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ORIGINAL ARTICLE

Fertility preservation and fertility treatment in transgender adolescents and adults in a Swedish region, 2013–2018

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STUDY QUESTION: In a transgender population referred for fertility consultation, which factors influence the decision to cryopreserve oocytes and sperm?

SUMMARY ANSWER: Previous hormonal treatment, gender affirmation surgery and sexual orientation were associated with the decision to undergo fertility preservation and transgender women underwent fertility preservation more frequently than transgender men.

WHAT IS KNOWN ALREADY: It is well-known internationally that fertility preservation and fertility treatment are increasingly requested by transgender men and women. Factors affecting their decisions as well as treatment differences between transgender women and transgender men have been reported, but many studies have had low participation rates and small sample sizes.

STUDY DESIGN, SIZE, DURATION: This retrospective cohort study, conducted during 2013–2018, included 78 transgender women (assigned male at birth and referred for sperm cryopreservation) and 164 transgender men (assigned female at birth referred for oocyte cryopreservation).

PARTICIPANTS/MATERIALS, SETTING, METHODS: In 2013, the previous requirement for sterilization before completion of a legal gender change was removed in Sweden. All fertile-aged transgender men and transgender women referred to a tertiary care centre for consultation concerning fertility preservation, fertility treatment or hysterectomy were identified from administrative systems. Demographic, medical and treatment data were extracted from electronic medical records and from an ART database. Logistic regression was applied to analyse factors affecting the decision to cryopreserve gametes among transgender men and transgender women.

MAIN RESULTS AND THE ROLE OF CHANCE: A majority of transgender men (69.5%) and transgender women (82%), wanted to become parents. Fertility preservation was less frequent in transgender men than in transgender women (26.2% versus 75.6%, respectively). No individuals among those primarily referred for hysterectomy opted for cryopreservation of oocytes. Among transgender men, young age, no previous hormonal treatment and stating homosexual orientation were independent factors associated with the decision to cryopreserve oocytes. Among transgender women, the decision to undergo gender affirmation surgery and stating heterosexual orientation were independent factors associated with a decision to refrain from fertility preservation. Fertility treatments, using IUI or IVF with donor sperm, were mainly performed in partners of transgender men. Ten live births were reported in the group of transgender men and two for transgender women.

LIMITATIONS, REASONS FOR CAUTION: The main limitation is the retrospective nature of the study, with missing data for many variables. The short study period and the study population being too young to permit observation of long-term outcomes of fertility preservation and fertility treatments are reasons for caution.

WIDER IMPLICATIONS OF THE FINDINGS: Our results confirm that fertility preservation has been requested by transgender people since the change in Swedish legislation in 2013. Information about aspects of fertility early in the transition process is important, since hormonal and surgical treatments may have a large impact on the decision to undergo fertility preservation. It is important to train fertility clinic staff to identify and handle the specific obstacles, as well as address the need for information and support that transgender people may have when planning for fertility preservation, fertility treatment and pregnancy.

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Key words: gender dysphoria / transgender / fertility preservation / cryopreservation / oocyte cryopreservation / sperm cryopreservation / fertility treatment / hysterectomy / sexual orientation

WHAT DOES THIS MEAN FOR PATIENTS?

In 2013, the previous requirement for sterilization before completion of a legal gender change was removed in Sweden. The new law enables people to make their own decisions concerning surgical treatment, fertility preservation and fertility treatment for parenthood. We wanted to know whether transgender individuals in Sweden have used these possibilities. Here, all individuals assigned female at birth who were referred for egg (oocyte) cryopreservation are called transgender men, and all individuals assigned male at birth and referred for sperm cryopreservation are called transgender women. We found that a majority (69.5% in transgender men and 82.1% in transgender women) wanted to become parents. Cryo-preservation of oocytes was less frequent than cryopreservation of sperm (26% versus 76%). An early discussion about fertility is important, since the factors we identified that may have a large impact on the decision to undergo fertility preservation were previous hormonal treatment and planned or completed gender affirmation surgery. Fertility treatments and pregnancies were mainly found in partners of transgender men. These findings may be useful for transgender persons and will hopefully increase their quality of healthcare by improving knowledge among healthcare providers.

Introduction

Gender dysphoria is defined as psychological distress or discomfort caused by incongruence between a person's gender assigned at birth and the gender with which he/she identifies him- or herself (Coleman *et al.*, 2012). Sweden was the first country in the world to enact legislation for legal gender change (Swedish Law (1972:19)). This law required a person to be unmarried and sterilized in order to complete the legal gender change. However, this requirement was abandoned according to the new amended Swedish law dated 1 July 2013 (Swedish Law (2013:405); Payne and Erbenius, 2018).

The estimated prevalence of gender dysphoria diagnosis during the last 50 years has increased (Dhejne *et al.*, 2014; Arcelus *et al.*, 2015; Rafferty et al., 2018) and is now higher among the younger general population, with a predominance of transgender men (Aitken *et al.*, 2015; Butler *et al.*, 2018). In Sweden, there was a pronounced increase in the incidence of applications for legal gender change after 2000 (Dhejne *et al.*, 2014). The number of people with diagnoses related to gender dysphoria increased threefold (from 464 to 1365) between 2007 and 2013; the corresponding figure was fivefold (from 14 to 78) for people aged <18 years (National Guidelines from the National Board of Health and Welfare Sweden, 2015).

Recent studies have indicated that between one- and two-thirds of transgender adolescents express a desire to have children in the future (Auer *et al.*, 2018; Baram *et al.*, 2019; Nahata et al., 2020). Genital gender affirmation surgery, such as penectomy and orchidectomy in transgender women or hysterectomy with bilateral oophorectomy in transgender men, lead irreversibly to sterility. Gender-affirming hormonal therapy (GAHT) most often comprises oestrogen combined with peripheral androgen receptor blockade for transgender women and testosterone for transgender men. GAHT has negative effects on fertility and the knowledge about reversal of these effects after treatment cessation is still limited (De Roo et al., 2016; Adeleye et al., 2019; Moravek, 2019; Moravek *et al.*, 2020). A high occurrence of sperm abnormalities was found, especially after previous GAHT, in a recent large prospective study on sperm quality in transgender women (Rodriguez-Wallberg *et al.*, 2021). International guidelines recommend that all transgender people receive fertility counselling before GAHT (Coleman *et al.*, 2012; Ethics Committee of the American Society for Reproductive Medicine, 2015; Finlayson *et al.*, 2016; Hembree *et al.*, 2017; Rafferty et al., 2018). Legislation on assisted reproduction and healthcare services varies considerably between the European countries, according to the ESHRE Guideline Group on Female Fertility Preservation (ESHRE Guideline Group on Female Fertility Preservation et al., 2020). In Sweden, referral for fertility consultation prior to initiation of GAHT is recommended. Concurring with national and international guidelines, fertility preservation and fertility treatment are offered in Sweden and subsidized within the national healthcare system.

The most common available options for fertility preservation are cryopreservation of sperm obtained through masturbation in the case of transgender women, and cryopreservation of oocytes after ovarian stimulation in the case of transgender men (James-Abra *et al.*, 2015). In the current study, all individuals assigned female at birth referred for oocyte cryopreservation are referred to as transgender men; and all individuals assigned male at birth and referred for sperm cryopreservation are referred to as transgender women.

Cryopreservation of embryos for transgender men requires sperm from a partner or a sperm donor and in Sweden, this is only permitted

to achieve a pregnancy within a stable relationship. Cryopreservation of testicular or ovarian tissue, albeit still considered experimental, might be a future option (De Roo *et al.*, 2016; Schneider *et al.*, 2019; Grin *et al.*, 2021).

Transgender women and transgender men have the same option of donor sperm treatment of a partner. According to the current Swedish legislation, treatment of a partner with IUI or IVF/ICSI, with fresh or cryopreserved sperm, are the options for transgender women to become genetically related parents. Transgender men who decide to retain their reproductive organs have the option of genetically related pregnancies and childbearing using their own oocytes after discontinuing androgen therapy (Light *et al.*, 2014; Leung *et al.*, 2019). During the study period, neither embryo donation nor double donation (oocytes and sperm) were legal in Sweden, where surrogacy is currently prohibited, limiting the options for genetic parenthood for some couples (Stenfelt *et al.*, 2018).

