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## Bone health in transgender people

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2020

### **document version**

Publisher's PDF, also known as Version of record

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### **citation for published version (APA)**

Wiepjes, C. M. (2020). *Bone health in transgender people: Short-term and long-term effects of hormonal treatment on bone mineral density, metabolism, geometry, and fractures*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

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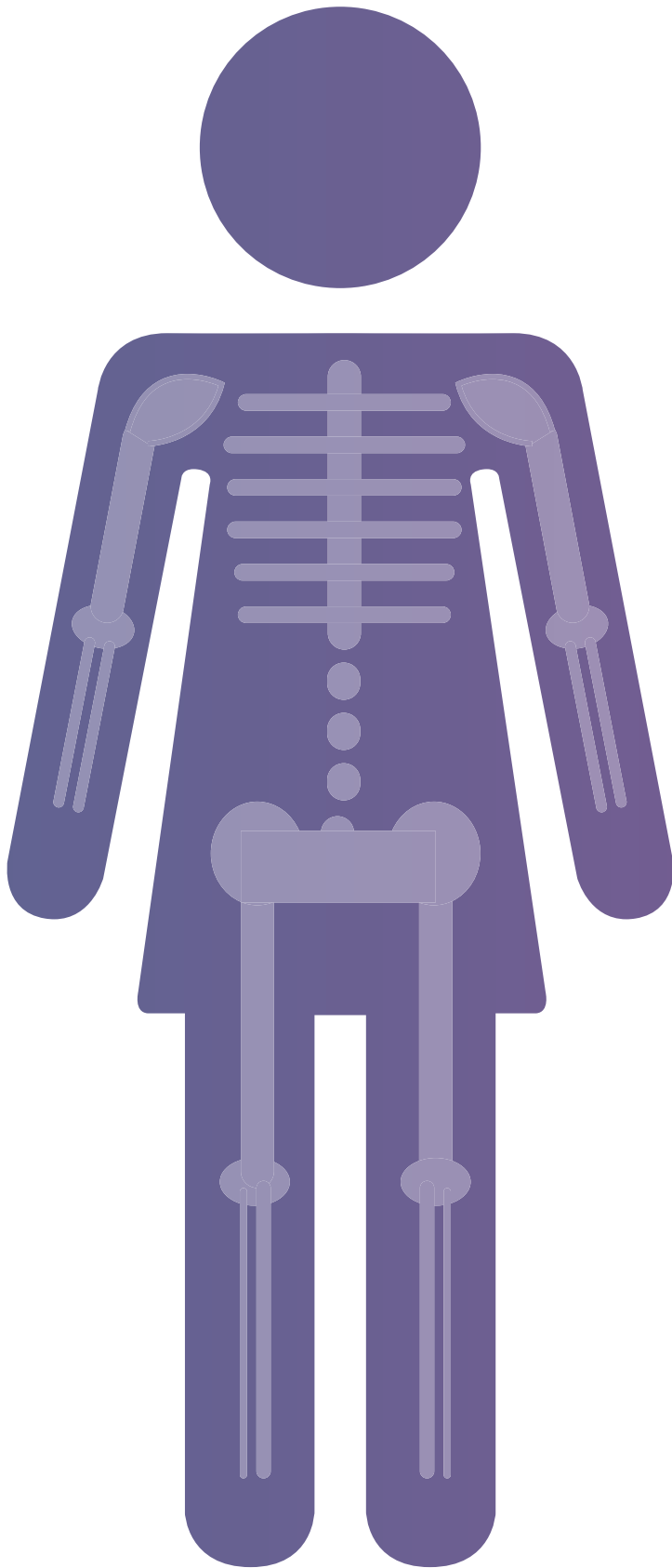
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# Chapter 6

Change in grip strength in trans people  
and its association with lean body mass and  
bone density

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*Endocr Connect.* 2019 Jun 1.

## Abstract

**Objective:** Gender-affirming hormonal treatment (HT) in trans people changes physical appearance. Muscle mass and strength are important aspects of physical appearance, but few data exist on the effect of HT on grip strength and muscle mass. This study aimed to investigate the change in grip strength in trans people during the first year of HT, to study possible determinants of this change, and to study the associations between changes in grip strength, lean body mass, and bone mineral density (BMD).

**Design and methods:** A multicenter, prospective study was performed, including 249 transwomen and 278 transmen. Grip strength, lean body mass, and BMD were measured at baseline and after one year.

**Results:** After one year of HT, grip strength decreased with -1.8kg (95%CI -2.6; -1.0) in transwomen and increased with +6.1kg (95%CI +5.5; +6.7) in transmen. No differences in grip strength change was found between age groups, BMI groups, hormonal administration routes, or hormone concentrations. In transmen, increase in grip strength was associated with increase in lean body mass (per kg increase in grip strength: +0.010 kg, 95%CI +0.003; +0.017), while this was not found in transwomen (per kg increase in grip strength: +0.004 kg, 95%CI -0.000; +0.009). Change in grip strength was not associated with change in BMD in transwomen and transmen.

**Conclusions:** After one year of HT, grip strength decreased in transwomen, and increased in transmen. In transmen only, change in grip strength was associated with change in lean body mass.

