Successful oocyte cryopreservation using letrozole as an adjunct to stimulation in a transgender adolescent after GnRH agonist suppression

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Objective: To report a successful case of ovarian hyperstimulation and oocyte cryopreservation in a transgender male adolescent after suppression with a gonadotropin-releasing hormone (GnRH) agonist while using the aromatase inhibitor letrozole to maintain low serum estradiol.

Design: Case report.

Setting: Division of Reproductive Endocrinology and Infertility, Washington University in St. Louis School of Medicine, St Louis,

Patient(s): A 15-year-old Tanner II transgender male adolescent with a GnRH agonist implant.

Intervention(s): The GnRH agonist implant was removed. The patient was given letrozole (5 mg daily) while undergoing ovarian stimulation with an antagonist protocol. After oocyte retrieval, the patient began taking testosterone.

Main Outcome Measure(s): Successful oocyte cryopreservation with minimal changes in breast budding.

Result(s): The patient's peak serum estradiol concentration was 510 pg/mL. Twenty-two mature oocytes were cryopreserved. Small increases in breast budding occurred between baseline and the time of oocyte retrieval.

Conclusion(s): We successfully used letrozole to maintain low serum estradiol in a transgender male adolescent during ovarian stimulation. Maintaining low estradiol to minimize pubertal development and possibly prevent gender dysphoria symptoms may make oocyte cryopreservation more desirable for transgender male adolescents. (Fertil Steril® 2021;116:522-7. ©2021 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Transgender, transgender male adolescent, oocyte cryopreservation, fertility cryopreservation, letrozole, aromatase inhibitor

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■ ransgender youth who plan to take gender-affirming hormones before undergoing natal puberty often are first given a gonadotropinreleasing hormone (GnRH) agonist to delay pubertal progression. Some of these patients may desire fertility preservation with sperm or oocyte cryopreservation but may be concerned that puberty will progress during treatment as a result of stopping GnRH agonist treatment and a subsequent increase in endogenous estradiol. For transgender male youth, this concern is based on the fact that the peak serum estradiol concentration can reach

1000-4000 pg/mL during a typical oocyte retrieval cycle. Moreover, in certain patients at risk of hyperstimulation, estradiol concentrations can be even higher if care is not taken to avoid hyperstimulation. Thus, strategies are needed to stimulate the ovaries effectively while maintaining a low estradiol concentration.

One potential strategy is to provide transgender male youth with the nonsteroidal aromatase inhibitor letrozole, which prevents the peripheral conversion of androgens to estradiol. As letrozole can keep estrogen and progesterone concentrations low, it is a

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TABLE 1

Timeline of events before, during, and after ovarian stimulation.

December 2019

March 2020 April 2020 May 2020 June–July 2020

August 2020

Planned stimulation start; delayed because of COVID19.
Leuprolide acetate (3.75 mg IM) administered to suppress pubertal progression.
Leuprolide acetate (3.75 mg IM) administered to suppress pubertal progression.
Controlled ovarian stimulation and retrieval. Letrozole (5 mg) administered during controlled ovarian stimulation. Testosterone therapy initiated and first menses occurred.

Additional vaginal bleeding occurred. Depo-Provera (150 mg IM) administered for menstrual suppression. Letrozole (2.5 mg daily orally) restarted to delay epiphyseal plate closure while on testosterone.

Removal of histrelin implant.

Note: IM = intramuscular.

Martin. Transgender male adolescent egg freezing after GnRH agonist use. Fertil Steril 2021

standard part of ovarian hyperstimulation protocols in patients with breast cancer who have estrogen or progesterone-receptor positive disease. In breast cancer patients, letrozole has not been shown to reduce mature oocyte yield (1). Although a case series described the use of letrozole in adults (2), we found no publications in the PubMed database describing the use of letrozole in ovarian stimulation cycles in transgender male youth.