The earlier reported use of fertility preservation varies from 10% to 82% in transgender women and from 0% to 17% in transgender men according to one meta-analysis which includes studies worldwide (Baram *et al.*, 2019). However, lower frequencies of fertility consultation and fertility preservation have been noted among transgender adolescents (Nahata *et al.*, 2017; Auer *et al.*, 2018; Lai *et al.*, 2020). Barriers to fertility preservation were discomfort with masturbation among transgender women and the invasiveness of procedures among transgender men (Chen *et al.* 2017; Nahata *et al.*, 2017; Baram *et al.*, 2019). Other considerations, such as varying desire for parenthood, individual experiences of gender dysphoria, cost and a wish not to delay the medical transition, influenced decisions concerning fertility preservation (Chen *et al.*, 2017, 2019). In a recent study, higher percentages of fertility consultation (91%) and fertility preservation (38%) in transgender girls than observed in earlier studies were reported from the Netherlands (Brik *et al.*, 2019). So far, a limited number of studies on this issue have been conducted, most of them outside Sweden. Prior to the change in Swedish law, described in a recent Swedish study (Armuand *et al.*, 2020), there was no legal way to have biological children after a legal gender change. The new law enables the individual's own decisions concerning surgical treatment, fertility preservation and fertility treatment for genetic and biological parenthood. We found it valuable to investigate whether people with gender dysphoria in Sweden have utilized these possibilities.

Objectives

Our aim was to study the transgender population referred for fertility consultation and their decisions to undergo fertility preservation and fertility treatment after the 2013 change in legislation. We aimed to explore and identify characteristics predictive for the decision to undergo fertility preservation, as well as to assess the results of fertility preservation and fertility treatments.

Materials and methods

We conducted a retrospective cohort study analysing data from the charts of transgender individuals referred for fertility consultation, including discussion of fertility preservation, fertility treatment and hysterectomy. We also retrieved data on the results of fertility treatments, in terms of pregnancies and live births.

Study population

The Department of Reproductive Medicine at Sahlgrenska University Hospital in Gothenburg, Sweden, is a referral centre for our region and covers a population of 1.7 million. All patients of fertile age with International Classification of Disease (ICD)-10 codes for gender dysphoria (transsexualism (F64.0), other gender identity disorders (F64.8) or unspecified gender identity disorder (F 64.9)), referred for fertility consultation between January 2013 and December 2018, were considered for inclusion. Inclusion criteria were age under 40 years for transgender men and age under 56 years for transgender women. Individuals with one of the F.64 ICD-10 codes for gender dysphoria were identified in the hospital database. Based on the personal identification number held by every resident of Sweden, individual medical data were retrieved from four different databases. In the current study, for simplicity and clarity, and regardless of the F.64 ICD10 specific coding, all individuals assigned female at birth and referred for oocyte cryopreservation are referred to as transgender men; and all individuals assigned male at birth and referred for sperm cryopreservation are referred to as transgender women. Both study groups included individuals with different gender identity disorders.

Available fertility preservation options for transgender women were cryopreservation of sperm, obtained through masturbation or retrieved surgically by testicular sperm aspiration (TESA) or percutaneous epididymal sperm aspiration (PESA), in cases of very low sperm count or azoospermia. Fertility preservation options for transgender men included cryopreservation of oocytes or embryos, preceded by transvaginal oocyte aspiration after ovarian stimulation, according to a GnRH antagonist protocol with the addition of Letrozole. In this study, only cryopreservation of oocytes and semen were requested and is hereafter referred to as fertility preservation.

Variables

Extracted data included patients' age at referral, somatic, psychiatric and neuropsychiatric diagnoses, duration of previous GAHT, obesity (BMI $\geq$ 30 kg/m^2), previous pregnancies and parity, occupation, educational level, relationship status and sexual orientation. Sexual orientation possibilities included heterosexual, homosexual, bisexual, pansexual, asexual and undecided orientation. For data analysis purposes, we dichotomized the sexual orientation variable, with the following two categories: heterosexual and non-heterosexual (which includes homosexual, bisexual, pansexual, asexual and undecided options). The data also included history of gender affirmation surgery, comprising mastectomy, hysterectomy, breast augmentation and genital surgery in this study. Genital gender affirmation surgery comprised phalloplasty and metoidioplasty for transgender men and orchiectomy, penectomy and vaginoplasty for transgender women. These surgical variables could either consist of a decision to undergo, or of having undergone, surgery. Data on desire to become a parent and on planned method of achieving parenthood, as well as on reasons to decline fertility preservation, were also extracted from medical records.

Variables related to fertility preservation included number of ovarian stimulation cycles, number of ejaculations and number of cryopreserved oocytes or semen straws. The semen parameters volume, total sperm count, sperm concentration and sperm motility were assessed according to World Health Organization (WHO) reference values. Sperm abnormalities were defined according to WHO criteria

(Cooper et al., 2010). Three groups were created: one with normal parameters, a second group with at least one deviating parameter, and a third group with azoospermia (absence of spermatozoa in the ejaculate). The number and outcomes of fertility treatments were noted and included type of treatment, achieved pregnancy, miscarriage and live birth.

Ethics

The study was approved by the Swedish Ethical Review Authority (permit number 2019-03399, 14 August 2019).

Statistics

Statistical analyses were performed using the IBM Statistical Package for the Social Sciences (SPSS), version 22.0 for Windows (IBM, NY, USA). The χ^2 test or Fisher's exact test was used for categorical variables and the Mann–Whitney U test was applied for continuous variables. All tests were two-sided and a *P*-value of <0.05 was considered statistically significant. Univariable logistic regression analyses for the dependent variable 'cryopreservation of gametes' were performed and presented as odds ratio (OR) and 95% CI. The number of covariates to be included in the multivariable logistic regression analyses was limited by the size of the smallest group (number of events or non-events). The final inclusion of pre-specified covariates in the multivariable analyses was based on the significance level in the univariable analyses, the likelihood for interaction between covariates and the frequency of missing values. The maximum number of covariates to be included was limited by the number of events in each analysis. Furthermore, the covariate 'desire to have children' was excluded from both multivariable analyses, since it can be regarded as a prerequisite for a decision to undergo fertility preservation. Results were presented with adjusted OR and 95% CI. Descriptive statistics were presented as mean, SD, median, minimum and maximum values (continuous variables) or as number and percentage (categorical variables).

Results

During the study period, 265 individuals were referred and all 242 who attended the fertility consultation were included in the transgender study population. Two-thirds were transgender men and one-third were transgender women. The demographic characteristics of the study population are presented in Table I. The transgender men had more often started their hormonal treatment and initiated their gender affirmation surgery than the transgender women. Heterosexual orientation was more common among the transgender men, while homosexual orientation was stated more often among the transgender women.

Transgender men

Of 175 referred transgender men, the 164 who attended a first visit constitute the transgender men study population (Fig. 1). Reasons for referral were fertility consultation (n = 119), request for partner treatment (n = 6) and request for hysterectomy (n = 39). The 11 transgender men who did not attend a first visit only differed with respect to age, compared to the study group (mean 20.0 versus 23.9 years, $P = 0.03$).

Request for hysterectomy was the reason for referral in 39 cases, all of whom had a fertility consultation. These individuals were older than those referred primarily for fertility consultation (mean 26.8 versus 23.0 years, $P < 0.001$). All of them decided not to undergo fertility preservation and they were excluded from further analysis. Twenty-one did undergo hysterectomy (Fig. 1).

