The Amsterdam Cohort of Gender Dysphoria Study (1972–2015): Trends in Prevalence, Treatment, and Regrets

Chantal M. Wiepjes,^{1,2} Nienke M. Nota,^{1,2} Christel J. M. de Blok,^{1,2} Maartje Klaver,^{1,2} Annelou L. C. de Vries,^{2,3} S. Annelijn Wensing-Kruger,^{2,4} Renate T. de Jongh,¹ Mark-Bram Bouman,^{2,5} Thomas D. Steensma,^{2,4} Peggy Cohen-Kettenis,^{2,4} Louis J. G. Gooren,^{1,2} Baudewijntje P. C. Kreukels,^{2,4} and Martin den Heijer, MD, PhD^{1,2}

ABSTRACT

Background: Over the past decade, the number of people referred to gender identity clinics has rapidly increased. This raises several questions, especially concerning the frequency of performing gender-affirming treatments with irreversible effects and regret from such interventions.

Aim: To study the current prevalence of gender dysphoria, how frequently gender-affirming treatments are performed, and the number of people experiencing regret of this treatment.

Methods: The medical files of all people who attended our gender identity clinic from 1972 to 2015 were reviewed retrospectively.

Outcomes: The number of (and change in) people who applied for transgender health care, the percentage of people starting with gender-affirming hormonal treatment (HT), the estimated prevalence of transgender people receiving gender-affirming treatment, the percentage of people who underwent gonadectomy, and the percentage of people who regretted gonadectomy, specified separately for each year.

Results: 6,793 people (4,432 birth-assigned male, 2,361 birth-assigned female) visited our gender identity clinic from 1972 through 2015. The number of people assessed per year increased 20-fold from 34 in 1980 to 686 in 2015. The estimated prevalence in the Netherlands in 2015 was 1:3,800 for men (transwomen) and 1:5,200 for women (transmen). The percentage of people who started HT within 5 years after the 1st visit decreased over time, with almost 90% in 1980 to 65% in 2010. The percentage of people who underwent gonadectomy within 5 years after starting HT remained stable over time (74.7% of transwomen and 83.8% of transmen). Only 0.6% of transwomen and 0.3% of transmen who underwent gonadectomy were identified as experiencing regret.

Clinical Implications: Because the transgender population is growing, a larger availability of transgender health care is needed. Other health care providers should familiarize themselves with transgender health care, because HT can influence diseases and interact with medication. Because not all people apply for the classic treatment approach, special attention should be given to those who choose less common forms of treatment.

Strengths and Limitations: This study was performed in the largest Dutch gender identity clinic, which treats more than 95% of the transgender population in the Netherlands. Because of the retrospective design, some data could be missing.

Conclusion: The number of people with gender identity issues seeking professional help increased dramatically in recent decades. The percentage of people who regretted gonadectomy remained small and did not show a tendency to increase. Wiepjes CM, Nota NM, de Blok CJM, et al. The Amsterdam Cohort of Gender Dysphoria Study (1972–2015): Trends in Prevalence, Treatment, and Regrets. J Sex Med 2018;XX:XXX-XXX.

Copyright © 2018, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

Key Words: Transgender; Prevalence; Regret; Gender-Affirming Hormones; Gender-Affirming Surgery

⁴Department of Medical Psychology, VU University Medical Center, Amsterdam, the Netherlands;

Copyright © 2018, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

https://doi.org/10.1016/j.jsxm.2018.01.016

Received December 8, 2017. Accepted January 28, 2018.

¹Department of Endocrinology, VU University Medical Center, Amsterdam, the Netherlands;

²Center of Expertise on Gender Dysphoria, VU University Medical Center, Amsterdam, the Netherlands;

³Department of Child and Adolescent Psychiatry, VU University Medical Center, Amsterdam, the Netherlands;

⁵Department of Plastic, Reconstructive, and Hand Surgery, VU University Medical Center, Amsterdam, the Netherlands

2

INTRODUCTION

Gender dysphoria (GD) refers to the distress related to a marked incongruence between one's assigned sex at birth and the experienced gender later in life.¹ In this study, we define transwomen as having a male birth assignment and transmen as having a female birth assignment who might receive medical treatment to adapt their physical characteristics to their experienced gender. This treatment can include puberty suppression (PS), gender-affirming hormonal treatment (HT), and gender-affirming surgery.

It has been widely observed that the transgender population is growing and broadening.^{2,3} This increase in the transgender population raises several questions, especially concerning the frequency of performing gender-affirming treatments with irreversible effects and regret from such interventions.