In this case report, we describe our experience using letrozole to maintain low serum estrogen during controlled ovarian hyperstimulation in an adolescent transgender male presenting for fertility preservation.

CASE REPORT

The patient is a 15-year-old transgender male who had been on pubertal blockers since age 10. At age 12, he received a histrelin implant, which contains a GnRH agonist (Vantas; Endo Pharmaceuticals Solutions, Inc., Wilmington, DE). At age 14, the patient was referred by his pediatric endocrinologist to reproductive endocrinology and infertility for fertility preservation. He and his mother presented to investigate the option of cryopreserving oocyte, but were concerned that the patient might progress through female puberty if his histrelin implant was removed and his estrogen concentration were to elevate during ovarian stimulation. A previous case report described stimulation with the GnRH agonist implant in place (3). Histrelin implants are approved for one year of use, but typically are effective for up to two years. Since the patient had his implant in for two years already and was planning on having his implant removed before starting testosterone therapy, the decision was made to undergo stimulation after the removal of the implant. Once the patient decided to proceed with ovarian stimulation, a multidisciplinary team including specialists in pediatric endocrinology, reproductive endocrinology, social work, and psychiatry met several times to discuss logistics and choose the best approach. Written consent was obtained from the patient and his mother to write this case report.

The patient's histrelin implant was removed in December 2019 (Table 1) and 2 months later his antimüllerian hormone concentration was 2.62 ng/mL, follicle-stimulating hormone

was 3.6 mIU/mL, estradiol was 23 pg/mL, and luteinizing hormone (LH) was 1.3 mIU/mL (Table 2). At this time, his antral follicle count measured by transabdominal ultrasound was 25 and his breasts were Tanner Stage II with atrophic tissue.

Although ovarian stimulation was planned to begin in March 2020, stimulation was delayed because of COVID19related closures. In April 2020 and May 2020, the patient received monthly injections of depot leuprolide (3.75 mg). In June 2020, he began a controlled ovarian stimulation protocol using a GnRH antagonist as described elsewhere (4). At this time, he began taking letrozole orally (5 mg daily). At stimulation baseline, his estradiol concentration was undetectable, transabdominal antral follicle count was 25, and breasts were Tanner Stage III with 3.5 \times 3.5 cm of tissue on the right and 3.5 × 3.0 cm on the left. After 5 days of stimulation, the patient's estradiol concentration still was undetectable and no follicular growth was noted, so his gonadotropin dose was increased. He received a total of 2550 IU recombinant follicle-stimulating hormone (rFSH) and 2175 IU human menopausal gonadotropin (HMG) over 12 days. His peak estradiol concentration was 510.4 pg/mL. When the lead follicle was \geq 20 mm (Table 2 and Fig. 1), an injection of 5000 IU human chorionic gonadotropin (hCG) was given to trigger follicular maturation and resumption of meiosis. Human chorionic gonadotropin was chosen instead of leuprolide acetate because the patient had been on depot leuprolide acetate before stimulation, raising the concern that he might not make enough endogenous LH to trigger final oocyte maturation. A low dose of hCG was used to reduce the risk of severe ovarian hyperstimulation syndrome. Oocytes were retrieved 36 hours later. Of the 36 oocytes obtained, 22 were mature and were cryopreserved. During the procedure, the patient had a small hymenal ring abrasion that did not require

When evaluated on the day of retrieval, breast development remained at Tanner Stage III, though breast tissue had increased to 4.5×5 cm on the right and 4.5×4.5 cm on the left. The patient started testosterone therapy 3 days after oocyte retrieval. He was to take letrozole orally (2.5 mg daily) for growth optimization by delaying epiphyseal plate closure. However, because of a miscommunication, he stopped the