Demography of the group attending fertility consultation

Among the 125 transgender men referred primarily for fertility consultation or due to a request for partner treatment, 43 (34.4%) decided to undergo and completed fertility preservation. The remaining 82 (65.6%) decided against fertility preservation. Demographic variables in the groups, based on the decision to undergo fertility preservation, are shown in Table II. Transgender men who underwent fertility preservation were younger and more often students in or after elementary school, compared with the group who did not. Furthermore, they had less often started hormonal treatment. Mastectomy was common in both groups. Subjects deciding to undergo fertility preservation were less often living in a relationship and defined themselves more often as homosexual. Among those who underwent fertility preservation, it was more common to accept carrying a pregnancy themselves. The desire to have children was high in both groups.

The most frequent somatic diagnoses were asthma and polycystic ovary syndrome. Among the psychiatric diagnoses, depression and anxiety were the most common. The two most common neuropsychiatric diagnoses were attention deficit disorder (ADD) and attention deficit and hyperactivity disorder (ADHD).

High age and severe comorbidity were reasons for the clinic to decline fertility preservation (11.5%). Patients' stated that reasons not to undergo fertility preservation were unwillingness to delay or stop hormonal treatment (5%), plan for partner treatment (21.5%), reluctance to undergo physical examination, and failure to adhere to the work-up to confirm the gender dysphoria diagnosis (11%). Reasons were not stated in 51%.

Factors affecting the decision to undergo fertility preservation

Univariable logistic regression analyses of transgender men revealed that young age, not having started hormonal treatment, being a student, having a low educational level, not having a partner, stating homosexual orientation and desire to have children were positively associated with a decision to undergo fertility preservation. Table III presents the underlying data used for the univariable analyses (Fig. 2). In the multivariable analysis, higher age (adjusted OR 0.86 (95% CI 0.77–0.95), $P = 0.004$), and previous hormonal treatment (adjusted OR 0.07 (95% CI 0.01–0.40), $P = 0.002$) were independent factors reducing the likelihood of deciding to undergo fertility preservation, while stating homosexual orientation (adjusted OR 9.21 (95% CI 2.35–36.04), $P = 0.001$) was an independent positive predictive factor. The covariate 'not having a partner' was also included in the model but did not remain independently predictive.

Fertility preservation results

Forty-three patients chose and successfully completed cryopreservation of oocytes (missing data from one person treated abroad). The first ovarian stimulation cycle in 42 individuals resulted in a mean of

Table I Demographic characteristics for all transgender patients attending for their first fertility consultation.

Variable	Transgender men* n = 164	Transgender women* n = 78	*P*-value
Age, years, *mean (SD)*	23.9 (5.8)	24.4 (6.6	0.52[1]
median (min; max)	23 (13; 40)	23 (13; 51)	
Obesity, (BMI $\geq$ 30 kg/m^2), *n (%)*	21 (12.8)	7 (9.0)	0.51
Missing	11 (6.7)	5 (6.4)	
Concurrent diagnoses, *n (%)*			
Neuropsychiatric	46 (28.0)	14 (17.9)	0.12
Psychiatric	81 (49.4)	35 (44.9)	0.60
Somatic	41 (25.0)	14 (17.9)	0.29
Previous hormonal treatment, *n (%)*	74 (45.1)	17 (21.8)	0.001
Gender affirmation surgery, *n (%)*	141 (86.0)	33 (42.3)	<0.001
Any surgery, planned or completed			
Genital gender affirmation surgery	(8 + 6 + 5)/162	(18 + 8)/77	<0.001
Completed	8 (4.9)	18 (23.1)	
Partly completed	6 (3.7)	–	
Waiting list	5 (3.0)	8 (10.3)	
Missing	2 (1.2)	1 (1.3)	
Mastectomy	136 (82.9)	N/A	
Waiting list	5 (3.0)	–	
Missing	1 (0.6)	–	
Breast augmentation	N/A	25 (32.1)	
Waiting list	–	3 (3.8)	
Missing	–	1 (1.3)	
Hysterectomy	38 (23.2)	N/A	
Waiting list	4 (2.4)	–	
Occupation, *n (%)*			
Student	81 (49.4)	31 (39.7)	0.15
Employed	57 (34.8)	25 (32.1)	(Student versus all others, excluding missing)
Unemployed	5 (3.0)	13 (16.7)	
Sick leave	10 (6.1)	7 (9.0)	
Welfare benefit	3 (1.8)	–	
Other	2 (1.2)	1 (1.3)	
Missing	6 (3.7)	1 (1.3)	
Education, *n (%)*			
Elementary school, not completed	7 (4.3)	4 (5.1)	0.16
Elementary school, completed	36 (22.0)	14 (17.9)	(Elementary school versus all others, excluding missing)
Secondary school	59 (36.0)	43 (55.1)	
University	14 (8.5)	7 (9.0)	
Other education	2 (1.2)	3 (3.8)	
Missing	46 (28.0)	7 (9.0)	
Children, *n (%)*			
Biological child/children	4 (2.4)	1 (1.3)	
Partner has child/children	9 (5.5)	1 (1.3)	
No children	151 (92.1)	76 (97.4)	0.18
Relationship, *n (%)*			
None	77 (47.0)	53 (67.9)	0.04
Heterosexual	54 (32.9)	5 (6.4)	(None versus all others, excluding missing)
Same-sex relationship	16 (9.8)	16 (20.5)	
Missing	17 (10.4)	4 (5.1)	

(continued)

Table I Continued

Variable	Transgender men* n = 164	Transgender women* n = 78	*P*-value
Sexual orientation, *n (%)*			
Heterosexual	78 (47.6)	9 (11.5)	<0.001
Homosexual	28 (17.1)	37 (47.4)	(Heterosexual versus all others)
Bisexual	8 (4.9)	14 (17.9)	
Pansexual	4 (2.4)	1 (1.3)	<0.001
Asexual	6 (3.7)	–	(Homosexual versus all others, excluding missing)
Undecided	9 (5.5)	10 (12.8)	
Missing	31 (18.9)	7 (9.0)	
Desire to have children, *n (%)*			
Yes	114 (69.5)	64 (82.1)	0.24
No	19 (11.6)	–	(Yes versus all others, excluding missing)
Not sure	16 (9.8)	12 (15.4)	
Missing	15 (9.1)	2 (2.6)	
Previous pregnancies, *n (%)*		N/A	
Birth	3 (1.8)	–	
Miscarriage	1 (0.6)	–	
Termination of pregnancy	1 (0.6)	–	

N/A, not applicable.
*In the current study, all individuals assigned female at birth referred for oocyte cryopreservation are referred to as transgender men; and all individuals assigned male at birth and referred for sperm cryopreservation are referred to as transgender women.
[1]The χ^2 test or Fisher's exact test were used for categorical variables and the Mann–Whitney U test was applied for continuous variables (in this table only age). All tests were two-sided and a *P*-value of <0.05 was considered statistically significant.

12.6 retrieved oocytes (range 0–30). Three patients without oocyte recovery in the first treatment cycle underwent a second stimulation cycle with successful retrieval (mean: 12.0 oocytes, range 2–17).

Outcomes of fertility treatment

So far, 1 of 43 oocyte cohorts have been utilized and resulted in pregnancy, and several couples are awaiting fertility treatment. A total of 15 pregnancies have occurred among the 164 transgender men (9.1%), resulting in 10 live births, one ongoing pregnancy and four miscarriages (Fig. 1). In two cases, pregnancies have been achieved after IUI with donor sperm. The remaining pregnancies required IVF/ICSI treatment with donor sperm. In all cases but one, the pregnancy was carried by a partner.

Transgender women

Of 90 referred transgender women, 78 attended a first visit, and they constitute the transgender women study population (Fig. 3). One was primarily referred for fertility treatment of a partner, while the remaining 77 were referred for fertility consultation. The 12 non-attendees did not differ in any demographic aspect, compared with the study population.

Demography of the group attending fertility consultation

The 59 transgender women who decided to undergo fertility preservation (76%) had to a lesser extent decided to undergo gender affirmation surgery (Table IV). Individuals deciding to undergo fertility preservation were less likely to identify themselves as heterosexual, compared with the group not undergoing fertility preservation. Transgender women were rarely living with children and the desire to have children was high in both groups. Asthma was the most common somatic diagnosis. Depression and anxiety were the most common psychiatric diagnoses, and ADHD and ADD were the most common neuropsychiatric diagnoses.