## Introduction

According to the DSM-criteria, gender dysphoria (GD) is defined as the incongruence between a person's assigned sex at birth and the experienced gender.<sup>(1)</sup> GD often has a strong impact on the person's psychological wellbeing. Therefore, most trans people prefer treatment to change physical appearance, for example gender-affirming hormonal treatment (HT) with or without gender-affirming surgery.

Grip strength and muscle mass are good indications of the masculinity of the body. A decrease in grip strength and muscle mass could lead to a more feminine body for transwomen (male-to-female trans people), while an increase in grip strength and muscle mass indicates a more masculine body for transmen (female-to-male trans people). Besides the importance of physical appearance, a change in grip strength and muscle mass also might be important in the prevention of sarcopenia (the age-related loss of muscle mass)<sup>(2)</sup>, and dynapenia (the age-related loss of muscle strength).<sup>(3)</sup>

Earlier studies on effects of HT in trans people focused on bone mineral density (BMD) and body composition. These studies found an increase in lean body mass in transmen and a decrease in lean body mass in transwomen.<sup>(4, 5)</sup> BMD increased in both transwomen and transmen.<sup>(6)</sup> A study in cis gender people found grip strength to be a predictor of bone mass.<sup>(7)</sup> Possibly, a change in BMD in trans people is associated with a change in grip strength. Some studies described the change in grip strength<sup>(8, 9)</sup>, however, sample sizes of these studies were small and possible influences on these changes, for example age, body mass index (BMI), administration routes of HT, and sex hormone concentrations during HT, have not been studied.

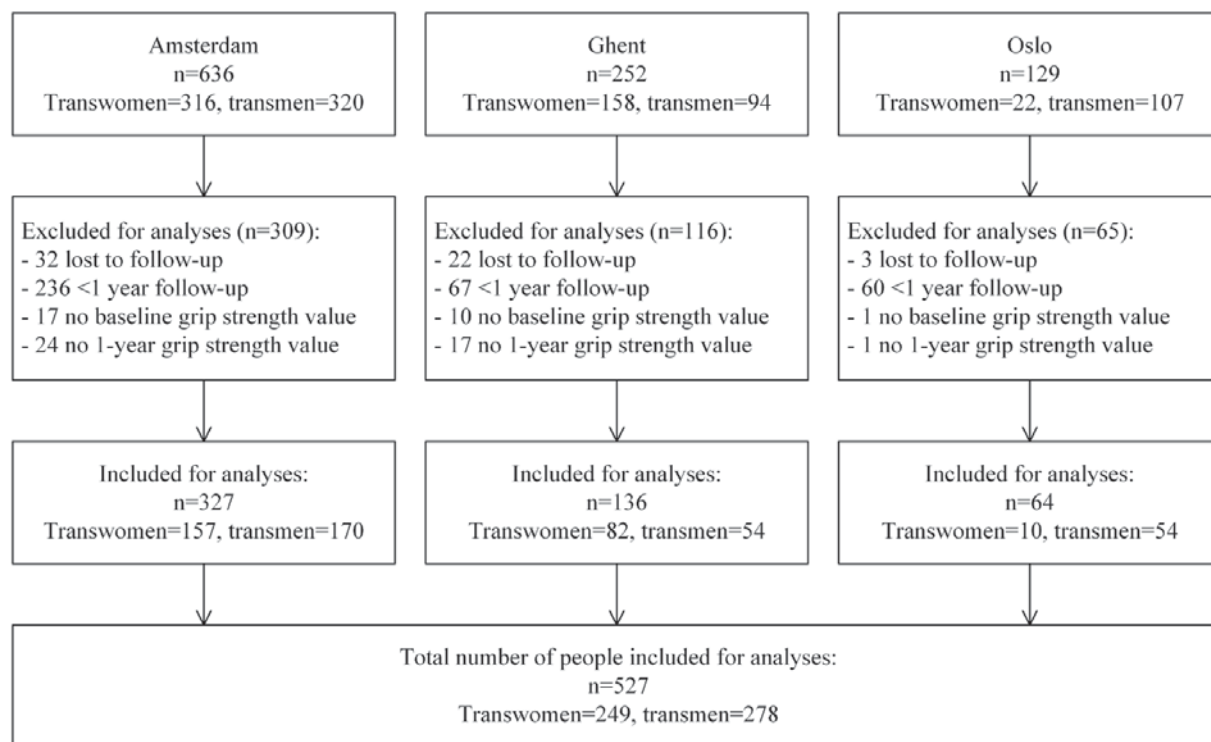
The aim of this study is to investigate the time course of change in grip strength in trans people in the first year of HT, to study possible determinants of this change, and to study the reciprocal associations between changes in grip strength, lean body mass (as an approximation of muscle mass), and BMD.