TABLE 2 Medication dosing, lab values, and ultrasound findings before, during, and after stimulation. Ultrasound Medication Dosing Serum Testing Findings Left GnRH Right rFSH Uterine Antagonist Letrozole hCG **FSH** ovarian ovarian Cycle Day (IU) HMG (IU) (IU) AMH (ng/mL) (mIU/mL) E2 (pg/mL) lining (mm) follicles (mm) follicles (mm) (mcg) (mg) Let ovary: $18 \times 11 \times 18$ AFC 15 < 10 10 < 10 8 < 10Right ovary: $12 \times 9 \times 8$ AFC 10 < 102.62 26 21 weeks prior 3.6 1.8 2.1 3.1 1–5 <5 <5 15 < 10 8 < 10 150 225 150 150 5 6 7–9 225 225 150 10 150 5 108.6 13.5, 12.5, 12.5, 12, 12, 11.5, 10, 9.5 12.5, 10.5, 10.5, 9.5, 9 11 12 13 225 225 225 225 225 5 5 5 250 250 15, 14.5, 13, 13, 12, 10.5, 10.5 20, 18, 16, 16, 15.5, 15, 14, 14, 14, 14, 13, 12, 11.5, 11, 10.5, 10 19, 18.5, 18.5, 15, 14.5, 14, 12, 11.5, 11, 10.5 345.5 (3.2x) 510.4 13.5, 13, 11, 11, 10.5, 10.5, 10 14 5 5000 16 5 Oocyte retrieval

Note: AMM = antimullerian from one; E2 = estractiol; FSH = follicle-stimulating from one; GnRH = gonadotropin-releasing from one; hCG = from an chorionic gonadotropin; HMG = from a menopausal gonadotropin; HSH = recombinant follicle-stimulating from one.

Martin. Transgender male adolescent egg freezing after GnRH agonist use. Fertil Stenii 2021.

FIGURE 1



Transabdominal ultrasound on cycle day 12 with both ovaries in transverse view

Martin. Transgender male adolescent egg freezing after GnRH agonist use. Fertil Steril 2021.

letrozole. One week after stimulation, his estradiol concentration was 97.8 pg/mL.

The morning after the patient received the hCG trigger, he experienced shortness of breath and sudden cramping abdominal pain without nausea. The symptoms resolved <30 minutes after onset. His mother reported that, in the past, he occasionally experienced anxiety that presented as shortness of breath. The abdominal pain was localized to the right lower quadrant and was likely because of enlarged ovaries. Because this pain resolved spontaneously and almost immediately, our concern for ovarian torsion was diminished.

Approximately 4 days after retrieval, the patient experienced a menstrual period lasting 6 to 7 days with 3 days of moderate flow. He felt cramping and fatigue for approximately 1 week. His mother noted that he would not have been able to attend school if it had been in session. The patient experienced an additional episode of vaginal bleeding 1 month after this initial period. At that time, the estradiol concentration was undetectable, FSH was 10 mIU/mL, LH was 5.5 mIU/mL, testosterone was 228 ng/dL, and free testosterone was 22.7 ng/dL. These values were consistent with male puberty. In addition, the estradiol was likely low because of the letrozole use, which he restarted a few days before the blood tests. The patient was counseled on menstrual suppression regimens and opted for 150 mg intramuscular Depo-Provera. Menstrual bleeding has stopped. After being on testosterone for 3 months, his breast tissue was atrophic.

During the stimulation, the patient had support from his family, a case manager, his pediatric endocrinologist, and the reproductive endocrinology and infertility team. Since starting testosterone, the patient has been feeling very positive. Overall, he and his family were satisfied with their decision to cryopreserve oocytes.

DISCUSSION

In the United States in 2017, 0.7% of those aged 13–17 years (approximately 150,000 individuals) identified as transgender

(5). The Endocrine Society and the World Professional Association for Transgender Health have provided clear guidelines and recommendations surrounding the use of GnRH agonist therapy and gender-affirming hormonal therapy for transgender individuals (6, 7). Additionally, both of these societies recommend counseling on fertility preservation before initiating testosterone or estrogen therapy. However, those working in the field of reproductive endocrinology and infertility need to learn more about how to apply our treatments safely and effectively and to set expectations adequately about the process to transgender youth and adults.