Nineteen transgender women declined fertility preservation. High age and patient's failure to attend for follow-up were reasons for the clinic to decline fertility preservation (11%). Patients' stated reasons not to undergo fertility preservation were unwillingness to interrupt or delay hormonal treatment (16%), plan for partner treatment (5%), and failure to adhere to the workup to confirm the gender dysphoria diagnosis (21%). Reasons were not stated in 47%.

Factors affecting the decision to undergo fertility preservation

In the univariable analyses of transgender women, gender affirmation surgery and stating heterosexual orientation were negatively associated with the decision to undergo fertility preservation, while there was a positive association for desire to have children. There was a borderline significant negative association with previous hormonal treatment. Table III presents the underlying data used for the univariable analyses (Fig. 4). The sample size, with 19 declining fertility preservation, allowed two covariates to be included in the model. In the multivariable analysis, the decision to postpone or not to undergo gender affirmation surgery (adjusted OR 0.20 (95% CI 0.06–0.72), $P = 0.013$) and stating non-heterosexual orientation (adjusted OR 0.16 (95% CI 0.03–0.82), $P = 0.027$) were independent predictive factors for the decision to undergo fertility preservation.

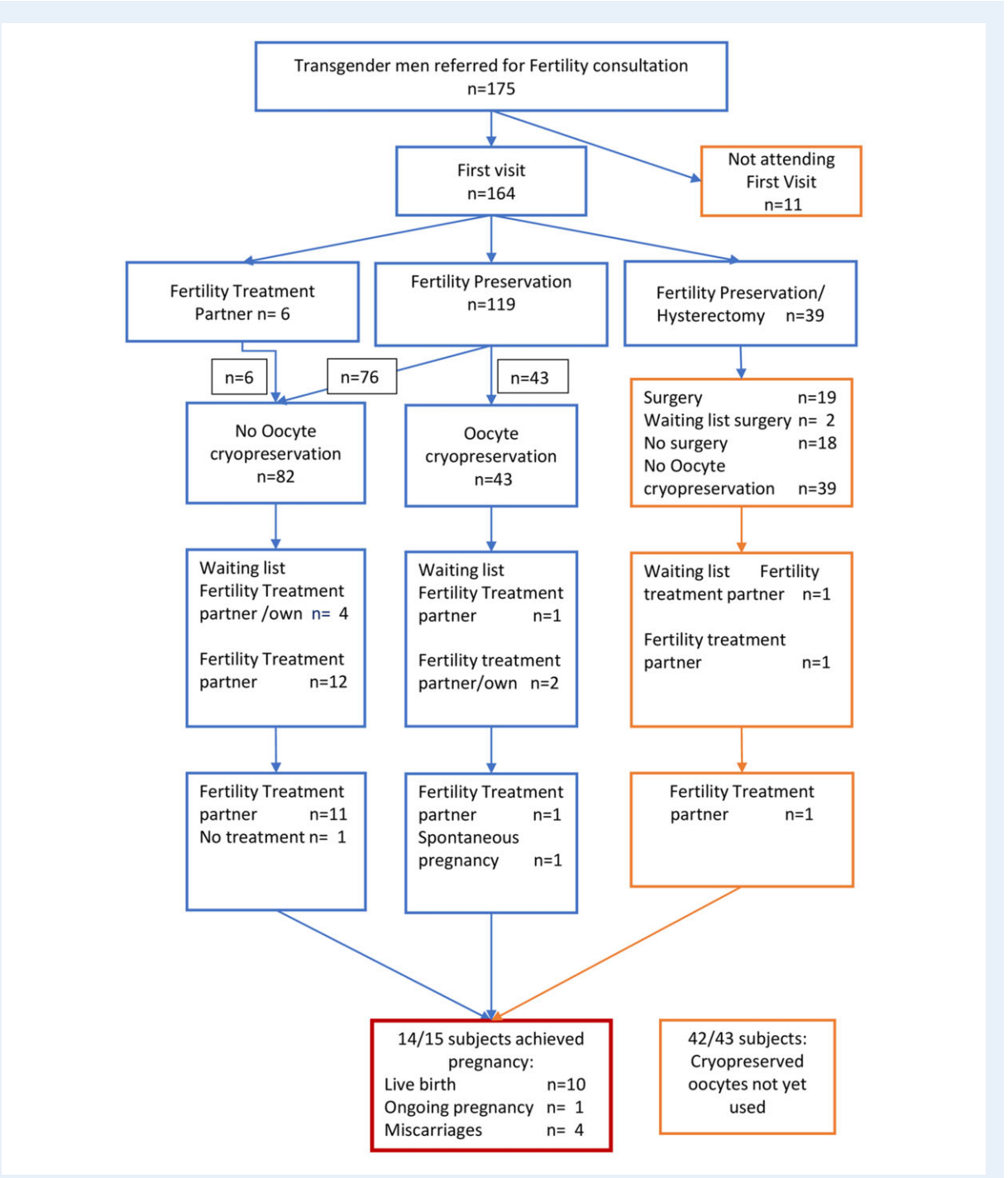

Figure 1. Flowchart of transgender men referred for fertility consultation and outcomes of fertility preservation and fertility treatments. In the current study, all individuals assigned female at birth referred for oocyte cryopreservation are referred to as transgender men.

Fertility preservation results

Fifty-nine transgender women attempted, and 53 successfully completed, cryopreservation of sperm with two or three collections. Six attempted cryopreservation repeatedly, but with no retrieval of sperm, owing to azoospermia. Four of these had azoospermia after 3 months of discontinued hormonal treatment, while two had had no previous hormonal treatment. In one case, both TESA and PESA were attempted and in one case only TESA

Table II Demographics of transgender men* referred for fertility consultation.

Variable	Oocyte cryo-preservation n = 43	No oocyte cryo-preservation n = 82	*P*-value
Age, years, *mean (SD)*	19.9 (4.3)	24.6 (5.4)	<0.001[2]
median (min; max)	18 (13; 32)	24 (15; 39)	
Obesity, (BMI ≥30 kg/m^2), *n (%)*	5 (11.9)	11 (14.1)	1.00
Missing	1	4	
Concurrent diagnoses, *n (%)*			
Neuropsychiatric	14 (32.6)	20 (24.4)	0.40
Psychiatric	23 (53.5)	40 (48.8)	0.71
Somatic	12 (27.9)	19 (23.2)	0.66
Previous hormonal treatment, *n (%)*	2 (4.7)	38 (46.3)	<0.001
Gender affirmation surgery, *n (%)*	34 (79.1)	70 (85.4)	0.45
Any surgery, planned or completed			
Genital gender affirmation surgery			1.00
Completed	0	2 (2.4)	
Partly completed	1 (2.4)	0	
Waiting list	1 (2.4)	3 (3.7)	
Missing	1		
Mastectomy	31 (73.8)	68 (82.9)	0.61
Waiting list	3 (7.1)	2 (2.4)	
Missing	1		
Hysterectomy	4 (9.3)	15 (18.3)	0.13
Waiting list	0 (0)	2 (2.4)	
Occupation, *n (%)*			
Student	28 (68.3)	36 (46.2)	0.03
Employed	9 (22.0)	32 (41.0)	(Student versus all others)
Unemployed	2 (4.9)	1 (1.3)	
Sick leave	2 (4.9)	5 (6.4)	
Welfare benefits	0 (0)	3 (3.8)	
Other	0 (0)	1 (1.3)	
Missing	2	4	
Education, *n (%)*			
Elementary school not completed	5 (13.2)	2 (3.8)	0.001
Elementary school completed	19 (50.0)	13 (24.5)	(Elementary school versus higher education)
Secondary school	12 (31.5)	29 (54.7)	
University	2 (5.3)	9 (17.0)	
Missing	5	29	
Previous pregnancies, *n (%)*			1.00
Birth	1 (2.3)	2 (2.4)	(Any pregnancy versus none)
Miscarriage	1 (2.3)	0	
Termination of pregnancy	0	1 (1.2)	
Children, *n (%)*			0.22
Biological child/children	2 (4.7)	2 (2.4)	(Living with versus no children)
Partner child/children	0	8 (9.8)	
No children	41 (95.3)	72 (87.8)	
Relationship, *n (%)*			
Heterosexual	8 (21.1)	36 (46.2)	0.01
Same sex relationship	3 (7.9)	7 (9.0)	(Partner versus none)
No partner	27 (71.1)	35 (44.9)	
Missing	5	4	