There are no reliable estimations of the current prevalence of transgender people who actually have received gender-affirming treatment (including HT), because most recent studies are based on questionnaires4,5 or data about gender-affirming surgery only.^{6,7} In most countries transgender care is performed by multiple health care providers (eg, university clinics or general practitioners), which makes it difficult to provide these numbers. In contrast, in the Netherlands, more than 95% of the transgender population has received treatment in only 1 center, the gender identity clinic at the VU University Medical Center (VUmc; Amsterdam, the Netherlands), currently known as the Center of Expertise on Gender Dysphoria.⁸⁻¹⁰ This center started treating adults in 1972. From 1987 to 2002, children and adolescents were seen by a mental health specialist in the Utrecht University Medical Center (Utrecht, the Netherlands). After they were considered eligible, they could receive medical treatment in the VUmc, which consisted of PS (usually by gonadotropin-releasing hormone analogues), followed by HT (see Kreukels and Cohen-Kettenis¹¹ for the treatment protocol for adolescents diagnosed with GD). After 2002, the Utrecht clinic stopped seeing adolescents and the diagnostics were performed in the VUmc. Adult people are referred to a psychologist or psychiatrist for the diagnostic phase after an initial screening. People diagnosed with GD can start HT if they are considered eligible. HT consists of testosterone for transmen and estrogens, often combined with antiandrogens, for transwomen. In the 1st year of HT, checkups are performed every 3 months. After a minimum of 12 months of HT, gender-affirming surgery can be performed, including mastectomy and hysterectomy with oophorectomy in transmen and breast augmentation and vaginoplasty (including orchiectomy) in transwomen. After gonadectomy (oophorectomy or orchiectomy), people are usually seen every 1 to 2 years for clinical follow-up.

In the present study we included the complete population seen at the gender identity clinic of the VUmc from 1972 through December 2015 to assess the current prevalence of transgender people who received medical treatment, the frequency of specific medical treatments performed, and the numbers of people who received HT in line with their sex assigned at birth because they regretted undergoing gonadectomy.

METHODS

Study Design and Patient Selection

After approval of the local ethics committee, a retrospective medical record review was performed to identify all people seen in our gender identity clinic from 1972 until December 2015. Data were collected from the hospital registries of the VUmc. The total study population was defined as people who had been diagnosed with 1 of the following International Classification of Diseases diagnoses: 302.5 (transsexualism), 302.6 (gender identity disorder not otherwise specified), or 302.85 (gender identity disorder in adolescent or adult) according to the 9th edition or F64 (gender identity disorders) according to the 10th edition.¹² In addition, the administrative employees of our gender identity clinic registered everyone who was referred to our gender identity clinic since the early 1970s. People reported on this list also were included in the study population. Some people of this study population have been described in previous studies.^{9,13-18} People were excluded from the study if they had been registered at our gender identity clinic but had actually never visited the clinic or if they had presented with other complaints than gender identity issues. Because of the retrospective design and the large study population, necessity for informed consent was waived by our local ethics committee.

Hospital Registries

The hospital registries store clinical data obtained during regular patient care performed in our center, including medical diagnoses (since 1985), medication prescriptions (since 2000), surgical interventions (since 2006), laboratory test results (since 2004), radiology results (since 1993), and visit dates (since 2007). The 1st visit was defined as the 1st appointment with the psychologist, psychiatrist, pediatrician, endocrinologist, or gynecologist for health care related to gender identity.

Clinical Data Collection

Not all data were available from the hospital registries, particularly older data or surgeries performed in other centers. To generate the most reliable results, the medical records of all people who composed the study population were checked. All people were classified as transwomen or transmen (based on the sex assigned at birth), and date of birth and death were noted. The following categories were included: the individual was in the diagnostic stage, the individual did not start HT, or the individual was on HT. Start of HT was defined as the 1st date gender-affirming hormones were prescribed by a physician in our gender identity clinic after a confirmed GD diagnosis, irrespective of previous gender-affirming hormone use. Of the people who started HT, baseline and follow-up data, including

Amsterdam Cohort of Gender Dysphoria Study

1st visit, medical history, medication use, prior gender-affirming hormone use, start date and type of PS and HT, and date of gonadectomy, were collected. Some people regretted the interventions they had undergone. Transwomen who started testosterone treatment after vaginoplasty or transmen who started estrogen treatment after oophorectomy and expressed regret were categorized as those who experienced regret. Reasons for regret as reported in their medical records were noted. Dates were set to the 1st of the month and personal identification data were removed from the research database.

