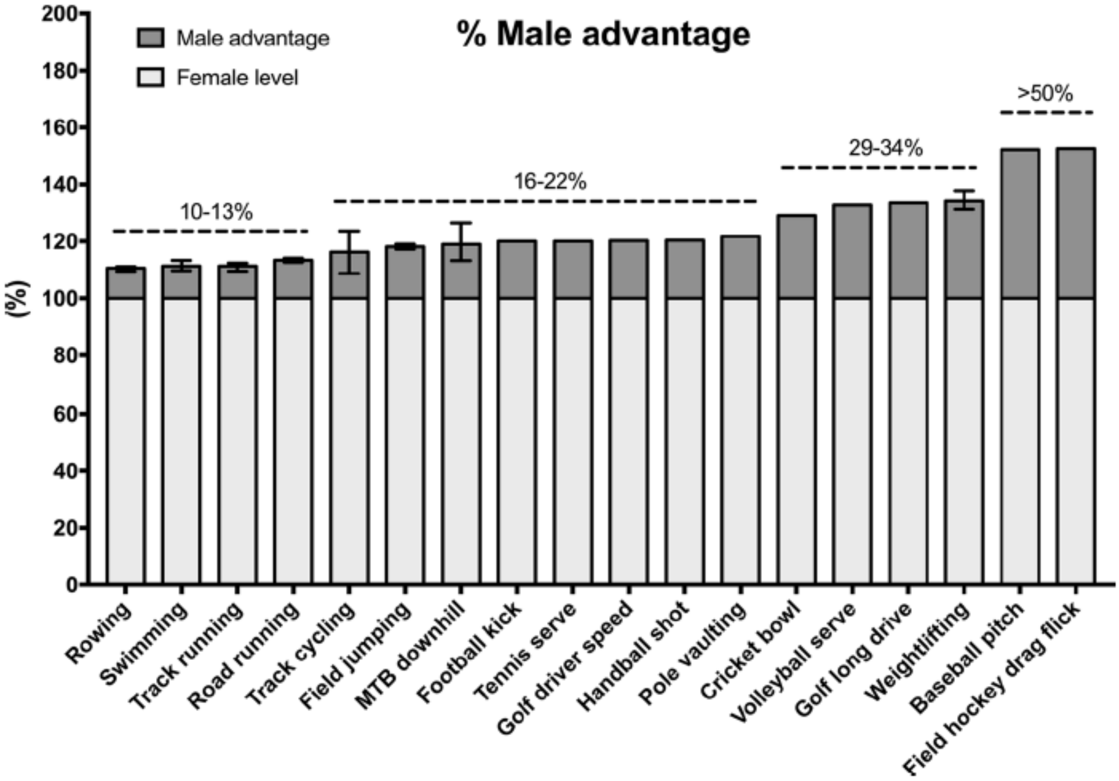

Figure 1. Male performance advantage over females across various sporting events. The female level is set to 100%. The metrics were compiled from publicly available databases (from Hilton and Lundberg, 2021).

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 few cycling disciplines can be compared over time in terms of performance. In track sprint, the gender gap has been stable since 1993 and estimated at approximately 8.7% (Thibault et al., 2010). 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).

Comparing the world records, world bests or performance during the UCI World Championships in different cycling disciplines is a good way to estimate the performance disparity between male and female riders (Table 1). Whether the performances are compared in sprint or endurance disciplines, the sex-based difference is estimated on average to 10 to 13%.

	Men	Women	Gap (%)
Track			
Flying 250 m Sprint (sec)	9.686	10.804	11.5%
Flying 200 m Time Trial (sec)	9.1	10.154	11.5%
Flying 500 m Time Trial (sec)	24.758	28.970	17%
250 m Time Trial, standing start (sec)	16.949	18.247	7.7%
1000 m Time Trial (min:sec)	0:57.813	1:06.144	14.4%
Flying last 2000 m Individual Pursuit (min:sec)	2:02.992	2:11.457	6.8%
4000 m Team Pursuit (min:sec)	3:42.032	4:04.242	10%
Hour record (km)	56.792	49.254	-13%
Road			
Time Trial (min:sec)	40:02.78	44:28.60	11%

Table 1. Sex differences in World records, World bests and best performances during the last UCI World Championships in Track and Road cycling.

By analogy, we can look at sex differences in performances during the cycling part of 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 a slight 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 10-13% in track cycling and 11-13% 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.

II. Key factors at the origin of sporting performance advantages in males

We have now a lot of scientific evidence to consider that the sex differences in athletic performance after puberty are mainly 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).

The onset of male puberty is associated with a sex-related divergence in sport performance, due to the testosterone-induced changes in muscle mass, strength/power, anthropometric variables and hemoglobin levels in males (Handelsman, 2017). The sex-based differences in sports performance between males and females are mainly explained by the biological effects of elevated 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 positively affected by testosterone (except in shooting, archery, etc.).