(continued)

Table II Continued

Variable	Oocyte cryo-preservation n = 43	No oocyte cryo-preservation n = 82	*P*-value
Sexual orientation, *n (%)*			
Heterosexual	18 (47.4)	48 (64.9)	0.10
Homosexual	14 (36.8)	7 (9.5)	(Heterosexual versus all others)
Bisexual	2 (5.3)	5 (6.8)	
Pansexual	1 (2.6)	3 (4.1)	0.001
Asexual	0	5 (6.8)	(Homosexual versus all others)
Undecided	3 (7.9)	6 (8.1)	
Missing	5	8	
Desire to have children, *n (%)*			
Yes	40 (95.2)	60 (78.9)	0.02
Not sure	2 (4.8)	12 (15.8)	(Yes, versus all others)
No	0	4 (5.3)	
Missing	1	6	
Plan for parenthood, *n (%)*			
Subject carries pregnancy	11 (29.7)	6 (8.5)	0.01
Partner carries pregnancy	1 (2.7)	27 (38.0)	(Carry pregnancy versus all other options)
Internal surrogacy	5 (13.5)	9 (12.7)	
External surrogacy	2 (5.4)	1 (1.4)	
Adoption	0	3 (4.2)	
Not sure	18 (48.7)	25 (35.2)	
No wish for children	0	4	
Missing	6	7	

*In the current study, all individuals assigned female at birth referred for oocyte cryopreservation are referred to as transgender men.
[2]The χ^2 test or Fisher's exact test were used for categorical variables and the Mann–Whitney U test was applied for continuous variables (in this table only age). All tests were two-sided and a *P*-value of <0.05 was considered statistically significant.

was attempted. All cases were assessed and examined according to clinical azoospermia routines, including hormonal and genetic analysis.

Outcomes of fertility treatment

In the study population of 78 transgender women, three pregnancies have occurred, achieved through partner treatment with IVF/ICSI (3.8%), resulting in two live births and one miscarriage. Cryopreserved sperm was utilized in two cases.

Discussion

In our study of 164 transgender men and 78 transgender women who attended a fertility consultation, 26.2% of the transgender men and 75.6% of the transgender women attempted fertility preservation. All but six transgender women with azoospermia successfully achieved cryopreservation of gametes. In transgender men, younger age, no previous hormonal treatment and homosexual orientation were associated with the decision to undergo fertility preservation. Among the transgender women, not choosing gender affirmation surgery and stating a non-heterosexual orientation were associated with the decision to undergo fertility preservation. Fertility treatments in 14 individuals resulted in 15 pregnancies and 10 live births among the transgender men and their partners. The partners of three transgender women have achieved three pregnancies, two of which resulted in live births.

Concurring with previous studies, we found a higher proportion of fertility preservation among the transgender women, compared with the transgender men. Varying fertility preservation rates among transgender men (0–16.7%) and transgender women (9.6–81.8%) were found in a systematic review (Baram *et al.*, 2019). The same review found that studies with participants referred for fertility consultation at fertility centres reported higher fertility preservation rates than other studies (Armuand *et al.*, 2017; Baram *et al.*, 2019). Two studies found low rates of fertility preservation among transgender adolescents, most of whom declined fertility preservation prior to starting hormonal treatment (Chen *et al.*, 2017; Nahata *et al.*, 2017). Nearly all participants in an Australian study with a low rate (7%) of fertility preservation stated that the procedure should be offered to all transgender and non-binary individuals, but many were worried about the cost (Riggs and Bartholomaeus, 2018). In a recent study from the Netherlands including 35 young transgirls with a mean age of 14.8 years, 91% attended fertility consultation and 34% attempted fertility preservation (Brik *et al.*, 2019). This is a higher percentage than reported in previous studies although the authors did not explain this finding. However, increasing knowledge of fertility preservation methods among healthcare providers and young adults in the transgender community might be a plausible explanation. Methods are evolving and

Table III Distribution of events (fertility preservation decision) in relation to different covariates.

Covariate	Value		Transgender men*		Transgender women*	
			n (%) of events	Missing n	n (%) of events	Missing n
Age	Men	Women				
(years)[3]	13 < 20	13 < 21	25 (64.1)	0	16 (72.7)	0
	20 < 25	21 < 26	11 (23.9)		25 (78.1)	
	25–39	26–51	7 (17.5)		18 (75.0)	
Obesity	BMI ≥30 kg/m^2		5 (31.3)	5	6 (85.7)	5
	BMI <30 kg/m^2		37 (35.6)		50 (75.8)	
Neuropsychiatric diagnosis	Yes		14 (41.2)	0	11 (78.6)	0
	No		29 (31.9)		48 (75.0)	
Psychiatric diagnosis	Yes		23 (36.5)	0	29 (82.9)	0
	No		20 (32.3)		30 (69.8)	
Somatic diagnosis	Yes		12 (38.7)	0	10 (71.4)	0
	No		31 (33.0)		49 (76.6)	
Hormonal treatment	Yes		2 (5.0)	0	10 (58.8)	0
	No		41 (48.2)		49 (80.3)	
Gender affirmation surgery	Yes		34 (32.7)	0	20 (60.6)	1
	No		9 (42.9)		38 (86.4)	
Genital gender affirmation surgery	Yes		2 (28.6)	1	16 (61.5)	1
	No		40 (34.2)		42 (82.4)	
Mastectomy	Yes		34 (32.7)	1	N/A	N/A
	No		8 (40.0)			
Hysterectomy	Yes		4 (19.0)	0	N/A	N/A
	No		39 (37.5)			
Breast augmentation	Yes		N/A	N/A	16 (57.1)	1
	No				42 (85.7)	
Occupation	Student		28 (43.8)	6	25 (80.6)	1
	Employed/all others[4]		13 (23.6)		33 (71.7)	
Education	Elementary school		24 (61.5)	34	13 (72.2)	7
	Higher education[5]		14 (26.9)		41 (77.4)	
Living with children	Yes		2 (16.7)	0	2 (100.0)	0
	No children		41 (36.6)		57 (75.0)	
Relationship status	In a relationship		11 (20.4)	9	14 (66.7)	4
	No		27 (43.5)		42 (79.2)	
Sexual orientation	Heterosexual		18 (27.3)	13	4 (44.4)	7
	Others[6]		20 (43.5)		49 (79.0)	
	Homosexual		14 (66.7)	13	29 (78.4)	7
	Others[7]		24 (26.4)		24 (70.6)	
Desire to have children	Yes		40 (40.0)	7	51 (79.7)	2
	No/not sure		2 (11.1)		6 (50.0)	

*In the current study, all individuals assigned female at birth referred for oocyte cryopreservation are referred to as transgender men; and all individuals assigned male at birth and referred for sperm cryopreservation are referred to as transgender women.
[3]In tertiles of population.
[4]Others include unemployed, sick leave, social welfare and other.
[5]Higher education includes levels above elementary school.
[6]Include homosexual, bisexual, pansexual and undecided.
[7]Include heterosexual, bisexual, pansexual and undecided.

improving, which might also increase interest in fertility preservation among the transgender population in the future.