To our knowledge, this is the first case report describing the use of an aromatase inhibitor to maintain low estrogen concentrations during ovarian stimulation of a transgender male adolescent who had been on GnRH agonist therapy to prevent pubertal progression. Moravek (8) describes rising levels of estradiol during stimulation as concerning for transgender men and suggests using letrozole to reduce this concern. In a qualitative study, transgender youth expressed feelings of dysphoria when considering oocyte cryopreservation (9). Armuand et al. (2) described using letrozole during ovarian stimulation in transgender men ages 19-35 years. Despite using letrozole, Armuand et al. (2) report that these men experienced gender dysphoria, but were able to cope with these feelings effectively. The investigators point out that the procedure itself was not distressing to patients, but the experiences leading up to retrieval that linked transgender men to their incongruent sex assigned at birth, such as breast tenderness and transvaginal ultrasounds, were distressing (2). Our patient found the minimal degree of breast progression and menstruation distressing; however, he did not report gender dysphoria or suicidal ideation during the stimulation. In a systematic review, Baram et al. (10) also suggest using letrozole to maintain low levels of estrogen. Letrozole has been used effectively in patients with estrogen- and progesteronereceptor positive breast cancers undergoing ovarian stimulation. Letrozole appears not to reduce mature oocyte yield (1) and generally is a well-tolerated oral medication. To further minimize estrogen rise, a GnRH agonist can be used instead of hCG to trigger oocyte maturation (11).

A prior case report described ovarian stimulation in a transgender male adolescent who retained his histrelin implant (3). Although that team considered removing the histrelin implant, the family was concerned about the psychologic effects of removal and opted to keep the implant in place (3). During the stimulation, a "low slow" approach was used in providing rFSH and HMG. Although the stimulation was successful, only four mature oocytes were obtained. After speaking with that team about their experience, we decided to start with a higher dose of rFSH and HMG. We obtained 22 mature oocytes. This robust response may have been because we removed the histrelin implant and started at a higher dose of rFSH and HMG. Histrelin implants can be left in place while testosterone therapy is started. Our patient had his implant removed in December 2019, two years after placement. The histrelin implant is approved for one year; however, it may be effective for up to two years if left in place. The implant often is not covered by insurance and can cost approximately \$5400 if paid for out of pocket (12).

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ORIGINAL ARTICLE: FERTILITY PRESERVATION

The hypothalamic-pituitary-gonadal axis typically resumes function 3 and 6 months after implant removal. If within two years of implant placement, some patients choose to keep the implant in place while starting testosterone. In the initially planned timeline, stimulation was to begin in March 2020; however, this was delayed because of the COVID19 pandemic. The patient took GnRH agonist injections while waiting for our clinic to resume nonemergent procedures.

There are other fertility preservation options for transgender males apart from oocyte cryopreservation. Data show that transgender male adults desire biological children (13). One study reported 35.9% of surveyed transgender adolescents desired biological children and 26.3% were unsure if they wanted biological children (14). Although oocyte cryopreservation before testosterone therapy as an adolescent is one option, some patients may choose to delay oocyte cryopreservation until adulthood. Stimulation is typically performed after stopping testosterone for 3-6 months (15, 16), however, a recent case report described successful stimulation immediately after testosterone cessation (17). For those not interested in undergoing oocyte cryopreservation, ovarian tissue cryopreservation is another option that could be performed during gender-affirming surgery, however, there is not much data regarding outcomes after testosterone use (8).

We encountered a few minor challenges during this case. First, we used an abdominal probe instead of a transvaginal probe for sonographic monitoring to assess follicular development. Second, we had a low level of concern for not being able to access the patient's ovaries on the day of retrieval given his low body mass index. However, we had discussed this possibility with the family ahead of time. We also discussed with the patient and his family ahead of the retrieval that the probe could cause a vaginal laceration at the time of oocyte retrieval. Although the patient did have a small hymenal ring abrasion, which was likely caused during the vaginal preparation with normal saline and a speculum, we did not need to suture it.