Despite only very few experimental data, the general consensus is that differences in testosterone levels is currently the most important factor contributing to the performance differences between male and female athletes (Handelsman, 2018). This view is supported by the results of 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.

> The sex differences in athletic performances emerge from puberty. The men's physical advantages in muscle mass, strength/power, speed and endurance are largely explained by the circulating testosterone concentrations that are on average 15-20 times higher than in women.

III. Determining 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, which promote fair competition for all athletes irrespective of their gender identity.

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 (Table 2).

1- Maximal oxygen uptake.

There is substantial evidence demonstrating that successful professional road cyclists possess very high values of the absolute or normalized maximal oxygen uptake ($\dot{V}O_2max$) (~74 mL/kg/min) and a lactate threshold (LT2) (~90% of $\dot{V}O_2max$) (Faria et al., 2005).

Absolute $\dot{V}O_2max$ values 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 is significantly lower in FT (74.4 ± 3.0 $mL \cdot kg^{-1} \cdot min^{-1}$) than in TT, all-terrain (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).

	aerobic	muscle power	biomechanics
Road			
rouleur/punch	+++	++	+
sprint	+	+++	++
mountain	+++	+++	+
time trial	+++	++	++
BMX racing	+	+++	+
MTB			
XCO	+++	++	++
downhill	+	++	+
Track			
sprint	+	+++	++
pursuit	+++	++	++

Table 2. Physiological determinants of performance in several cycling disciplines

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$\dot{V}O2max$ is not only a limiting factor for road cycling, but also for all other endurance disciplines, including 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. Blood lactate concentration at various cycling intensities is also highly predictive of endurance, especially the maximal lactate steady state (MLSS), the highest exercise intensity at which blood lactate concentration remains stable (Faria et al., 2005). It has been shown that the LT2-$\dot{V}O_2$ relationship 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- 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.

3- 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 the Onset of Blood Lactate Accumulation (OBLA) 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).

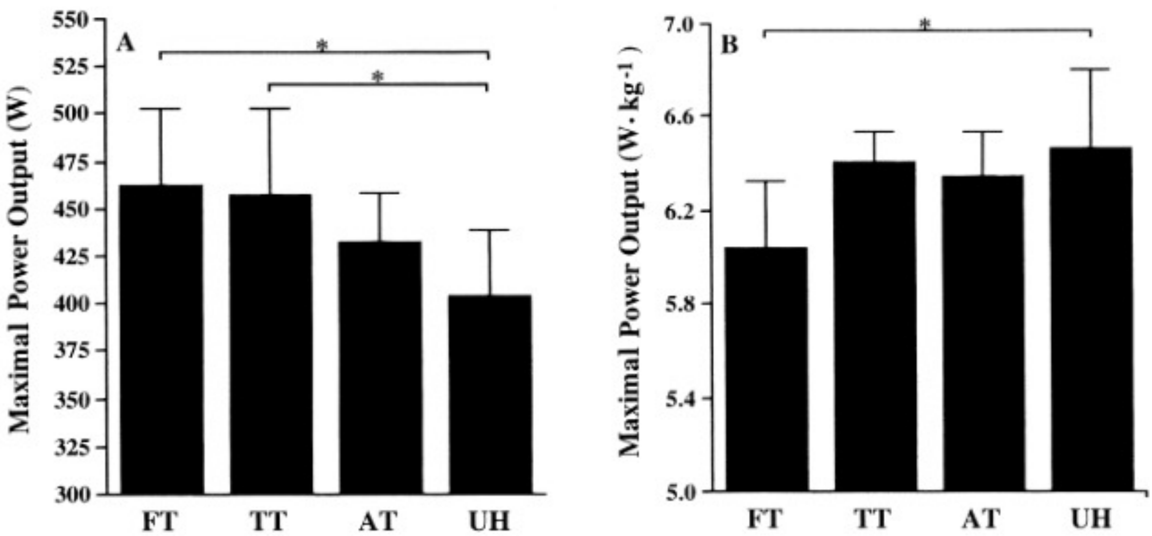

Figure 2. Maximal power output (Wmax) values 1 (Mean +/- SD) for flat terrain (FT, N = 5), time trial (TT, N = 4), all terrain (AT, N = 6), and uphill (UH, N = 9) specialists. A: absolute values; B: relative to body mass. * denotes a significant difference ($P < 0.05$) between groups. (from Padilla et al., 1999).

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).

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.

5. Implications of shape and alignment of bones in lower limbs.

It has been shown that the shape and alignment of long bones in lower limbs are mainly dictated by the level of circulating testosterone during puberty (Sutherland et al., 2012). Several sexually dimorphic features exist of both upper and fore limbs, but likely the most important dimorphism for performance in cycling concerns the Q-angle at the knee. The Q-angle is the angle between the direction of pull for the quadriceps and the patellar tendon, which extends down past the patella to attach to the front of the tibia (Figure 3). This arrangement allows the quadriceps to use the patella as a pulley to straighten the leg, as happens when one pushes down on the pedal of a bike. Knee extension against resistance is a motion used in all cycling disciplines. The greater Q-angle observed in female athletes is at the origin of a greater lateral force on the patella, and less force for the extension of the leg. For the strength produced by the quadriceps, male athletes can extend their legs with greater force than female athletes (Figure 4).