## Material and methods

### Study design and study population

This study is part of the European Network for the Investigation of Gender Incongruence (ENIGI) study, a multicenter prospective cohort study, including treatment centers in Amsterdam, Ghent, Oslo, and Florence using the same treatment protocol. The study design is published previously<sup>(10,11)</sup> and the study is registered at <https://clinicaltrials.gov/ct2/show/NCT01072825>. In short, people were included from 2010 until April 2016. The included people were 18 years and older and gave informed consent. People could participate in this study when they started with HT, if they did not use gender-affirming hormones before the start of HT, and if they spoke the native language. During the first

year of treatment, the people were seen every 3 months. For the current study, only data from Amsterdam, Ghent, and Oslo were analyzed, as grip strength was not assessed in Florence. People were included if their grip strength was measured at baseline and after 12 months. For the analyses on lean body mass and BMD, people were included if a dual-energy X-ray absorptiometry (DXA) was performed at baseline (range 4 months before to 4 months after baseline) and after 12 months (range 10 to 14 months) of HT. People from Oslo were excluded from the analyses on lean body mass and BMD, because a different type of DXA scanner was used (Oslo: Lunar (GE Lunar, Madison, WI, USA); Amsterdam and Ghent: Hologic Discovery A (Hologic Inc, Bedford, MA, USA)). In total, 1,017 participants were included in the overall study. After exclusions due to unknown grip strength values at baseline or 12 months ( $n=60$ ), a follow-up of less than one year ( $n=363$ ), or lost to follow-up ( $n=57$ ), a total of 249 transwomen and 278 transmen were included in our analyses (Figure 1).



**Figure 1.**  
Inclusion flowchart

Transwomen were treated with the anti-androgen cyproterone acetate (CPA) 50 mg daily, in combination with two to four mg oral estradiol valerate a day, or 100 mcg/24h estradiol patch twice a week. People older than 40 years were advised to be treated with transdermal estrogens, because of thrombosis risk.<sup>(12)</sup> Transmen were treated with testosterone. They could choose between testosterone gel (50 mg daily), testosterone esters (250 mg intramuscular every two to three weeks), or testosterone

undecanoate (1000 mg intramuscular every 12 weeks).

The Medical Ethics Review Committee of Ghent approved the study protocol. Local Ethical Review Committees approved participations in the other centers.

### **Clinical data collection**

Grip strength was measured in kilograms (kg), using an adjustable hand-held standard grip device, a Jamar Dynamometer.<sup>(10,13)</sup> The grip strength of the dominant hand was measured twice and the highest value was noted. These measurements were performed at baseline and after three months, six months, nine months, and twelve months of HT. However, from Oslo only data at baseline and after 12 months were available.

Body weight and height were measured at every visit. People were measured without shoes and in light indoor clothes. BMI was calculated by weight divided by the square of body height.

### **DXA**

A whole-body DXA was performed to measure lean body mass of the arms and the legs. Outcomes of body composition were determined using manufacturer-supplied algorithms. The specific arm and leg regions were defined with software from Hologic.

Absolute BMD values were obtained for lumbar spine (L1–L4, LS), total hip (TH), and femoral neck (FN). The same type of DXA device was used in Amsterdam and Ghent (Hologic Discovery A, Hologic Inc., MA, USA) and software version 13.5.3 was used.

### **Laboratory measurements**

Venous blood samples were obtained in the morning at baseline, after three months of HT, and after 12 months of HT. As the results were also used during clinical care, assays with higher quality were implemented when they were available. In order to compare the new and old values likewise, conversion formulas were generated by the endocrine laboratory.

In Oslo, testosterone and estradiol were determined using a competitive immunoassay (ECLIA, Roche Diagnostic, Indianapolis, USA) with a lower limit of quantitation (LOQ) of 0.1 nmol/L (2.6 ng/dL) and 18.4 pmol/L (5.0 pg/mL), and a coefficient of variation (CV) of 5 and 7%, respectively. In Ghent, an E170 Modular (E2 Gen II, Roche Diagnostics, Germany) was used for testosterone (LOQ 0.4 nmol/L [11.5 ng/dL], CV 2.6%) and estradiol (LOQ 92 pmol/L [25.1 pg/mL], CV 3.2%). For estradiol, it was updated in March 2015 to an E170 Modular (E2 Gen III, Roche Diagnostics, Germany) with a conversion formula of Gen III = 6.687940 + 0.834495 \* Gen II. In Amsterdam, estradiol was measured using a competitive immunoassay (Delfia, ParkinElmer, Wallac Oy, Turku, Finland) with a LOQ of 20 pmol/L (5.4 pg/mL) and a CV of <13% until July 2014. Thereafter, an LC-MS/MS (VUmc, Amsterdam, the

Netherlands; LOQ 20 pmol/L [5.4 pg/mL], CV <7%) was used, with a conversion formula of LC-MS/MS=1.60\*Delfia-29. Testosterone was measured using a radioimmunoassay (RIA, Coat-A-Count, Siemens, Los Angeles, CA, USA; LOQ 1 nmol/L [28.8 ng/dL], CV <10%) until January 2013. After that, it was measured using a competitive immunoassay (Gen III, Architect, Abbott, Abbott Park, IL, USA) with a LOQ of 0.1 nmol/L (2.9 ng/dL) and a CV <10%. Two conversion formulas were generated: <8 nmol/L: Architect=1.1\*RIA+0.2; >8 nmol/L: Architect=1.34\*RIA-1.65.

### Statistical analyses

Results are presented as mean with standard deviation (SD) in case of normal distribution, or median with interquartile range (IQR) for non-normally distributed data, and percentages. In case of non-normally distributed data, a log transformation was performed before further analyses.