Statistical Analysis

The total number of people visiting the clinic each year and their median age were reported separately for transwomen and transmen and were stratified for age at the 1st visit: children were younger than 12 years, adolescents were 12 to 18 years old, and adults were at least 18 years old. The percentage of people who started HT within 5 years after the 1st visit was reported for each year. The prevalence was calculated for people at least 12, at least 16, 12 to 18, 18 to 30, 30 to 50, and at least 50 years old by using the total number of people in these age groups who received medical treatment in our center until 2015, excluding deceased people. The total populations of these age groups in the Netherlands in 2015 were provided by the Central Bureau of Statistics of the Netherlands. The percentage of people who underwent gonadectomy within 5 years after starting HT was reported. For calculation of the total percentage of the study population who had undergone gonadectomy, only people at least 18 years old who used HT for at least 1.5 years were included, because these were requirements for surgery. People who regretted their medical transition are reported as the percentage of the total population of transwomen and transmen who underwent gonadectomy. In adults, time from 1st visit to start of HT or gonadectomy, if applicable, are expressed as median days with interquartile range (IQR). Total follow-up time was calculated for every individual who started HT and was expressed as years from the 1st visit to the last visit. Prevalence with 95% CI was calculated using OpenEpi.¹⁹ All other analyses were performed using STATA 13.1 (StataCorp, College Station, TX, USA).

RESULTS

1st Visit

6,793 people presented for gender-affirming treatment, with more transwomen (65.2%) than transmen (34.8%; Table 1). The number of people attending the gender identity clinic increased over time (Table 2), whereas the median age of adults at the time of their 1st visit decreased (Figure 1). The median age at the 1st visit was younger for adult transmen (25 years; IQR = 21-35 years) than for adult transwomen (33 years; IQR = 25-42 years). Although historically more transwomen than transmen presented for treatment, more transmen than

Tab	le 1	. Treatmer	t patterns	of total stu	ly i	population,	stratified	for age	e groups	; and fo	r transwomen	and	transmen*	

	Transwomen	Transmen	Total	Ratio of transwomen to transmen
Total study population, N (%)	4,432 (65.2)	2,361 (34.8)	6,793 (100)	1.9:1
Adults (≥18 y)	3,809	1,624	5,433	2.3:1
Age (y) [†] , median (IQR; max)	33 (25–42; 81)	25 (21–35; 73)	31 (23–41; 81)	
Started HT ⁵ , %	68.9	72.9	69.9	
Underwent gonadectomy , %	75.3	83.8	77.7	
Adolescents (12–18 y)	330	482	812	0.7:1
Age (y) [†] , median (IQR)	16 (15—17)	16 (15—17)	16 (15—17)	
Started PS [‡] , %	28.7	50.8	41.0	
Stopped PS, %	4.1	0.7	1.9	
Started HT ^s without PS, %	33.9	30.8	32.2	
Underwent gonadectomy , %	79.5	77.2	78.2	
Children (<12 y)	293	255	548	1.1:1
Age (y) [†] , median (IQR)	8 (7–10)	9 (8–11)	9 (7—10)	
Started PS ^{‡,¶} , %	33.6	49.1	40.3	
Regret [#] , % (n)	0.6 (11)	0.3 (3)	0.5 (14)	2.0:1

HT = gender-affirming hormonal therapy; IQR = interquartile range; max = maximum; PS = puberty suppression.

*From 1987 through 2002, children and adolescents were seen at the Utrecht University Medical Center and then at the VU University Medical Center only if they could begin medical treatment.

[†]Age is defined as the age at the 1st visit to the VU University Medical Center, Amsterdam.

[‡]Only those who reached the age of eligibility (usually \geq 12 years old) could undergo PS.

⁵Only in people at least 16 years old.

^{||}Only people treated with gender-affirming hormones for at least 1.5 years and at least 18 years old (orchiectomy in transwomen and oophorectomy in transmen).

[¶]Those who were too old (\geq 18 years) after the diagnostic phase for PS could begin directly with HT.

[#]Only those people who underwent gonadectomy.