CONCLUSION

Specialists should consider using letrozole as an adjunct to the controlled ovarian hyperstimulation protocol when stimulating ovaries for fertility preservation in transgender male adolescents. We were successful in stimulating this patient who was transitioning from using a GnRH agonist implant to testosterone therapy. This case report catalogs the unique needs of each of the four phases of the oocyte cryopreservation process (prestimulation, stimulation, procedural, and postprocedural) that are necessary for preparing these patients. Although we demonstrate the utility of using letrozole in a transgender adolescent, letrozole could also be used in transgender male adults. We note the importance of including a multidisciplinary team to ensure the patient's well-being

during a stressful time. Finally, we note that a strategy to keep estradiol low may make the oocyte cryopreservation process more appealing to transgender male youth, allowing them the opportunity to preserve their fertility.

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Criopreservación satisfactoria de ovocitos utilizando Letrozol como adyuvante para la estimulación ovárica en un adolescente transgénero tras supresión con agonista de GnRH.

Objetivo: Comunicar un caso exitoso de hiperestimulación ovárica y criopreservación de ovocitos en un varón adolescente transgénero tras supresión con agonista de homona liberadora de gonadotrpinas (GnRH-a) con utilización concomitante del inhibidor de aromatasa Letrozol para mantener el estradiol sérico bajo.

Diseño: Comunicación de un caso.

Entorno: División de Endocrinología Reproductiva e Infertilidad, Universidad de Washington en la escuela de medicina de St Louis, St Louis, Missouri.

Paciente(s): Varón adolescente transgénero de 15 años, Tanner II con un implante de GnRH-a.

Intervención(es): Se retiró el implante de GnRH-a. El paciente recibió Letrozol (5 mg diarios) mientras se realizaba estimulación ovárica con un protocolo de antagonistas. Después de la recuperación de ovocitos, el varón empezó a tomar Testosterona.

Medida(s) del resultado(s) principal(es): ovocitos criopreservados con éxito con cambios mínimos em el desarrollo mamario.

Resultado(s): El pico de estradiol sérico del paciente fue de 510 pg/mL. Se criopreservaron 22 ovocitos maduros. Se observó un pequeño incremento en el desarrollo mamario entre el inicio del tratamiento y la recuperación de ovocitos.

Conclusión(es): Se utilizó Letrozol con éxito para mantener bajo el nivel de estradiol sérico en un varón adolescente transgénero durante la estimulación ovárica. Mantener el estradiol sérico bajo para minimizar el desarrollo puberal y probablemente prevenir síntomas de disforia de género podría hacer más deseable la criopreservación de ovocitos para los varones adolescentes transgénero.

Palabras clave: Transgénero, varón adolescente transgénero, criopreservación de ovocitos, criopreservación de fertilidad, letrozol, inhibidor de aromatasa.

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Experience of Chest Dysphoria and Masculinizing Chest Surgery in Transmasculine Youth

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OBJECTIVES: Transmasculine individuals, those assigned female sex at birth but who identify as masculine, have high rates of suicidal behavior and often suffer from chest dysphoria (discomfort and distress from unwanted breast development). Growing numbers of transmasculine youth are pursuing definitive treatment with masculinizing chest surgery (MCS), and adult studies reveal marked benefits of MCS, although little is known about the impact of chest dysphoria on transmasculine youth or the optimal timing of MCS. In this study, we aimed to explore youth experiences of chest dysphoria and the impact of MCS.

METHODS: Transmasculine youth aged 13 to 21 were recruited from a pediatric hospital-based gender clinic. Participants completed a semistructured qualitative interview exploring the experience of chest dysphoria and thoughts about or experiences with MCS. Interview transcripts were coded by 3 investigators employing modified grounded theory, with the median interrater reliability at $\kappa = 0.92$.