Because this difference results from strict osteological factors not related to muscle mass, an athlete whose bones achieved their mature shape during a period of high circulating testosterone would retain an advantage that could contribute to physical performance in cycling.

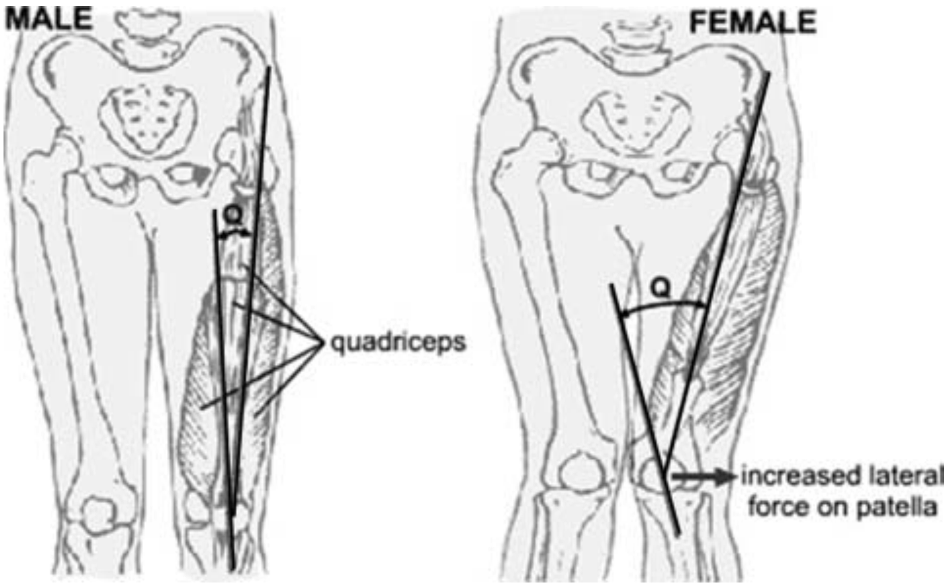

Figure 3. The Q-angle defined as the angle between the direction of pull of the quadriceps muscle and the direction of the patellar tendon. (from Sutherland et al., 2012).

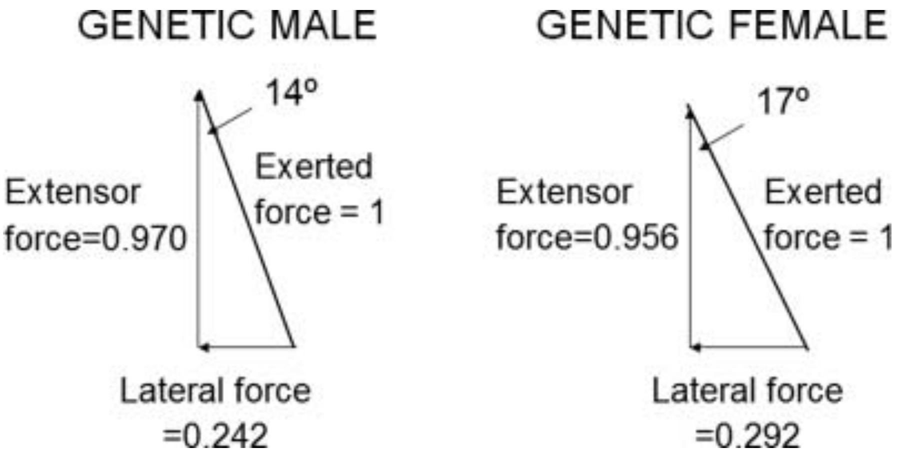

Figure 4. With a larger Q-angle (right part of the figure), a greater lateral force is generated on the patella, and a lower force is generated for the extension of the leg. (from Woodland and Francis, 1992).

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.) (Table 2). Moreover, biomechanical factors such as the shape and arrangement of long bones in forelimbs could account for cycling performances.

IV. Is the male performance advantage lost when blood testosterone concentrations are significantly reduced by GAHT in TransWomen?

Whether TransWomen should be allowed to compete in the female category and if so, under what conditions, is currently extremely controversial. In addition to their well-known anabolic consequences on lean body mass, androgens also stimulate erythropoiesis mental drive, aggressiveness and affect the shape and alignment of long bones in the limb. 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 at the best 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 differences between TransWomen who have received transition treatment (i.e. GAHT and eventually surgical sex reassignment) and CisWomen are less clear, mainly due to a lack of available experimental data in athletes. Unfortunately, there are no prospective studies investigating the changes in athletic performance in transgender athletes with GAHT after puberty. Studies in non-athletic TransWomen report changes in lean body mass, muscle cross-sectional area, muscular strength, haemoglobin and/or haematocrit, during the GAHT treatment, all of which are of relevance for cycling performance.