	, , , ,				
	lst visit, n	Started HT*, %	Age (y) at start of HT, median (IQR)	Previous HT, %	Underwent gonadectomy [†] , %
Transwomen (≥18 y)					
1972–1979	119	89.9	33 (26–40)	16.8	79.4
1980–1984	189	88.4	33 (25–40)	12.6	71.9
1985–1989	319	75.9	31 (25–39)	15.3	76.5
1990—1994	392	65.8	30 (25–41)	20.5	76.7
1995–1999	522	65.5	34 (27–41)	26.6	78.7
2000-2004	605	56.0	38 (30–45)	29.2	67.3
2005-2009	476	61.6	39 (29–47)	22.9	68.6
2010-2014	926 (138 [‡])	60.9 [‡]	32 (23—42) [‡]	29.8 [‡]	NA
Transmen (≥18 y)					
1972–1979	30	96.7	24 (21–30)	10.3	72.4
1980–1984	69	84.1	24 (21–32)	3.5	82.8
1985–1989	105	84.8	24 (21–30)	1.1	79.8
1990—1994	142	69.0	27 (21–33)	7.1	88.8
1995—1999	177	65.0	29 (24–37)	7.0	88.7
2000-2004	207	63.3	32 (26–39)	5.3	87.0
2005-2009	185	63.8	29 (23–37)	3.4	81.4
2010-2014	518 (70 [‡])	71.4 [‡]	24 (21–37) [‡]	O [‡]	NA

Table 2. Description of adult study population for every 5-year cohort

HT = gender-affirming hormonal therapy; IQR = interquartile range; NA = not applicable.

*People who started HT within 5 years after the 1st visit.

[†]People who had this procedure within 5 years after the start of HT.

[‡]Only in people who had their 1st visit 5 years before December 31, 2015 (n = 138 transwomen; n = 70 transmen).

transwomen applied for treatment in 2015. This change in sex ratio was mainly due to the increase in adolescent transgender boys, because the ratio of transwomen to transmen in adults remained stable over time.

Prevalence and Treatment

At the end of 2015, 3,838 transgender people at least 16 years old had received medical treatment and were not deceased. Because the total population of people at least 16 years old in the Netherlands in 2015 was 13,870,426, the prevalence was 27.7 per 100,000 people (95% CI = 26.8-28.6), or 1:3,600. Stratification for transwomen and transmen showed a prevalence of 36.4 (95% CI = 35.0-37.8) per 100,000 people (or 1:2,800) for men (transwomen) and 19.3 (95% CI = 18.3-20.3) per 100,000 people (or 1:5,200) for women (transmen). The calculation of prevalence numbers of people at least 12 years old and specific age groups are presented in Table 3.

The percentage of adult people who started HT within 5 years after the 1st visit decreased over time, whereas the percentage of people who underwent gonadectomy within 5 years after starting HT remained stable (Figure 2). Of the total study population at least 18 years old treated with HT for at least 1.5 years, 75.6% of transwomen (n = 1,742) and 82.4% of transmen (n = 885) underwent gonadectomy. The median time from the 1st visit to the start of HT for adults was 327 days (IQR = 36–570 days) and from the 1st visit to gonadectomy was 1,029 days (IQR = 679–1,465 days). The median

follow-up time for people treated with HT was 6.4 years (range = 0.4-41.6 years).

Of adolescents, 41.0% started PS, whereas only 1.9% of these adolescents stopped PS and did not start HT (Table 1). 32.2% of adolescents started directly with HT, because they were too old (\geq 18 years) to start with PS after the diagnostic phase.

Regret

Regret was identified in 0.6% of transwomen and 0.3% of transmen who underwent gonadectomy. The characteristics of these people are presented in Table 4. Their ages at start of HT ranged from 25 to 54 years, and they expressed their regrets 46 to 271 months after initiation of HT. Reasons for regret were divided into social regret, true regret, or feeling non-binary. Transwomen who were classified as having social regret still identified as women, but reported reasons such as "ignored by surroundings" or "the loss of relatives is a large sacrifice" for returning to the male role. People who were classified as having true regret reported that they thought gender-affirming treatment would be a "solution" for, for example, homosexuality or personal acceptance, but, in retrospect, regretted the diagnosis and treatment.

DISCUSSION

The aim of this study was to generate a dataset of all individuals who presented to our clinic for gender-affirming care from 1972 to 2015. We found that the number of people with

Amsterdam Cohort of Gender Dysphoria Study



Figure 1. Number of people and median age for each year, stratified for transwomen and transmen and for children (<12 years), adolescents (12–18 years), and adults (\geq 18 years). Age is defined as age at the 1st visit to the VU University Medical Center, Amsterdam. From 1987 through 2002, children and adolescents were seen at the Utrecht University Medical Center and then at the VU University Medical Center only if they could begin medical treatment.

gender identity issues who sought professional help increased dramatically in recent decades and that the median age of adults at presentation decreased. The ratio of transwomen to transmen remained stable over the years for adults, whereas in adolescents the population of transgender boys increased compared with the population of transgender girls. Currently, more transgender boys than transgender girls are seen. This phenomenon also has been described by Aitken et al.¹⁷ The age at the 1st visit was