Many different factors related to the decision to decline fertility preservation have been reported in earlier studies. In our study, there were several reasons to decline fertility preservation; however, the reasons were unknown in about 50% in both groups. In previous studies, barriers to fertility preservation often differed between transgender men and transgender women, but both groups had experienced a negative impact of poor attitudes and knowledge among health care providers (Armuand *et al.*, 2017; Baram *et al.*, 2019; Chiniara *et al.*,

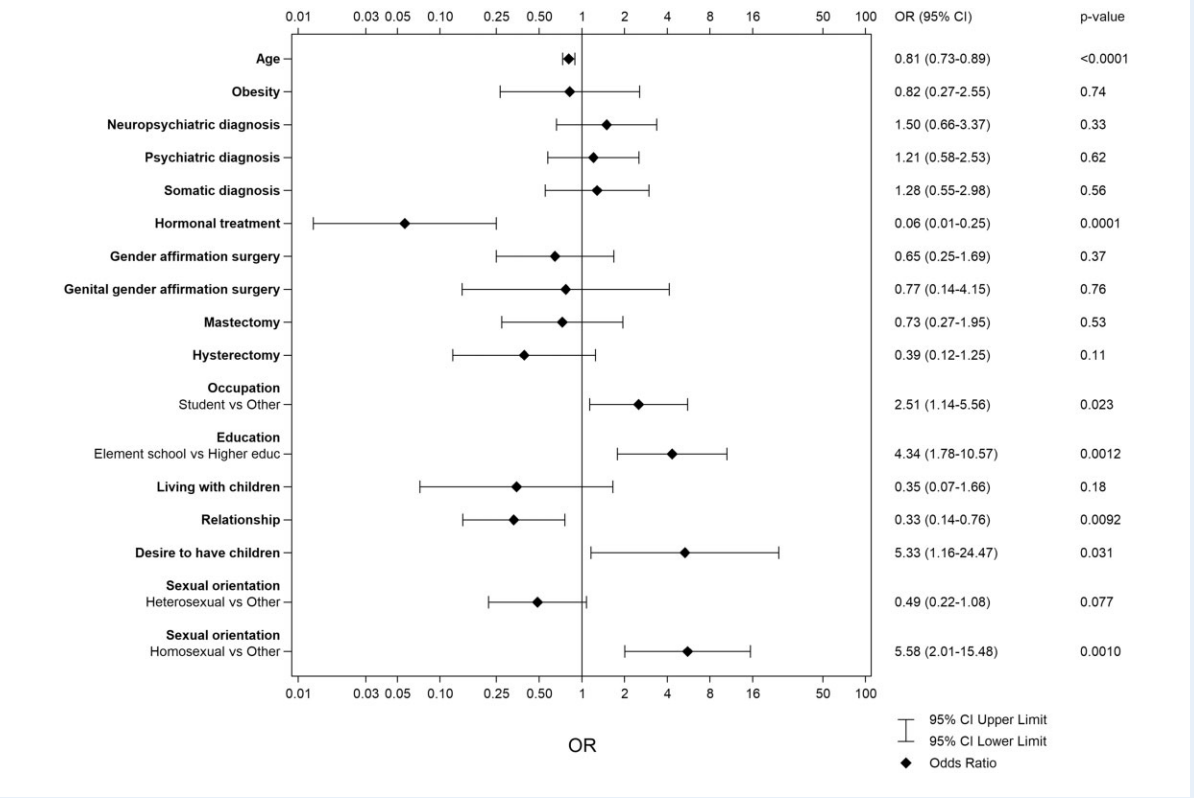

Figure 2. Univariable logistic regression analysis for the dependent variable cryopreservation of oocytes among transgender men attending fertility consultation. In the current study, all individuals assigned female at birth referred for oocyte cryopreservation are referred to as transgender men.

2019). Concerns related to stopping or delaying hormonal treatment have been investigated in previous studies, finding that the impact on fertility preservation decisions varies (Armuand *et al.*, 2017; Nahata *et al.*, 2017; Chiniara *et al.*, 2019; Persky *et al.*, 2020). In our study, 4.9% of the transgender men and 15.8% of the transgender women stated that concerns related to changes in hormone treatment was their reason to decline fertility preservation. These concerns might also have been an undisclosed factor among those where no specific reason for decline was found. Cost of procedure was a significant barrier to fertility preservation in several reports (Chen *et al.*, 2017; Riggs and Bartholomaeus, 2018). Fertility preservation is covered by the Swedish healthcare system and cost is thus an unlikely factor behind declining fertility preservation in the Swedish transgender population. In our study, adoption was a rare alternative for becoming a parent, in contrast to previous studies reporting that one-third to about half of people declining fertility preservation were considering adoption in the future (Nahata *et al.*, 2017; Chiniara *et al.*, 2019). The low cost and relatively easy access to fertility preservation in Sweden may be one important explanation for adoption being a rare parenthood alternative in our study.

Younger age was associated with the decision to undergo fertility preservation among the transgender men, but not the transgender women, in our study. To our knowledge, this finding has not been reported in previous studies. However, younger transgender girls were less likely to decide to undergo fertility preservation, according to Brik *et al.* (2019). In two earlier studies on transgender adolescents, there was no age difference between those who declined and those who decided on fertility preservation (Chen *et al.*, 2019; Persky *et al.*, 2020).

The transgender men deciding to undergo fertility preservation in our study were more often elementary school students. This variable is generally considered to be a proxy variable for socio-economic status but is most likely linked to age in our study. To our knowledge, there are few studies investigating the association between educational level and the decision to undergo fertility preservation. One study investigated factors affecting this decision in transgender adolescents, finding no difference in educational level between those who opted for and those who decided against fertility preservation (Chen *et al.*, 2019).

Many studies address concerns related to stopping or delaying hormonal treatment as a barrier to pursuing fertility preservation. We found an association between having started hormonal treatment and declining fertility preservation among the transgender men, but not among the transgender women. Another Swedish study focused on transgender men's experiences with fertility preservation and discontinuing hormonal treatment until menstruation resumed. The feminizing effects of interrupting hormonal treatment and of ovarian stimulation triggered the gender dysphoria (Armuand *et al.*, 2017). This indicates that discontinuation of hormonal treatment can be an obstacle among transgender men to pursue fertility preservation.