To examine the course of the change in grip strength during the first year, linear mixed model analyses were performed. The influence of age, differences in BMI, different administration routes of HT, and serum hormone concentrations, were analyzed. Age was divided into groups (<25 years, 25-40 years, ≥40 years), to stratify for accrual of grip strength, peak grip strength, and age-related decrease of grip strength. BMI was defined as underweight (<18.5 kg/m<sup>2</sup>), normal weight (18.5-25 kg/m<sup>2</sup>), and overweight (≥25 kg/m<sup>2</sup>). For analyses between differences in the administration route of HT, people who used the same administration route for at least nine months were included. Mean concentrations of estradiol and testosterone during HT were calculated by averaging the results of the measurements after three and after 12 months of HT. As different assays were used in the centers to determine estradiol and testosterone and no conversion formulas between the centers were available, it was not possible to analyze the estradiol and testosterone concentrations as absolute values. Therefore, center specific tertiles were created for estradiol and testosterone and were thereafter analyzed together. The center specific mean estradiol concentrations in transwomen were: first tertile 122 pmol/L (33 pg/mL, Amsterdam), 159 pmol/L (43 pg/mL, Ghent), and 167 pmol/L (46 pg/mL, Oslo); second tertile 233 pmol/L (63 pg/mL, Amsterdam), 248 pmol/L (68 pg/mL, Ghent), and 317 pmol/L (83 pg/mL, Oslo); and third tertile 405 pmol/L (110 pg/mL, Amsterdam), 572 pmol/L (156 pg/mL, Ghent), and 398 pmol/L (108 pg/mL, Oslo). The center specific mean testosterone concentrations for transmen were: first tertile 16 nmol/L (461 ng/dL, Amsterdam), 10 nmol/L (288 ng/dL, Ghent), and 15 nmol/L (432 ng/dL, Oslo); second tertile 28 nmol/L (806 ng/dL, Amsterdam), 16 nmol/L (461 ng/dL, Ghent), and 21 nmol/L (605 ng/dL, Oslo); and third tertile 54 nmol/L (1555 ng/dL, Amsterdam), 24 nmol/L (691 ng/dL, Ghent), and 33 nmol/L (950 ng/dL, Oslo).

The average of the right and left arm was calculated for the analyses on the lean body mass of the arms, and the average of the right and left leg was calculated to analyze the lean body mass of the legs. To evaluate the change of grip strength, lean body



mass, BMD, and serum creatinine after one year, the absolute and percentage difference between the baseline values and the values after 12 months were calculated. As these were normal distributed variables, linear regression analyses were performed to calculate the mean and 95% confidence interval (CI).

To study the association between changes in grip strength and changes in lean body mass, BMD, or creatinine concentrations, linear regression analyses were performed.

All analyses were performed separately for transwomen and transmen. Data was analyzed using STATA Statistical Software (Statacorp, College Station, Texas, USA, version 15.1). P-values <0.050 were considered statistically significant.

## Results

### Characteristics

The characteristics are shown in Table 1. No differences were found between included and excluded people in baseline grip strength, age, BMI, estradiol concentrations, testosterone concentrations, or smoking habits (Supplementary Table 1).

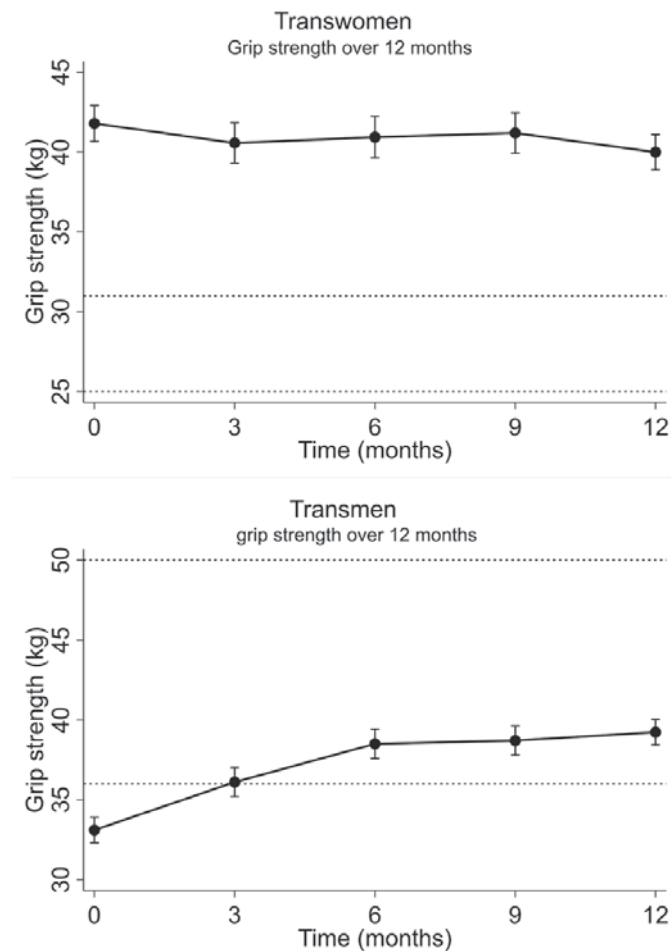
For the analyses on lean body mass, 171 transwomen and 154 transmen were included. For these analyses, excluded transwomen were younger (median age 26 years, IQR 21 to 34) than included transwomen (median age 31 years, IQR 23 to 42). Excluded transmen were younger (median age 22 years, IQR 19 to 25 ) and had a lower BMI (mean 24.3 kg/m<sup>2</sup>, SD 5.2) than included transmen (median age 28 years, IQR 20 to 33, and mean BMI 26.0 kg/m<sup>2</sup>, SD 5.5). No differences were found between included and excluded people in baseline grip strength, estradiol concentrations, testosterone concentrations, or smoking habits.