	Total population		Male sex assigned at (transwomen)	birth	Female sex assigned (transmen)	at birth
Age (y)	Per 100,000	l per	Per 100,000	l per	Per 100,000	l per
≥12	26.9 (26.1–27.8)	3,700	34.8 (33.5–36.2)	2,900	19.3 (18.3–20.3)	5,200
≥16	27.7 (26.8–28.6)	3,600	36.4 (35.0–37.8)	2,800	19.3 (18.3–20.3)	5,200
12—18	16.0 (13.9–18.4)	6,300	11.1 (8.8–14.1)	9,000	21.0 (17.7–25.1)	4,800
18–30	35.7 (33.5–38.2)	2,800	30.3 (27.4–33.4)	3,300	41.4 (37.9–45.1)	2,400
30–50	30.5 (29.0–32.2)	3,300	40.1 (37.6–42.8)	2,500	21.0 (19.2–23.0)	4,800
≥50	23.0 (21.9–24.2)	4,300	37.6 (35.5–39.8)	2,700	9.7 (8.7–10.8)	10,300

Table 3. P	revalence	numhers	specified	for	different	ane	arouns

*Data are presented as number (95% CI).

Table 4.	Characteristics	Table 4. Characteristics of people with regret	egret					
Case	Type	Year started HT	Age (y) at start of HT	Year of gonadectomy	Time after HT (mo)	Time after gonadectomy (mo)	Reversal surgery	Reason for regret
-	M-F-M	1978	31	679I	±153	±130	None	Social acceptance
2	M-F-M	1982	25	1984	±54	±27	Mastectomy	Social acceptance
м	M-F-M	1986	47	1988	±216	±197	Mastectomy	Social acceptance
4	M-F-M	1988	33	0661	±186	±167	None	True regret
ы	M-F-M	1988	38	0661	±70	±44	Mastectomy	Social acceptance
9	M-F-M	1661	41	1993	±67	±49	Mastectomy, vaginectomy, phalloplasty	Social acceptance
7	M-F-M	1661	38	1995	±271	±225	Mastectomy	True regret
Ø	M-F-M	1993	30	1994	±79	±61	None	Feels non-binary
σ	M-F-M	966L	33	1997	1 90	±73	Mastectomy, phalloplasty	True regret
Q	M-F-M	1997	43	666l	±46	±27	Mastectomy	True regret
E	M-F-M	2004	54	2007	±130	±92	Mastectomy, vaginectomy	True regret
21	F-M-F	1987	25	0661	±91	±50	Breast augmentation, remove testicular implants	True regret
5	F-M-F	0661	34	1993	±102	±74	Remove testicular implants	Feels non-binary
14	F-M-F	1993	31	1997	±258	±212	None	True regret
$F extsf{-}M extsf{-}F extsf{-}$	emale to male tc) female; $HT = horr$	$F ext{-}M ext{-}F=female$ to male to female; $HT=hormonal$ treatment; $M ext{-}F ext{-}$	F-M = male to female to male.	to male.			

6

older for adult transwomen than for transmen. The percentage of adult people starting HT within 5 years after the 1st visit decreased over time, whereas the percentage of people who underwent gonadectomy within 5 years after starting HT remained stable. Of the total population treated with HT, 77.8% underwent a gonadectomy. Only a very small percentage of people who underwent gonadectomy regretted their decision, expressed as the start of HT in line with their sex assigned at birth.

An explanation for the increase in referrals could be the increased attention in society and media, which contributes not only to awareness of the existence of GD and possibilities for medical treatment but also to greater social acceptance. In addition, information about transgender identities has become much more accessible through the internet within the past decade, which could lead to an earlier recognition of gender identity issues. Also, transgender and gender non-binary individuals might be more willing to access care and more access to care has become available.

The increase in the prevalence of people with GD who sought medical treatment in the Netherlands (1:11,900 transwomen and 1:30,400 transmen in 1990⁸ vs 1:2,800 transwomen and 1:5,200 transmen currently) suggests that the transgender population is dramatically increasing. The highest prevalence for transwomen was found for the 30- to 50-year age group (1:2,500), whereas that for transmen was found in the 18- to 30year age group (1:2,400). Transgender people in the Netherlands seem to experience a reasonable degree of acceptance owing to a tolerant social climate in contrast to many other countries.²⁰ For example, medical costs are reimbursed by medical insurance companies, and it is possible to change the legal sex status (even without gonadectomy). These points can lead to a lower threshold to seek help, making this study population useful for an adequate estimation of the current prevalence of people with GD who seek medical treatment. More than 95% of transgender people are treated in our gender identity clinic. However, not all transgender people seek medical help. Some use self-medication or go abroad for treatment. Therefore, these numbers might still be an underestimation of the real prevalence. Our data represent a population that actively sought help in a medical setting. In 2012, a Dutch study of non-clinical people reported that 0.6% (1:167) of those with male sex assigned at birth and 0.2% (1:500) of those with female sex assigned at birth reported an incongruent gender identity with a wish for hormones or surgery.²¹ However, that was a population-based study with a response rate of 20.9%, which could lead to non-response bias. In addition, the existence of incongruent gender identities was based on self-report and no detailed assessment of GD was performed, which could have led to higher prevalence rates.