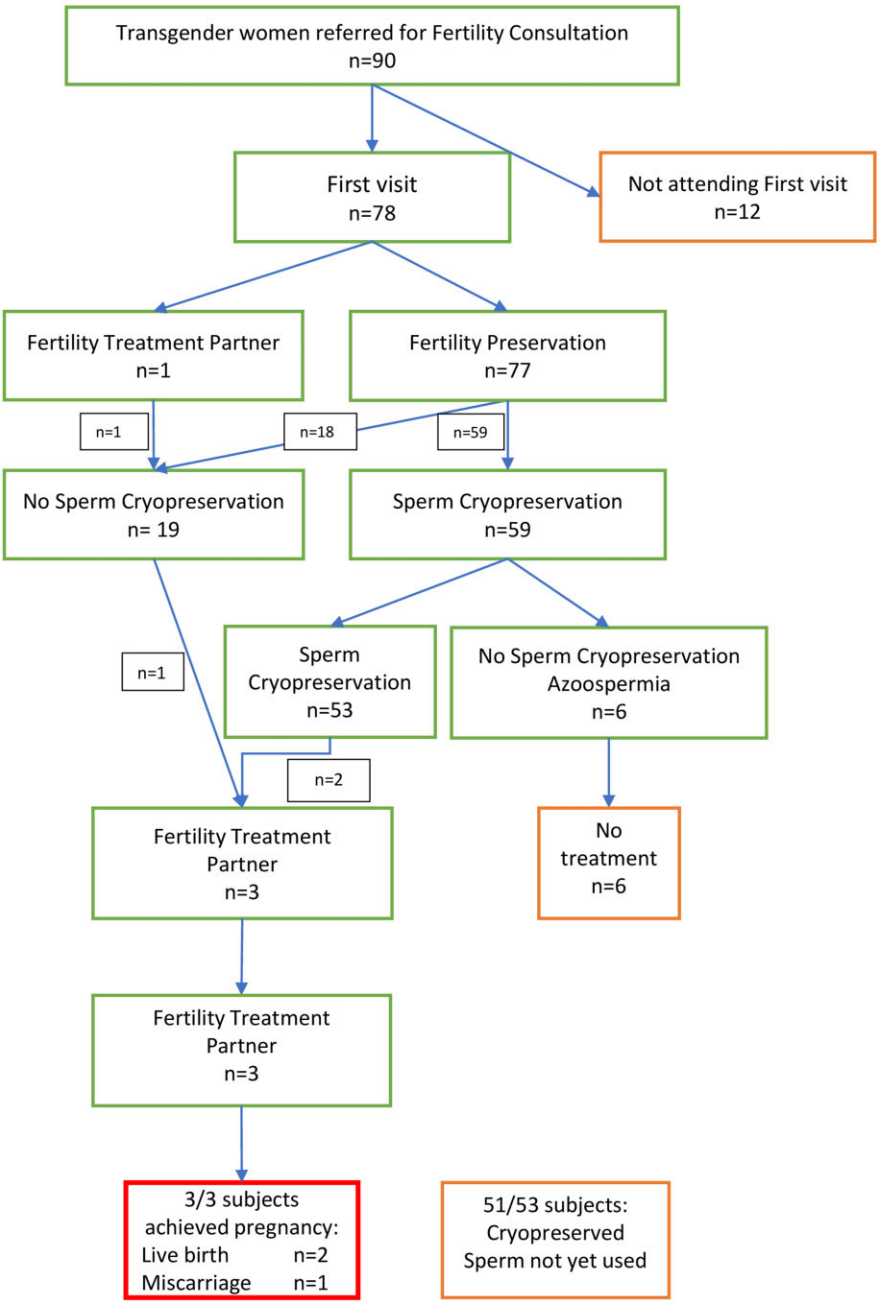

Figure 3. Flowchart of transgender women referred for fertility consultation and outcomes of fertility preservation and fertility treatments. In the current study, all individuals assigned male at birth and referred for sperm cryopreservation are referred to as transgender women.

Having been informed that hormonal treatment could alter fertility, none of the subjects in one study underwent fertility preservation despite substantial desire to become parents in the future (Chiniara *et al.*, 2019). A significantly higher rate of desire to have children before, compared with after, hormonal treatment has been reported among transgender men from Germany. Most of the transgender men had thoughts about fertility preservation prior to hormonal treatment, but only a few underwent treatment (Auer *et al.*, 2018). In a study on attitudes towards decision-making on fertility preservation, willingness to delay hormonal treatment in order to enable fertility preservation was much lower (3%) among transgender adolescents than among their parents (33%) (Persky *et al.*, 2020). All these findings support the need for fertility consultation prior to start of hormonal treatment, as well as indicating that the experienced urgency to start the medical transition might be a factor behind declining fertility preservation. However, in one study, there

Table IV Demographics of transgender women* referred for fertility consultation.

Variable	Semen cryo-preservation n = 59	No semen cryo-preservation n = 19	*P*-value
Age, years, *mean (SD)*	24.5 (6.1)	24.3 (8.3)	0.93[8]
median (min; max)	23 (13; 43)	22 (14; 51)	
Obesity (BMI ≥30 kg/m^2), *n (%)*	6 (10.7)	1 (5.9)	1.00
Missing	3	2	
Concurrent diagnoses, *n (%)*			
Neuropsychiatric	11 (18.6)	3 (15.8)	1.00
Psychiatric	29 (49.2)	6 (31.6)	0.20
Somatic	10 (16.9)	4 (21.1)	0.74
Previous hormonal treatment, *n (%)*	10 (16.9)	7 (36.8)	0.11
Gender affirmation surgery, *n (%)*			
Any surgery, planned or completed	20 (34.5)	13 (68.4)	0.02
Genital gender affirmation surgery			
Completed	10 (17.2)	8 (42.1)	0.06
Waiting list	6 (10.3)	2 (10.5)	
Missing	1	–	
Breast augmentation	14 (24.1)	11 (57.9)	
Waiting list	2 (3.4)	1 (5.3)	0.01
Missing	1	0	
Occupation, *n (%)*			
Student	25 (43.1)	6 (31.6)	0.43
Employed	18 (31.0)	7 (63.8)	(Student versus all others)
Unemployed	9 (15.5)	4 (21.1)	
Sick leave	5 (8.6)	2 (10.5)	
Other	1 (1.7)	0 (0)	
Missing	1	0	
Education, *n (%)*			
Elementary school not completed	3 (5.6)	1 (5.9)	0.75
Elementary school completed	10 (18.5)	4 (23.5)	(Elementary school versus higher education)
Secondary school	33 (61.1)	10 (58.8)	
University	6 (11.1)	1 (5.9)	
Other education	2 (3.7)	1 (5.9)	
Missing	5	2	
Children, *n (%)*			
Biological child/children	1 (1.7)	0 (0)	1.00
Partner child/children	1 (1.7)	0 (0)	(Living with versus no children)
No children	57 (96.6)	19 (100)	
Relationship, *n (%)*			
Heterosexual	4 (7.1)	1 (5.6)	0.37
Same sex relationship	10 (17.9)	6 (33.3)	(Partner versus none)
No partner	42 (75.0)	11 (61.1)	
Missing	3	1	
Sexual orientation, *n (%)*			
Heterosexual	4 (9.1)	5 (29.4)	0.04
Homosexual	29 (54.7)	8 (44.4)	(Heterosexual versus all others)
Bisexual	10 (18.9)	4 (22.2)	
Pansexual	1 (1.9)	0	0.59
Undecided	9 (17.0)	1 (5.6)	(Homosexual versus all others)
Missing	6	1	

(continued)

Table IV Continued

Variable	Semen cryo-preservation n = 59	No semen cryo-preservation n = 19	*P*-value
Desire to have children, *n (%)*			
Yes	51 (89.5)	13 (68.4)	0.06
Not sure	6 (10.5)	6 (31.6)	(Yes versus all others)
No	0	0	
Missing	2	0	
Plan for parenthood, *n (%)*			
Partner with subject's sperm	23 (40.4)	3 (15.8)	0.06
Surrogacy	1 (1.8)	1 (5.3)	(Partner versus all other options)
Adoption	0	4 (21.1)	
Not sure	33 (57.9)	11 (57.9)	
Missing	2	0	

*In the current study, all individuals assigned male at birth and referred for sperm cryopreservation are referred to as transgender women.
[8]The χ^2 test or Fisher's exact test were used for categorical variables and the Mann–Whitney U test was applied for continuous variables (in this table only age). All tests were two-sided and a *P*-value of <0.05 was considered statistically significant.

was no clear effect of hormonal treatment on fertility preservation decisions, and the most common reasons to decline fertility preservation were desire for adoption or lack of desire to have children in the future (Nahata *et al.*, 2017).

To our knowledge, our study is the first to evaluate gender affirmation surgery in relation to the decision for fertility preservation. We found that the decision to postpone or not to undergo gender affirmation surgery was associated with the decision to undergo fertility preservation among the transgender women, but not among the transgender men. It is important to bear in mind that this study was conducted over a number of years, and that most individuals had a fertility consultation at the start of their transition process, prior to any surgery.

The option to have children could depend on the assigned sex of the future partner.

In Sweden, neither double donation (oocyte and sperm or embryo) nor surrogacy was legal during the study period, which might have affected fertility preservation decisions in couples where neither could carry a pregnancy. Sexual orientation might have influenced the decision to pursue fertility preservation depending on the probability that gametes would be used in a future or current relationship, taking prevailing legislation into account.

According to our data, for transgender men, having a homosexual orientation was associated with the decision to undergo fertility preservation, while in transgender women a non-heterosexual orientation was associated with the decision to undergo fertility preservation. A previous study reported similar results, finding that transgender women in favour of fertility preservation more often identified themselves as lesbian or bisexual (De Sutter *et al.*, 2002). However, other studies have not shown any differences in sexual orientation related to decisions or attitudes towards fertility preservation (Brik *et al.*, 2019; Chiniara *et al.*, 2019).