The important question is the precise impact of GAHT on performance, in term of timing of changes of performance characteristics, and blood testosterone target values.

1- Muscle mass

Muscle mass and muscle strength/power are key parameters underpinning male performance advantages. Unfortunately, studies on the effects of GAHT 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).

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.

The loss of skeletal muscle mass in prostate cancer patients with androgen deprivation therapy could be an interesting clinical situation to consider in order to examine the impact of low blood testosterone levels on skeletal muscle properties. It has been shown that while a significant decline in muscle mass occurs following androgen deprivation therapy, the treatment-induced adverse effects are fully prevented by resistance exercise training (Overkamp et al., 2023; Nilsen et al., 2015).

Therefore, it follows that in TransWomen athletes, it can be hypothesized that a resistance-training program during the GAHT would mitigate muscle mass loss, as it is reported in prostate cancer patients.

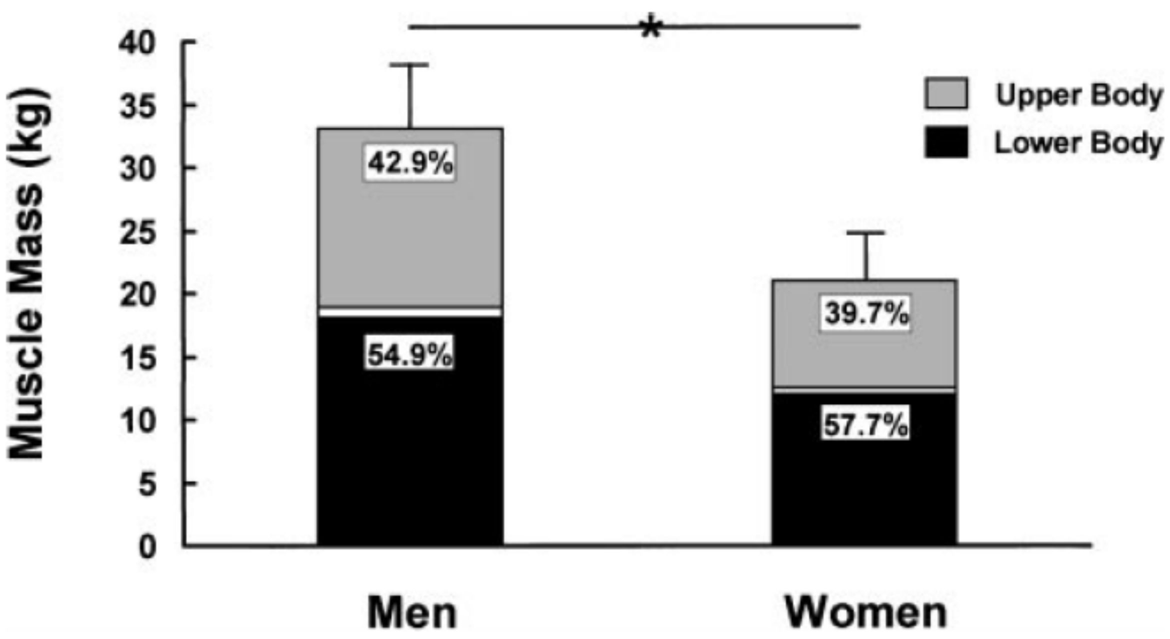

Figure 5. Skeletal muscle mass and distribution in CisMen and CisWomen. Values are means ± SE. (from Janssen et al., 2000).

In conclusion, there are large baseline differences in muscle mass between males and females (Figure 5), 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.

Results of studies in patients with androgen deprivation therapy suggest that the effects of GAHT on muscle mass may be strongly dependent on muscle activity. However, whether resistance training during GAHT could mitigate muscle mass loss in TransWomen athletes remains to be determined.

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 6). 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 ($P<0.05$).

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 (50^{th} 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.