An interesting finding is the percentage of children who were referred in childhood (before 12 years of age) and who started PS when the GD persisted and the eligibility criteria were fulfilled. This 40% of children who started PS is almost identical to the 39% of persistence of childhood GD reported in a previous



Figure 2. Top panel shows percentage of transgender adults beginning gender-affirming HT within 5 years after the 1st visit, stratified for transwomen and transmen. Bottom panel shows percentage of transgender adults with occurrence of gonadectomy within 5 years after starting HT for each year, stratified for transwomen and transmen. Year is defined as the year of the 1st visit. HT = gender-affirming hormonal treatment.

Dutch study (using a smaller cohort of children).²² In addition, the finding that the persistence is higher in natal girls (49.1%) compared with natal boys (33.6%) is in line with observations in previous follow-up studies on the persistence of GD in children (for an overview, see Ristori and Steensma²³).

Remarkably, we found a decrease over time in the percentage of referred adult people who actually started HT. This finding might be explained by the fact that in the past it was harder to find information about GD and its treatment, and only people with extreme types of GD managed to visit our gender identity clinic for treatment. Currently, owing to media attention and the internet, it is easier to access information about our gender identity clinic, making the threshold lower to search for help. This could have led to referrals of people with milder forms of GD and people who were not sure of their feelings and just wanted to explore these with a psychologist. Such people eventually might not pursue HT. Another explanation might be that not all transgender people want to undergo HT, such as transmen or people with a non-binary identity who only want a mastectomy.²⁴

By contrast, we noticed that the percentage of people who underwent gonadectomy within 5 years after the start of HT remained stable over time. At the start of the clinic in 1972, knowledge about transgender care was limited and only people who wished for a classic treatment, consisting of a diagnostic phase, HT plus social transitioning, and surgery (in this order), were treated. There was no room for partial treatments. Since the publication of the Standards of Care Version 6 in 2001, other types of treatment are offered.²⁵ In addition, in 2014, a change in Dutch law allowed transgender people without a wish to undergo gonadectomy to alter the sex on their birth certificate with a statement of an expert who declared that the individual was diagnosed with GD (Dutch civil law, article 1:28). Although these changes in clinical guidelines and the law might have led to a decrease in the number of transgender people choosing gonadectomy, the current results do not show this. However, the follow-up time of this study might be too short to notice such changes.

In the HT group, 22% of people who were eligible for surgery had not undergone gonadectomy. These numbers are comparable with a study from Sweden²⁶ but larger than in a study from Belgium,²⁷ in which approximately 15% of transwomen and transmen did not undergo gonadectomy. A possible wish to carry a child could change these numbers in the future, because fertility has become a more important issue.

Despite the large increase in treated transgender people, the percentage of people who underwent gonadectomy but regretted their decision was still very small (0.5%). In a review by Pfäfflin²⁸ in 1992, regret was reported by less than 1% of transmen and 1% to 1.5% by transwomen after gonadectomy. More recent studies have reported regret percentages of $0\%^{29,30}$ to $2\%^7$ and $6\%^{31}$ after gonadectomy. 13 of the 14 people who regretted gonadectomy had started HT from 1978 through 1997 and 1 started in 2004. At best, this indicates that the diagnostic and eligibility criteria for treatment have improved over the past decade. Another explanation might be the altered treatment protocol, which also allowed people to receive HT without gonadectomy. Our findings could be an underestimation of people with regret after gonadectomy, because some might choose to go elsewhere for reversal therapy or might experience regret without pursuing reversal surgery or HT. Regret might not always result in a desire for reversal therapy, as it may be hidden from others. In addition, in our population the average time to regret was 130 months, so it might be too early to examine regret rates in people who started with HT in the past 10 years.