For the analyses on LS BMD, 207 transwomen and 229 transmen were included. For TH and FN, 206 transwomen and 216 transmen were included. No differences were found between included and excluded transwomen. Excluded transmen were younger (median age 21 years, IQR 19 to 25) than included transmen (median age 24 years, IQR 21 to 31).

**Table 1. Characteristics of the study population.**

	Transwomen (n=249)		Transmen (n=278)	
	Baseline	During HT	Baseline	During HT
Age, years	28 (23 – 40)		23 (20 – 30)	
BMI, kg/m <sup>2</sup>	23.8 (4.5)	24.5 (4.4)	25.5 (5.6)	25.9 (4.8)
Smoking (% yes)	24.7	14.7	29.9	19.9
Alcohol (% yes)	44.8	44.6	55.3	55.8
Grip strength (kg)	41.8 (8.9)	40.0 (8.9)	33.1 (6.5)	39.2 (6.8)
Creatinine (µmol/L)	78.5 (10.8)	73.1 (10.6)	66.0 (9.0)	77.4 (10.6)
Hormone administration route*				
- Estradiol oral	-	134	-	-
- Estradiol transdermal	-	86	-	-
- Testosterone gel	-	-	-	52
- Testosterone undecanoate i.m.	-	-	-	130
- Testosterone esters i.m.	-	-	-	81
Estradiol concentrations, pmol/L				
- Amsterdam	105 (83 – 131)	225 (141 – 329)	142 (59 – 371)	180 (138 – 242)
- Ghent	109 (88 – 130)	246 (181 – 342)	166 (116 – 431)	134 (113 – 169)
- Oslo	120 (100 – 140)	257 (195 – 325)	280 (180 – 480)	168 (140 – 210)
Testosterone concentrations, nmol/L				
- Amsterdam	18.5 (14.0 – 23.0)	0.8 (0.6 – 0.9)	1.3 (1.0 – 1.7)	27.8 (19.5 – 39.0)
- Ghent	17.9 (13.5 – 21.5)	0.7 (0.5 – 1.1)	1.0 (0.7 – 1.3)	16.3 (11.2 – 21.1)
- Oslo	18.1 (12.2 – 20.4)	0.4 (0.4 – 0.6)	1.0 (0.8 – 1.3)	21.4 (16.7 – 28.5)

Data are presented as median with inter quartile range, mean with standard deviation, percentages, or absolute numbers. \* Only in people who used the same hormone administration route for >75% of the follow-up time. Abbreviations: n=number of people, BMI=body mass index, kg/m<sup>2</sup>=kilogram per square meter, i.m.=intramuscular.