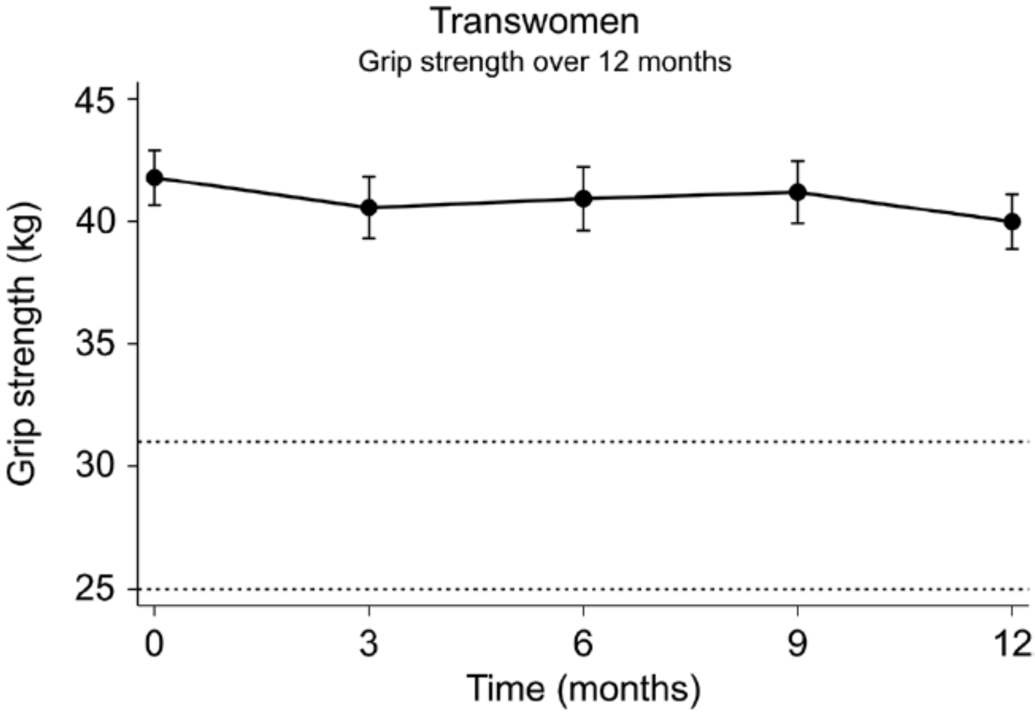

Figure 6. Change in grip strength during the first 12 months of gender-affirming hormonal treatment in TransWomen. Data are presented as means with 95% CI. The 25th and 75th percentiles of the reference populations are shown with dashed lines (25 kg and 31 kg, respectively) (From Scharff et al., 2019).

The effects of GAHT on muscle power were examined among 46 TransWomen military personnel (US Air Force), before and after they started their transition treatment (Roberts et al., 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 are trained regularly, and their continued service in the Air Force requires a certain level of physical fitness and performance. The results of this study are important, in particular because the effects of GAHT on physical performance are examined in regularly trained TransWomen, even if the level of physical training is different from that of athletes.

The assessment of physical performance was performed every 12 months, and included push-up and sit-up exercises, relevant for muscle power. The number of push-ups and sit-ups in 1 min is representative of muscular endurance and strength/power rather than just strength/power. These measures are relevant for sports that require sustained effort over time, such as cycling.

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). Given the high variability in the number of push ups in 1 min measured after 2 years of GAHT, and although the mean of push ups performed is not statistically different from the mean values measured in CisWomen, it is estimated that only 32% of TransWomen have performance values lower than those measured in CisWomen. ***Therefore, approximately 68% of TransWomen performed more push-ups in 1 min than the average measured on a population of CisWomen.***

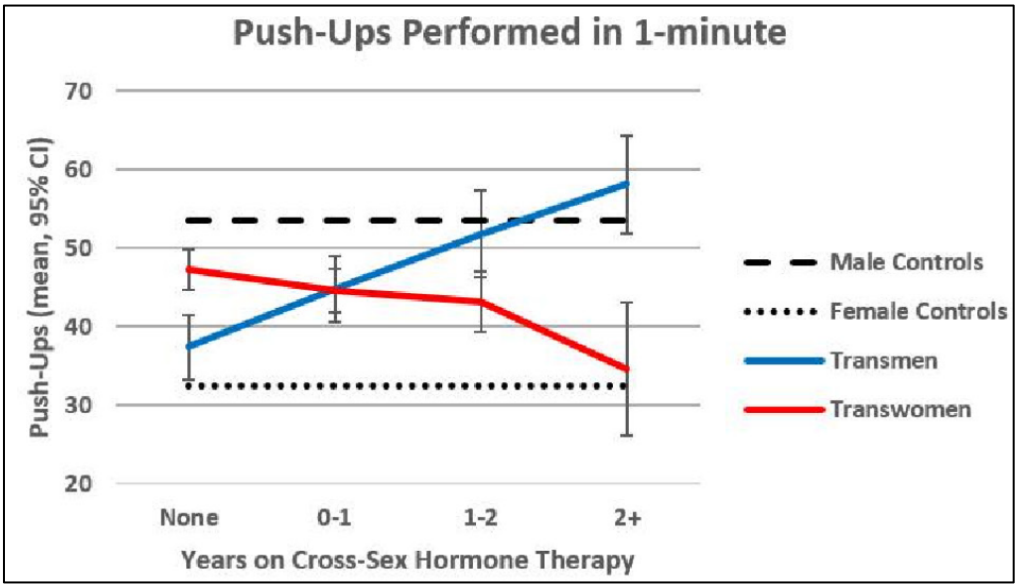

Figure 7. The effects of gender affirming treatment on the number of pus-ups performed in 1 min. Female controls = CisWomen. (From Roberts et al., 2020)