The Center of Expertise on Gender Dysphoria of the VUmc Amsterdam is the largest gender identity clinic in the Netherlands, where people of all ages, including children and adolescents, are treated. Life-time follow-up is recommended, making it a useful study population for collection of epidemiologic data and future long-term studies of treatment effects. However, there are some limitations. Because this is a retrospective chart review study, some data could be lacking. (i) Some people who once visited our clinic might not be reported in our database. However, we used several search strategies to identify the total study population, thereby decreasing the possibility of missing people. (ii) A large number of transgender people who had initially received treatment in our center were lost to follow-up. Although transgender people receive lifelong care, a large group (36%) did not return to our clinic after several years of treatment. Therefore, we could have missed some information on, for example, gonadectomies performed at other centers or people with regret.

CONCLUSIONS

We found that the prevalence of treated transgender people increased exponentially. Because of this growing population, it is necessary that health care providers outside university clinics also have knowledge about GD and its treatment, because HT can influence the course of several diseases^{32,33} and interact with several types of medication.³⁴ We also found that of all transgender people treated with HT, approximately 22% kept their gonads in situ. These people require special attention, because the long-term effects of HT on the testes, ovaries, and

uterus are not established. These topics and other possible complications, such as cancer risks, are subjects for further research.

ACKNOWLEDGMENT

The authors would like to thank Jos A.J. Megens for his role in accurate administrative work which helped us defining the study population.

Corresponding Author: M. den Heijer, MD, PhD, Department of Internal Medicine, Section Endocrinology, VU University Medical Center, PO Box 7057, 1007 MB Amsterdam, the Netherlands. Tel: +31-20-444-0530; Fax: +31-20-444-4313; E-mail: m.denheijer@vumc.nl

Conflicts of Interest: The authors report no conflicts of interest.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

STATEMENT OF AUTHORSHIP

Category 1

(a) Conception and Design

C.M. Wiepjes; N.M. Nota; C.J.M. de Blok; M. Klaver; R.T. de Jongh; P. Cohen-Kettenis; L.J.G. Gooren; B.P.C. Kreukels; M. den Heijer

(b) Acquisition of Data

C.M. Wiepjes; N.M. Nota; C.J.M. de Blok; M. Klaver; T.D. Steensma; B.P.C. Kreukels

(c) Analysis and Interpretation of Data

C.M. Wiepjes; N.M. Nota; C.J.M. de Blok; M. Klaver; A.L.C. de Vries; S.A. Wensing-Kruger; R.T. de Jongh; M. Bouman; T.D. Steensma; P. Cohen-Kettenis; L.J.G. Gooren; B.P.C. Kreukels; M. den Heijer

Category 2

(a) Drafting the Article

C.M. Wiepjes; N.M. Nota; P. Cohen-Kettenis; L.J.G. Gooren; B.P.C. Kreukels

(b) Revising It for Intellectual Content N.M. Nota; C.J.M. de Blok; M. Klaver; A.L.C. de Vries; S.A. Wensing-Kruger; R.T. de Jongh; M. Bouman; T.D. Steensma; P. Cohen-Kettenis; L.J.G. Gooren; B.P.C. Kreukels; M. den Heijer

Category 3

(a) Final Approval of the Completed Article

C.M. Wiepjes; N.M. Nota; C.J.M. de Blok; M. Klaver; A.L.C. de Vries; S.A. Wensing-Kruger; R.T. de Jongh; M. Bouman; T.D. Steensma; P. Cohen-Kettenis; L.J.G. Gooren; B.P.C. Kreukels; M. den Heijer