We have reported that one-third of the transgender men deciding to undergo fertility preservation would consider carrying a pregnancy in the future, while one-third of those who decided not to undergo fertility preservation preferred their partner to carry a pregnancy. In previous studies in transgender men with low frequencies of fertility preservation, very few—one to three percent—would be comfortable carrying a pregnancy in the future (Auer *et al.*, 2018; Chiniara *et al.*, 2019; Persky *et al.*, 2020). In the Chiniara *et al.* (2019) study, the option of insemination of a partner was considered by one-third, similar to the transgender men who did not undergo fertility preservation in our study (Auer *et al.*, 2018).

Some reports of transgender men carrying naturally conceived pregnancies have been published. Australian researchers created a questionnaire to assess the decision process around fertility preservation and reported that 64 of 409 transgender men were already parents and that 28% had given birth (Riggs and Bartholomaeus, 2018). A comprehensive study of pregnancies after transition reported previous testosterone treatment in 61% of 41 transgender men. All pregnancies were found to be naturally conceived with the pregnant individual's own oocytes (88%), and no differences were found in outcome of pregnancies, deliveries or births, related to prior testosterone treatment (Light *et al.*, 2014).

Fertility treatment and pregnancy outcomes

Data on results of fertility treatments and pregnancy outcomes in transgender couples are still limited. Our study confirms that the use of cryopreserved gametes for achieving pregnancy is limited so far in the transgender population. Most of the 18 pregnancies, resulting in 12 live births, occurred after IUI or IVF/ICSI treatments in partners of transgender men. In two recent reports on IVF in 10 couples, all achieved live births (Maxwell *et al.*, 2017; Leung *et al.*, 2019). Two couples used previously cryopreserved oocytes from transgender men and donor sperm for embryo donation to a partner (Maxwell *et al.*, 2017), which indicates that this procedure was legal. Embryo donation has been legal in Sweden since January 2018 and treatment of a partner with cryopreserved oocytes fertilized with donor semen has been possible since then. Encouraging data from previous

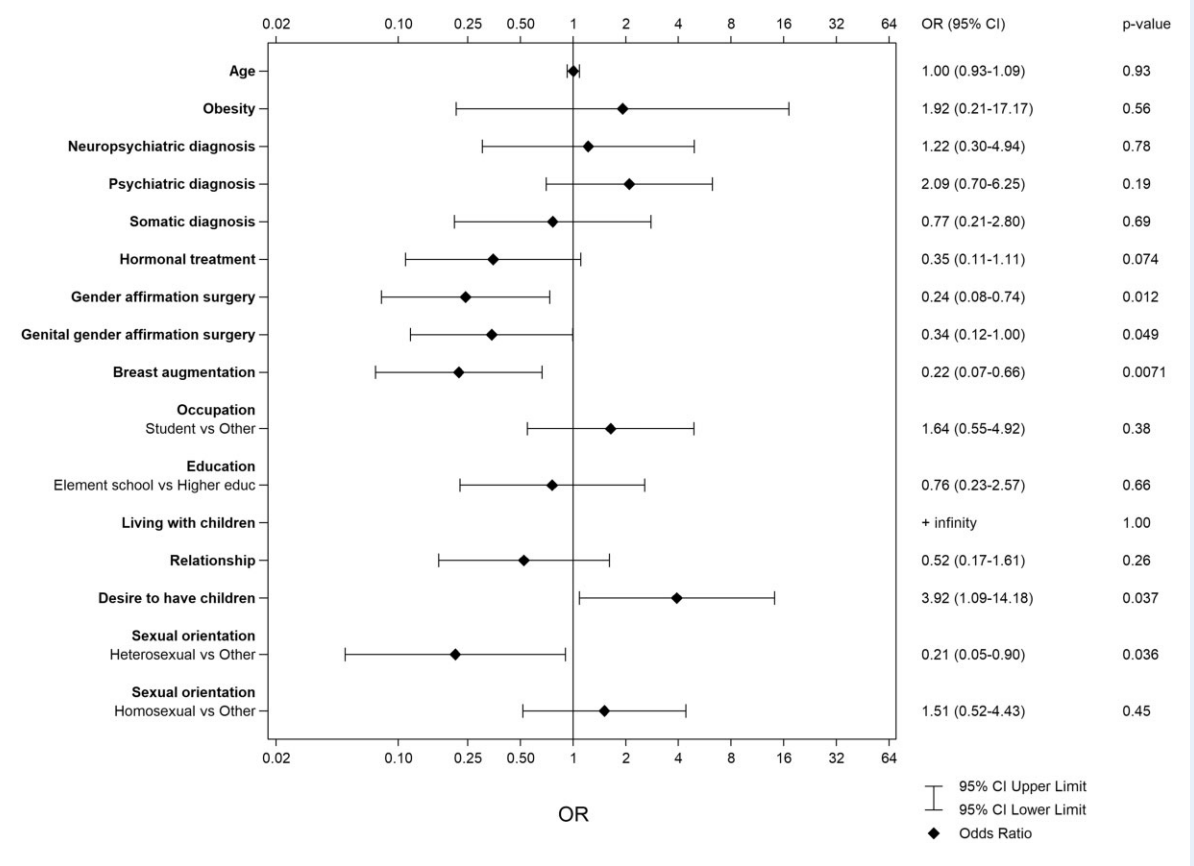

Figure 4. Univariable logistic regression analysis for the dependent variable cryopreservation of sperm among transgender women attending fertility consultation. In the current study, all individuals assigned male at birth and referred for sperm cryopreservation are referred to as transgender women.

studies also suggest that the effect of testosterone is reversible, and studies show similar outcomes in fertility treatments when transgender men with previous hormonal treatment are compared to those who have not started treatment (Light *et al.*, 2014; Mayhew and Gomez-Lobo, 2020).

Despite these encouraging data, there are nonetheless special obstacles and challenges for transgender men when planning for fertility preservation and pregnancy. As reported in a study from Sweden, transgender people had to deal with structural discrimination, gender norms and microaggressions in antenatal care, delivery and gender clinics. Access to quality care was dependent on the commitment and negotiation skills of the individual patient (Falck *et al.*, 2021). One study reports that transgender men's experiences of pregnancy loss could either resemble or differ from those in cisgender women (Riggs *et al.*, 2020). In a recent study, it was suggested that men, trans/masculine and non-binary people who are gestational parents acknowledge the specific challenges they face but engage in diverse practices that normalize their experiences of conception (Riggs *et al.*, 2021).

Study strengths

To the best of our knowledge, this is the largest clinical cohort studying both transgender men and transgender women with data on clinical outcomes of fertility preservation. The study population was recruited from one single university department of reproductive medicine, the recipient of all fertility consultation referrals for the transgender population in the region.

Study limitations

The main limitation is the retrospective nature of the study, with missing data for many variables. Reasons for caution are the short study period and the study population being too young to allow observation of fertility preservation and fertility treatment outcomes.

Conclusion

Our results confirm that fertility preservation has been requested after the 2013 change in Swedish legislation and that it has been more frequently used by transgender women than transgender men. Previous hormonal treatment, gender affirmation surgery and sexual orientation were associated with the decision to undergo fertility preservation. Fertility treatment and pregnancies with live births mainly occurred in partners of transgender men although the use of cryopreserved gametes was low. Information and discussion of aspects of fertility early in

the transition process is important, enabling transgender people to reflect on hormonal and surgical treatments in relation to fertility.

Data availability

The data underlying this article cannot be shared publicly due to the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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Authors' roles

All authors contributed to the conception and design of the study. E.M. and I.B. collected the data from administrative and medical databases. A.S. and E.M. performed the statistical analyses. All authors contributed to the analysis and interpretation of data. E.M. drafted the manuscript. A.S. and I.B. revised the manuscript and all authors approved the final version.

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Conflict of interest

None of the authors has any conflict of interest to declare.

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