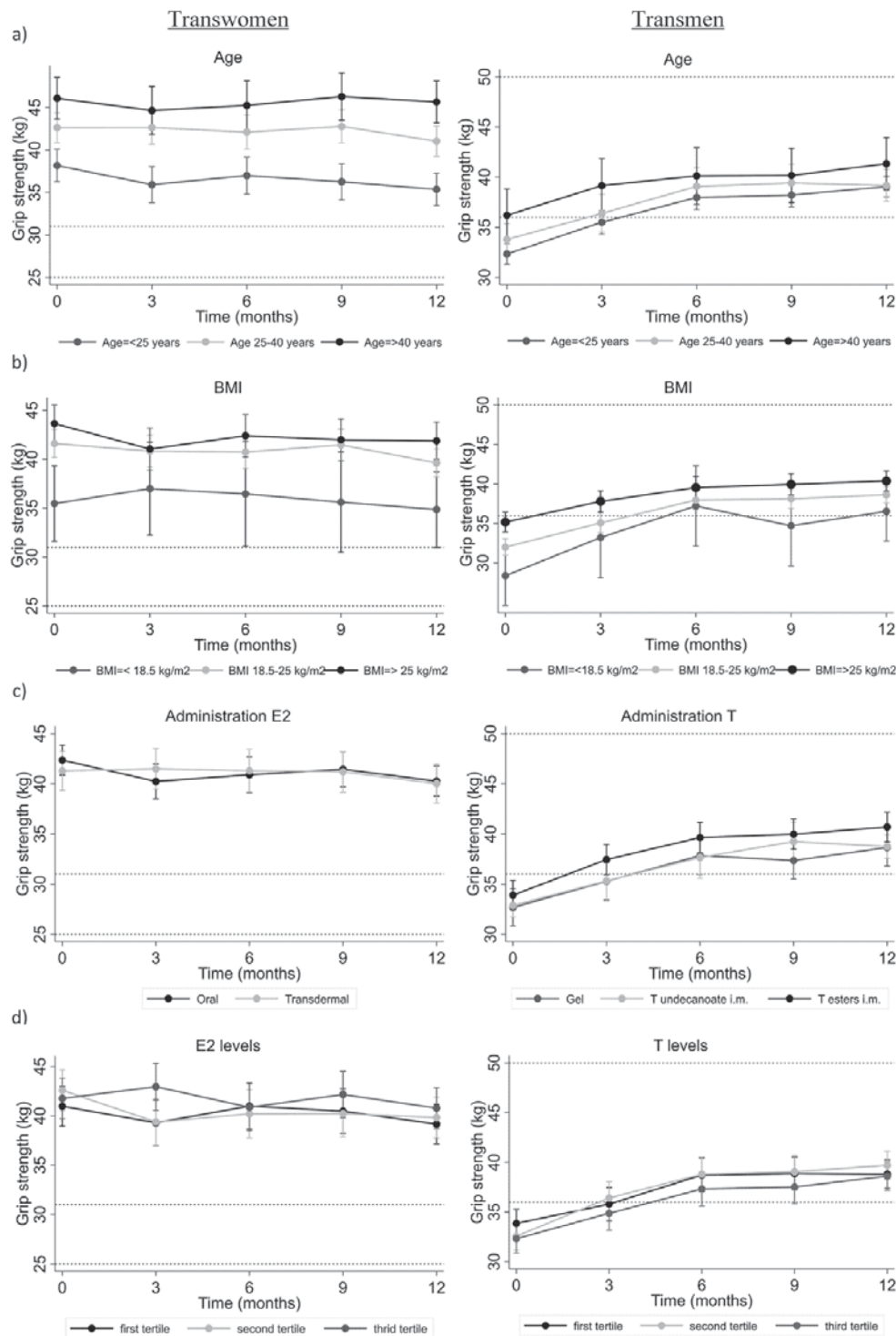


**Figure 2.**

Change in grip strength during the first 12 months of gender-affirming hormonal treatment in transwomen and transmen. Data are presented as means with 95% confidence interval. The 25<sup>th</sup> and 75<sup>th</sup> percentiles of the reference populations are shown with dashed lines. For transwomen the 25<sup>th</sup> percentile is 25 kg and the 75<sup>th</sup> percentile is 31 kg. For transmen the 25<sup>th</sup> percentile is 36 kg and the 75<sup>th</sup> percentile is 50 kg.<sup>(18)</sup> Abbreviations: kg= kilograms.

## Grip strength

In transwomen, grip strength decreased with  $-1.8$  kg (95% CI  $-2.6$  ;  $-1.0$ ), while in transmen, grip strength increased with  $+6.1$  kg (95% CI  $+5.5$  ;  $+6.7$ ). The course of the grip strength change over time is shown in Figure 2. For transwomen, 66% of the decrease in grip strength ( $-1.2$  kg) occurred in the last three months, while in transmen 49% of the increase ( $+3.0$  kg) occurred in the first three months. Change in grip strength did not vary between different age groups (Figure 3a), different BMI groups (Figure 3b), and different administration routes of HT (Figure 3c), for both transwomen and transmen. Change in grip strength did not vary between different hormone concentrations, either for transwomen or transmen (Figure 3d). No analyses on testosterone concentrations in transwomen could be performed, as testosterone was suppressed ( $<2$  nmol/L,  $<58$  ng/dL) in the majority of the transwomen (94%).

**Figure 3.**

Differences in change in grip strength for age groups, BMI groups, routes of hormonal administration, estradiol concentrations, and testosterone concentrations. Data are presented as means with 95% confidence intervals. Reference values (25<sup>th</sup> and 75<sup>th</sup> percentile) are based on the mean age of this population. For transwomen the 25<sup>th</sup> percentile is 25 kg and the 75<sup>th</sup> percentile is 31 kg. For transmen the 25<sup>th</sup> percentile is 36 kg and the 75<sup>th</sup> percentile is 50 kg.<sup>(18)</sup> a) Grip strength change over 12 months between age, adjusted for administration route. b) Grip strength change over 12 months between BMI groups. c) Grip strength change over 12 months between different administration routes, adjusted for age. d) Grip strength change over 12 months between different hormone concentrations. Abbreviations: BMI=body mass index, T=testosterone, E2=estradiol, kg/m<sup>2</sup>= kilogram per square meter, i.m.=intramuscular.

### Grip strength in relation to lean body mass

As reported previously in this study population <sup>(4)</sup>, a decrease in lean body mass was observed in transwomen and an increase in lean body mass was observed in transmen during the first year of HT.

Associations of change in grip strength with change in lean body mass are presented in Table 2. In transwomen, no associations between change in grip strength and change in arm or leg lean body mass was seen. In transmen, increase in grip strength was associated with an increase in arm lean body mass (per kg increase in grip strength: +0.010 kg, 95% CI +0.003 ; +0.017), but not with change in leg lean body mass.