REFERENCES

 American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

Amsterdam Cohort of Gender Dysphoria Study

- 2. Wylie K, Knudson G, Khan SI, et al. Serving transgender people: clinical care considerations and service delivery models in transgender health. Lancet 2016;388:401-411.
- **3.** Arcelus J, Bouman WP, Van Den Noortgate W, et al. Systematic review and meta-analysis of prevalence studies in transsexualism. **Eur Psychiatry 2015;30:807-815.**
- De Cuypere G, Van Hemelrijck M, Michel A, et al. Prevalence and demography of transsexualism in Belgium. Eur Psychiatry 2007;22:137-141.
- Esteva de Antonio I, Gomez-Gil E, Almaraz MC, et al. [Organization of healthcare for transsexual persons in the Spanish national health system]. Gac Sanit 2012;26:203-209 [in Spanish].
- 6. Caldarera A, Pfäfflin F. Transsexualism and sex reassignment surgery in Italy. Int J Transgend 2011;13:26-36.
- Dhejne C, Oberg K, Arver S, et al. An analysis of all applications for sex reassignment surgery in Sweden, 1960–2010: prevalence, incidence, and regrets. Arch Sex Behav 2014; 43:1535-1545.
- 8. Bakker A, van Kesteren P, Gooren L, et al. The prevalence of transsexualism in the Netherlands. Acta Psychiatr Scand 1993;87:237-238.
- 9. Van Kesteren P, Asscheman H, Megens J, et al. Mortality and morbidity in transsexual subjects treated with cross-sex hormones. Clin Endocrinol 1997;47:337-342.
- Cohen-Kettenis PT, Delemarre-van de Waal HA, Gooren LJ. The treatment of adolescent transsexuals: changing insights. J Sex Med 2008;5:1892-1897.
- Kreukels BP, Cohen-Kettenis PT. Puberty suppression in gender identity disorder: the Amsterdam experience. Nat Rev Endocrinol 2011;7:466-472.
- 12. World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: World Health Organization; 1993.
- Asscheman H, Giltay EJ, Megens JA, et al. A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. Eur J Endocrinol 2011; 164:635-642.
- 14. Asscheman H, Gooren LJG, Eklund PLE. Mortality and morbidity in transsexual patients with cross-gender hormone treatment. Metabolism 1989;38:869-873.
- Dekker MJ, Wierckx K, Van Caenegem E, et al. A European network for the investigation of gender incongruence: endocrine part. J Sex Med 2016;13:994-999.
- Kreukels BP, Haraldsen IR, De Cuypere G, et al. A European network for the investigation of gender incongruence: the ENIGI initiative. Eur Psychiatry 2012;27:445-450.
- 17. Aitken M, Steensma TD, Blanchard R, et al. Evidence for an altered sex ratio in clinic-referred adolescents with gender dysphoria. J Sex Med 2015;12:756-763.

- de Vries AL, Cohen-Kettenis PT. Clinical management of gender dysphoria in children and adolescents: the Dutch approach. J Homosex 2012;59:301-320.
- Sullivan KM, Dean A, Soe MM. OpenEpi: a web-based epidemiologic and statistical calculator for public health. Public Health Rep 2009;124:471-474.
- 20. Kuyper L. Transgenders in Nederland: prevalentie en attitudes. Tijdschr Seksuol 2012;36:129-135 [in Dutch].
- 21. Kuyper L, Wijsen C. Gender identities and gender dysphoria in the Netherlands. Arch Sex Behav 2014;43:377-385.
- Wallien MSC, Cohen-Kettenis PT. Psychosexual outcome of gender-dysphoric children. J Am Acad Child Adolesc Psychiatry 2008;47:1413-1423.
- 23. Ristori J, Steensma TD. Gender dysphoria in childhood. Int Rev Psychiatry 2016;28:13-20.
- 24. Beek TF, Kreukels BP, Cohen-Kettenis PT, et al. Partial treatment requests and underlying motives of applicants for gender affirming interventions. J Sex Med 2015;12:2201-2205.
- 25. De Cuypere G, Gijs L. Care for adults with gender dysphoria. In: Kreukels BPC, Steensma TD, de Vries ALC, eds. Gender dysphoria and disorders of sex development: progress in care and knowledge. New York: Springer Science + Business Media; 2014. p. 231-254.
- 26. Johansson A, Sundbom E, Hojerback T, et al. A five-year follow-up study of Swedish adults with gender identity disorder. Arch Sex Behav 2010;39:1429-1437.
- Wierckx K, Elaut E, Declercq E, et al. Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: a case-control study. Eur J Endocrinol 2013;169:471-478.
- 28. Pfäfflin F. Regrets after sex reassignment surgery. J Psychol Hum Sex 1993;5:69-85.
- 29. Vujovic S, Popovic S, Sbutega-Milosevic G, et al. Transsexualism in Serbia: a twenty-year follow-up study. J Sex Med 2009;6:1018-1023.
- Lawrence AA. Factors associated with satisfaction or regret following male-to-female sex reassignment surgery. Arch Sex Behav 2003;32:299-315.
- **31.** Imbimbo C, Verze P, Palmieri A, et al. A report from a single institute's 14-year experience in treatment of male-to-female transsexuals. J Sex Med 2009;6:2736-2745.
- 32. Johnson EL, Kaplan PW. Caring for transgender patients with epilepsy. Epilepsia 2017;58:1667-1672.
- **33.** Tauboll E, Sveberg L, Svalheim S. Interactions between hormones and epilepsy. **Seizure 2015;28:3-11.**
- Polderman KH, Gooren LJG, Asscheman H, et al. Induction of insulin resistance by androgens and estrogens. J Clin Endocrinol Metab 1994;79:265-271.