Prior to the transition treatment, there was no difference in sit-ups between TransWomen and CisMen (Figure 8). After 2 years of GAHT, the mean number of sit-ups in 1 min was not statistically different between TransWomen and CisWomen. These results confirm the decrease in strength/power with GAHT in TransWomen. However, given the variability of measures, it is estimated that after 2-2.5 years of GAHT, ***41% of TransWomen performed more sit-ups in 1 min than the mean measured on a population of CisWomen.***

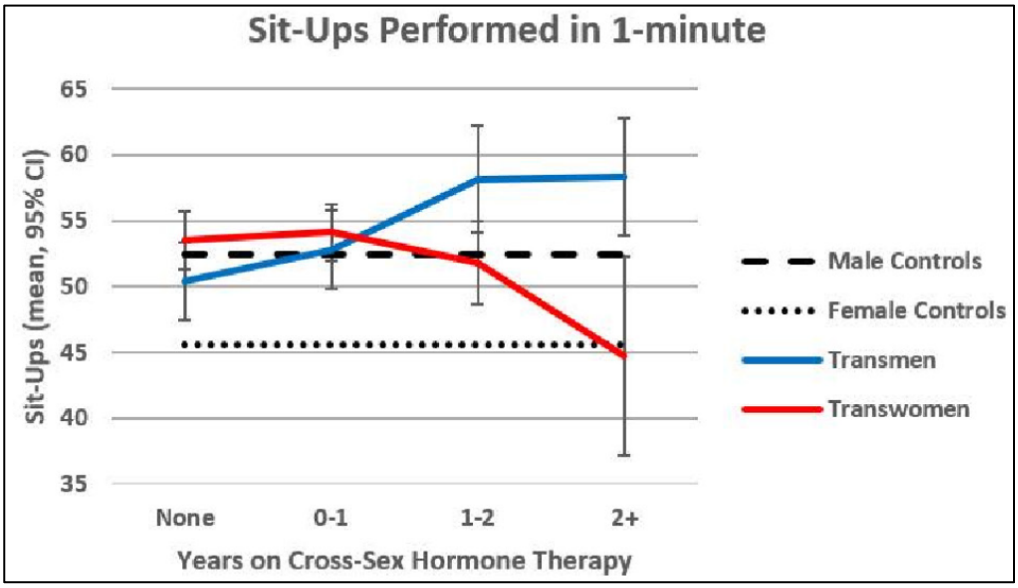

Figure 8. The effects of gender affirming treatment on the number of sit-ups performed in 1 min. Female controls = CisWomen. (From Roberts et al., 2020)

As reported in paragraph#IV.1, androgen deprivation therapy in prostate cancer patients is accompanied by reduced muscle mass and strength power. Several studies indicated that resistance training has beneficial effects on muscle strength in patients with prostate cancer receiving androgen deprivation therapy and successfully improves both the strength and power-generating capacity of knee extensor muscles (Galvao et al., 2006; Nilsen et al., 2016).

This situation of patients treated with androgen deprivation therapy may represent a good model of the effects of GAHT on muscle performance. Results from studies in these patients suggest that in transgender athletes, a resistance-training program during GAHT would mitigate the treatment-related decline in muscle strength/power, as it does in prostate cancer patients.

Only a slight decrease in muscle strength/power is reported in non-athletes TransWomen after 1 year (-4.75% of grip strength) or even after 8 years of GAHT (mean grip strength values 47% higher in TransWomen than the female reference values).

In regularly trained non-athletes TransWomen, the mean values of muscle strength/power markers are not significantly different from the mean values of a reference population of CisWomen after 2 years of GAHT. Despite this lack of statistical difference between TransWomen and CisWomen, it seems that 68% and 41% of TransWomen performed more push-ups and sit-ups in 1 min than CisWomen, respectively.

Although no studies have been performed in elite TransWomen athletes, future studies should evaluate the effects of resistance training during GAHT on the treatment-related decline in muscle strength/power.

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 $\dot{V}O_2max$ 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 GAHT 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.