**Table 2. Associations between change in grip strength (per kg increase) and lean body mass, bone mineral density, and creatinine, separately for transwomen and transmen**

	Transwomen		Transmen	
	Mean change (95%CI)	p-value	Mean change (95%CI)	p-value
Lean body mass				
- Arm	+0.004 kg (-0.000; +0.009)	0.079	+0.010 kg (+0.003; +0.017)	0.003
- Leg	+0.009 kg (-0.003; +0.021)	0.161	+0.014 kg (-0.002; +0.030)	0.078
Bone mineral density				
- Lumbar spine	+0.02 % (-0.05; +0.10)	0.556	+0.01 % (-0.08; +0.09)	0.900
- Total hip	+0.05 % (-0.01; +0.10)	0.112	-0.02 % (-0.09; +0.05)	0.630
- Femoral neck	+0.05 % (-0.03; +0.12)	0.201	+0.04 % (-0.06; +0.15)	0.401
Creatinine	-0.1 µmol/L (-0.2; +0.1) *	0.535	+0.2 µmol/L (+0.0; +0.4)	0.035

\* data shown is per kg decrease in grip strength

### Grip strength in relation to bone mineral density

As reported previously in this study population <sup>(6)</sup>, increases in LS BMD, TH BMD, and FN BMD were observed in transwomen, and increases in LS BMD and TH BMD, but not FN BMD, were observed in transmen during the first year of HT.

The associations of change in grip strength with change in bone mineral density are shown in Table 2. Change in grip strength was not associated with change in bone mineral density in both transwomen and transmen.

### Grip strength in relation to creatinine

Serum creatinine concentrations decreased with -5.0 µmol/L (95%CI -6.2 ; -3.8) in transwomen and increased with +11.1 µmol/L (95%CI +10.1 ; +12.2) in transmen. The associations of change in grip strength with change in creatinine are described in Table 2. In transmen, the increase in creatinine was associated with an increase in grip strength (per kg increase in grip strength: +0.2 µmol/L, 95%CI +0.0 ; +0.4). In transwomen, a decrease in creatinine tended to be associated with a decrease in grip strength (per kg decrease in grip strength: -0.1 µmol/L, 95%CI -0.2 ; +0.1).

## Discussion

In transwomen, a decrease in grip strength after one year of HT was found, while in transmen, an increase in grip strength after one year of HT was found. These changes were also found in the serum creatinine concentrations. Grip strength change did not vary between age groups, BMI groups, administration routes, and different hormone concentrations, for neither transwomen and transmen. Change in grip strength was associated with change in lean body mass in transmen but not in transwomen. Change in grip strength was not associated with a change in BMD.

In our study, transwomen decreased in grip strength, possibly due to the lack of testosterone. This is in agreement with a study in young men using gonadotropin-releasing hormone agonists, which found that muscle mass decreased by approximately one kilogram after 10 weeks.<sup>(14)</sup> The finding of an increase in grip strength in transmen is consistent with results from studies about testosterone replacement in hypogonadal men.<sup>(15)</sup> Testosterone has an effect on myoblast proliferation and myoblast differentiation, and testosterone increases the number of satellite cells, which promotes protein synthesis of muscle mass<sup>(16)</sup>. Thus, testosterone plays an important role in muscle mass and muscle strength. Accordingly, testosterone is not only important for muscle in men, but also for muscle in women. This is among others important for the prevention of dynapenia in older people.

The largest decrease in grip strength for transwomen took place in the last three months of HT, while the largest change for transmen took place in the first three months. The change in transmen is in line with a randomized controlled trial, that shows an increase in strength in the first 6 months, after the use of testosterone in healthy men  $\geq 60$  years old.<sup>(17)</sup> Interestingly, the time difference of the slow loss of grip strength in transwomen and the fast increase in transmen is opposite of what is observed for strength with training and detraining. It might possibly take longer for muscles to decrease in proteins due to lack of testosterone, than it is to increase due to administration of testosterone. However, to fully understand the difference, more research is necessary. After 12 months, the median grip strength of transwomen still falls into the 95<sup>th</sup> percentile for age-matched females. The median grip strength of transmen after 12 months falls into the 25<sup>th</sup> percentile of age-matched males.<sup>(18)</sup> Thus, transwomen are still stronger than average females and transmen are still weaker than average males. However, as this study is a follow-up of 12 months, transwomen and transmen might attain a grip strength value closer to the reference values of, respectively, females and males after a longer duration of HT.

No difference was found for grip strength change between age groups, BMI groups, and administration routes. A larger decrease in transwomen and a smaller increase in transmen was expected at age  $\geq 40$  years, because of the age related decrease of grip strength in combination with the lack of testosterone. However, our study

population of  $\geq 40$  years was not very old (mean age 49 years for transwomen and 47 years for transmen). Furthermore, our study suggests that change in grip strength was not related to mean serum hormone concentrations during the first year of HT. This finding is in line with a study on endocrine determinants in sarcopenia in 518 men aged 40-79 years, that found no association between total and bioavailable testosterone and the annual change in grip strength in men, after a follow-up of 4.3 years.<sup>(19)</sup> The finding that concentrations of testosterone and estradiol were not associated with the change in grip strength can be used to inform trans people that a higher dosage does not lead to a larger increase or decrease in grip strength. Also, because no relationship was found between change in grip strength and administration routes, trans people can make a more well informed decision when choosing between administration routes.