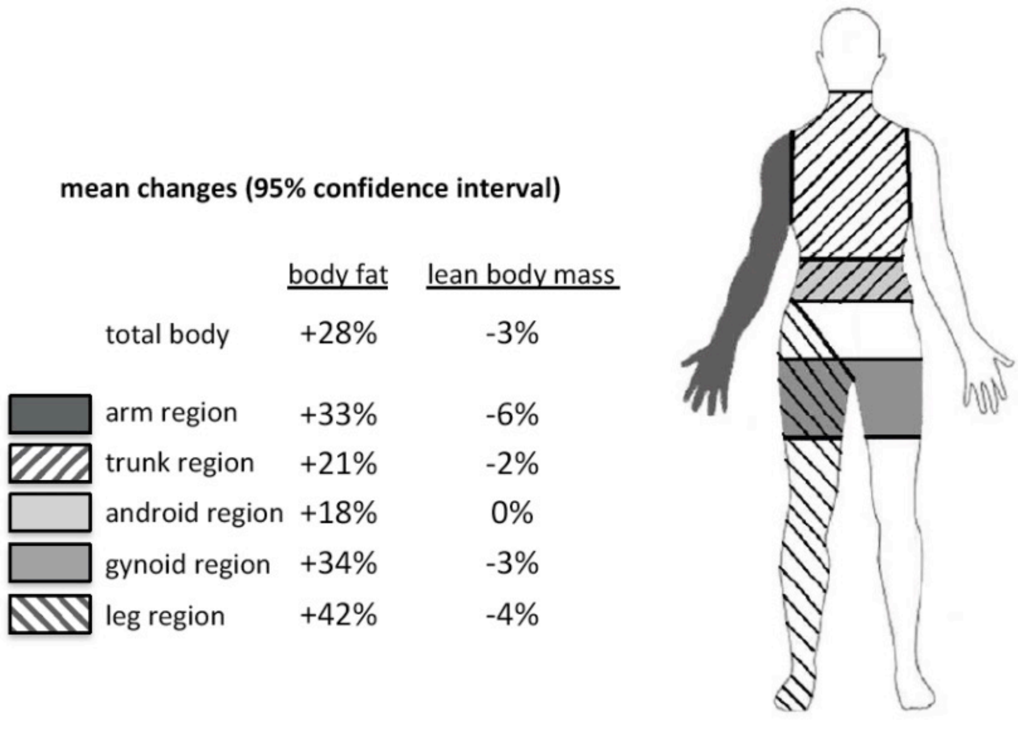

Figure 9. Percent changes in total and regional body fat and lean body mass in 179 non-athletes TransWomen (From Klaver et al., 2018).

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 9). 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 9). 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 9). 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.

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.

Impact on V̇O2max. In non-trained and non-athletes TransWomen, although the absolute values of V̇O2max remain higher than the values measured in CisWomen after more than 14 years of GAHT (mean 14.4 +/- 3.5 years), it is essential to note that the relative values of $\dot{V}O_2max$, expressed to body weight, are not significantly different from the values reported in CisWomen (Alvares et al., 2022). But as indicated by the Authors, 'their findings may not be applicable to populations that engage in regular intensive exercise' (i.e. especially in athletes).

In conclusion, the effects of testosterone suppression with GAHT on endurance performance markers need to be further examined in the future, especially in Cycling. However, given the rapid drop in the Hgb/Hct ratio compared with CisWomen baseline values, it is possible that GAHT adversely affects endurance performance in TransWomen, most likely negatively impacting endurance performance. Furthermore, although the majority of currently available 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 determining factors of performance.

However, the responses of $\dot{V}O_2max$, left ventricular size, stroke volume, cardiac output, lactate threshold, and exercise economy to GAHT in TransWomen athletes should be clarified in further studies.

4. Implications of shape and alignment of bones in lower limbs.

The alignment of long bones in lower limbs is one determinant the Q-angle values on the knee. The lower Q-angle values observed in male and TransWomen athletes is at the origin of a lower lateral force on the patella, and higher force for the extension of the leg in comparison with CisWomen athletes (Figure 4). Lower Q-angle values in men accounted for a 1.4% gain in quadriceps strength during leg extension, in comparison with women of similar stature and muscle mass.

The origin of this sex-related advantage is strictly related to osteological factors, and not to skeletal muscle mass or strength/power. It therefore seems highly unlikely that long-term GAHT would be able to reverse this advantage of osteological origin. The advantage related to the bone alignment in lower limbs on the force developed by the quadriceps during the leg extension, for the same muscle mass between TransWomen and CisWomen may be considered as small. However, given the repetition of contractions during a cycling event, it could have significant effects on performance.

> The small sex-difference in the extensor force generated by the quadriceps to extend the knee is a product of the masculine osteology. Such osteological advantage cannot be reversed by GAHT.

IV. Sport performance changes in TransWomen

In parallel with the changes in physiological capacities with GAHT, it is also important to evaluate the effects of these treatments on sports or exercise performances. Only 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.

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 of female distance runners 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 GAHT on 1.5 running performance were examined among 46 TransWomen military personnel, before and after they started their GAHT (Roberts 2020). Running times among TransWomen were similar to times among CisMen and faster than running performance among CisWomen prior to GAHT. Running times worsened among TransWomen after starting oestrogen administration and testosterone blockade, and became slower than performances in CisMen, but remained faster than CisWomen at all time points (Figure 10).