In transwomen, no association was found between change in lean body mass and change in grip strength, while it was only weakly associated in transmen. This is in contrast to a large cross-sectional and longitudinal perspective study of 847 participants aged 20-100 years, which found a strong correlation between grip strength and lean body mass.<sup>(20)</sup> However, this correlation was age dependent, and it was the strongest at 60 years old. People younger than 60 years appeared to be stronger than predicted with muscle mass and people older than 60 years appeared to be weaker. They also showed a stronger correlation between age and grip strength compared to age and muscle mass. Our population has a mean age of 25 years, this is significantly younger than 60 years, thus the correlation might be lower. Furthermore, change in grip strength was not associated to change in BMD. Therefore, change in BMD cannot be predicted by change in grip strength.

This is a large, multicenter, prospective study. Standardized measurements were used to measure grip strength, and there is a widespread age range. To our knowledge, this is the first study that describes the change in grip strength over the course of a year, and that examines possible influences on this change. However, our study also had some limitations. First, data about physical activity was only available in smaller subgroup of the study population and was therefore not analyzed. Therefore we could miss data that can partially explain the change in grip strength. However, in previous studies no change in physical activity was found in transwomen<sup>(8)</sup> and transmen<sup>(9)</sup> during the first year of HT. Second, possibly a true impact of testosterone concentrations on grip strength cannot be detected, since circulating testosterone concentrations were evaluated, instead of available testosterone in muscle cells.<sup>(21)</sup> In addition, the laboratory measurements were performed differently at the study centers and changed in two sites during follow-up. Although conversion formulas were generated and tertiles were used instead of absolute values, it might be that the variability in hormone concentrations affected the results. Last, it is questionable whether a decrease in grip strength in transwomen of almost 2 kg is clinically relevant. Nonetheless, transwomen possibly feel more feminine due to the decrease in muscle mass.<sup>(22,23)</sup> One study reported on the desired effects of HT

in transwomen in Indonesia, including reduced muscle mass.<sup>(23)</sup> A study in associations among masculinity, strength, and attractiveness shows a positive correlation between masculinity and grip strength, and a negative correlation between masculinity and attractiveness in young women.<sup>(24)</sup> This might indicate that a decrease in grip strength in women could influence the feeling of attractiveness. However, this may be dissimilar in transwomen. A questionnaire for transwomen and transmen would be of interest to investigate a possible satisfaction with the change in grip strength.

In conclusion, grip strength and lean body mass decreases in transwomen and increases in transmen, after 12 months of HT. This is interesting for the prevention of sarcopenia and dynapenia, since testosterone has a positive effect on muscle mass and grip strength. In addition, knowing the effects of HT on grip strength, its association with hormone concentrations and hormonal administration routes, and its relation with change in muscle mass and BMD, can help care providers and trans people with their expectations of HT. For further research, it would be interesting to evaluate the subjective satisfaction related to changes in grip strength, and to evaluate the change of grip strength after a longer follow-up to see if the grip strength will reach the grip strength reference values for women or men, for transwomen and transmen, respectively.



**Supplementary Table 1. Differences in characteristics between included and excluded transwomen and transmen**

	Transwomen			Transmen		
	Included (n=249)	Excluded (n=247)	p	Included (n=278)	Excluded (n=243)	p
Age, yr	28.5 (23.0 – 40.2)	28.0 (22.4 – 44.0)	0.977	23.0 (20.3 – 30.2)	22.2 (20.1 – 26.6)	0.084
BMI, kg/m <sup>2</sup>	23.8 (4.4)	23.5 (4.4)	0.478	25.3 (5.5)	25.3 (5.8)	0.945
Smoking, %yes	24.7	27.4	0.513	29.9	35.0	0.274
Alcohol, %yes	44.8	50.0	0.246	55.3	55.1	0.967
Baseline grip strength, kg	41.8 (8.9)	43.2 (9.1) (n=218)	0.084	33.1 (6.5)	34.0 (6.6) (n=215)	0.144
<b>Estradiol, pmol/L</b>						
- Amsterdam	105 (83 – 131)	96 (73 – 155)	0.907	142 (59 – 371)	397 (206 – 697)	0.053
- Ghent	109 (88 – 130)	93 (88 – 116)	0.468	166 (116 – 431)	128 (92 – 437)	0.721
- Oslo	120 (100 – 140)	100 (90 – 130)	0.307	280 (180 – 480)	275 (150 – 510)	0.810
<b>Testosterone, nmol/L</b>						
- Amsterdam	18.5 (15.0 – 23.0)	17.5 (15.0 – 22.5)	0.928	1.3 (1.0 – 1.7)	1.3 (0.5 – 1.7)	0.876
- Ghent	17.9 (13.5 – 21.5)	19.3 (13.2 – 23.6)	0.822	1.0 (0.7 – 1.3)	0.9 (0.7 – 1.3)	0.892
- Oslo	18.1 (12.2 – 20.4)	15.4 (11.6 – 20.1)	0.535	1.0 (0.8 – 1.3)	1.3 (0.8 – 1.6)	0.107
Creatinine (µmol/L)	78.5 (10.8)	77.0 (10.8)	0.266	66.0 (9.0)	65.0 (10.0)	0.363

Data are presented as median with inter quartile range, mean with standard deviation, or percentages.

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