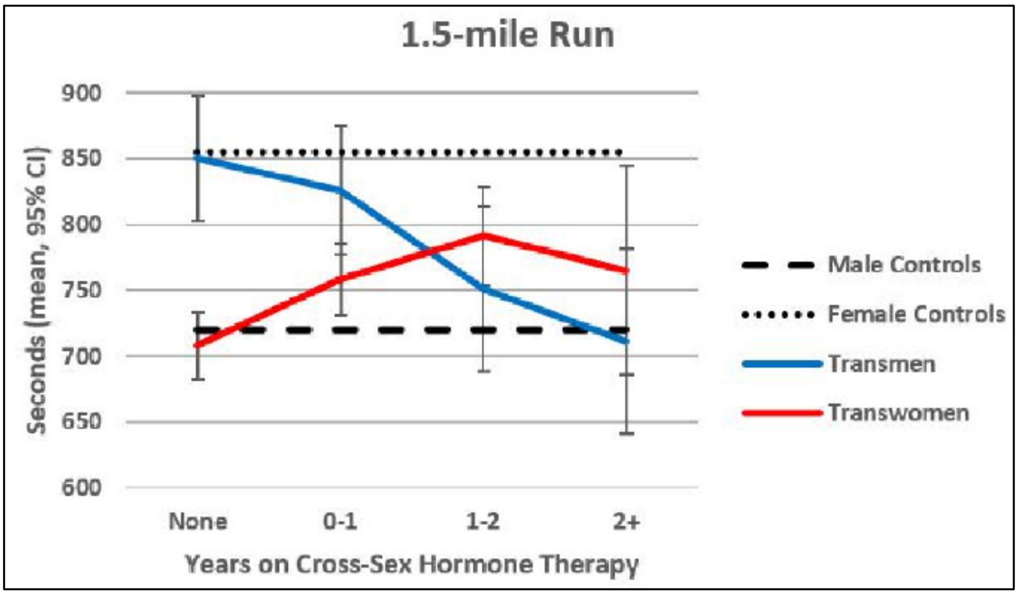

Figure 10. The effects of gender affirming treatment on the number of sit-ups performed in 1 min. Female controls = CisWomen. (From Roberts et al., 2020)

If these available data give interesting information on the changes reported in physical performance with GAHT, ***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.

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 athletes to compete with Cis-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 person. Similarly, it is clear that Cis athletes are not equal in terms of athletic abilities, including height, weight, coordination and many other parameters, including hormonal and metabolic factors. ***But it is critical that all competing athletes have a chance to succeed, even if that chance is not necessarily equal.***

Gender affirming hormonal treatments 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) (Table 3). The few existing experimental data confirm that GAHT 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. In the only study in which the effects of GAHT on physical performance are examined in regularly trained transgender women, even though the level of physical training is different from that of athletes, it is estimated that 68% of TransWomen performed more push ups in min and 41% more sit ups than CisWomen after more than 2 years of treatment.

aerobic	muscle power	biomechanics
↘	= or ↘	=
after 6-8 months	after > 2 years	

Table 3. Changes in the physiological determinants of cycling performances with GAHT.

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 bone alignment in the lower limbs. This osteological difference allows CisMen and TransWomen athletes to extend the leg with greater strength, which should have important implications for sports performance. Such anatomical differences give TransWomen an athletic advantage after puberty for certain sports, and cannot be reversed by GAHT in post-pubertal adults (Table 3). 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.

An important issue is that the current studies examined the changes in lean body mass, muscular strength, aerobic parameters and Hgb/Hct in non-athletic TransWomen following long-term GAHT. However, it is essential to keep in mind that there are no data on changes in cycling performance with GAHT, especially in well-trained subjects or top athletes. Therefore, the effects of GAHT on athletic performance in TransWomen athletes who engage in physical training during the gender affirming treatment remain unknown. While the existing studies examine the GAHT effects 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 essential to examine the changes in muscle mass and strength/power over time in TransWomen athletes, examine whether strength/power performance will reach the baseline values reported in Cisgender women, and test the impact on cycling performance.

VI. Final conclusion

Given the current body of knowledge,

1- only very few data exist on the changes in sport performance in TransWomen with GAHT, but none in cycling.

2- the scientific literature reports changes in the physiological determinants of performance with GAHT (i.e. lean body mass, muscle cross-sectional area, muscular strength/power, haemoglobin and/or haematocrit), but the vast majority in untrained TransWomen.

3- the sex differences in these determinants of performance in cycling, are either likely reversed after 6-8 months of GAHT (i.e. aerobic capacities), only slightly reversed after 2 years of hormonal treatment (i.e. muscle mass, strength/power), or unaffected by GAHT (bone leg shape and alignment).

Based on current knowledge, it is therefore **impossible to confirm**,

- that at least 2 years of GAHT with a target plasma testosterone concentration of 2.5 nM are sufficient to completely eliminate the advantages associated with the increase in testosterone during puberty in males,
- or that despite the hormonal transition treatment, an advantage persists on cycling performance after 2 years of GAHT.

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