RESULTS: Subjects (N = 30) were a mean age of 17.5 years, and 47% had undergone MCS. Youth reported that chest dysphoria triggered strong negative emotions and suicidal ideation, caused a myriad of functional limitations, and was inadequately relieved by testosterone therapy alone. All post-MCS youth reported near or total resolution of chest dysphoria, lack of regret, and improved quality of life and functioning.

CONCLUSIONS: We observed consensus that chest dysphoria is a major source of distress and can be functionally disabling to transmasculine youth. MCS performed during adolescence, including before age 18, can alleviate suffering and improve functioning. Additional research is needed to develop patient-reported outcome measures to assess the impact of chest dysphoria and MCS.

abstract





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Dr Mehringer conceptualized and designed the study, assisted with the design of data collection instruments, collected data, conducted analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Ms Harrison designed data collection instruments, coordinated data collection, collected data, conducted analyses, and reviewed and revised the manuscript; Mx Quain conducted analyses and reviewed and revised the manuscript; Dr Shea assisted with study design, informed data analyses, assisted with data interpretation, and reviewed and revised the manuscript; Dr Hawkins informed study conceptualization, assisted with study design, and reviewed and revised the manuscript; Dr Dowshen informed study conceptualization, assisted with study design, assisted with data interpretation, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

WHAT'S KNOWN ON THIS SUBJECT: Transmasculine youth have high rates of suicidal behavior. Studies in transmasculine adults reveal that chest dysphoria severely impacts quality of life and functioning and is greatly improved by masculinizing chest surgery; however, little is known about chest dysphoria in youth.

WMAT TRIS STUDY ADDS: This study is the first to describe the lived experience of chest dysphoria through the words of transmasculine youth themselves, and explores the impact of masculinizing chest surgery on quality of life and functioning in these youth.

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Transgender individuals face disproportionately high rates of negative health outcomes, including depression, anxiety, and suicidality. $\tilde{1}$ -3 Transmasculine individuals are those who were assigned female sex at birth but identify their gender as male or along the masculine spectrum. In a large multisite study published in 2018, researchers found that transmasculine youth had the highest prevalence of reported past suicide attempts among youth of any gender identity at 50.8%.4 It is imperative that we better understand the lived experience of transmasculine youth and the factors that contribute to these staggering rates of suicidality.

A phenomenon known to cause distress in many transmasculine individuals is chest dysphoria: physical and emotional discomfort and distress caused by the presence of unwanted breast development. Although the early use of gonadotropin-releasing hormone agonists for pubertal suppression can help to prevent breast development, the majority of transmasculine youth have already had significant irreversible breast development when presenting for gender-affirming care.5,6 As a temporizing measure, transmasculine individuals commonly bind their chests to create a more masculine chest contour, but this seldom provides adequate relief of chest dysphoria and often causes adverse health effects.7,8

Many transmasculine individuals ultimately choose to pursue masculinizing chest surgery (MCS), often referred to as "top surgery," in which unwanted breast tissue is removed to create a more masculine chest contour. Researchers of multiple studies of transmasculine adults have found high rates of satisfaction with MCS outcomes, low complication rates, and improvements in psychosocial and health outcomes. 9-15 Given the dramatic impact that MCS can have in

alleviating dysphoria and improving quality of life, it is widely accepted as a medically necessary procedure for many transmasculine individuals with chest dysphoria. 16,17 International best practice guidelines for the care of transgender individuals note that there are no specific age requirements for MCS and that timing of MCS should be based on the individual's physical and mental health status and goals for gender expression, 16,17 yet most US insurers limit coverage of MCS to those aged ≥18 years. 18

There has been limited investigation of the experience of chest dysphoria or outcomes of MCS in transmasculine youth. Olson-Kennedy et al¹⁹ described the Chest Dysphoria Scale, a novel measure of severity of chest dysphoria using a 17-item survey piloted on a cohort of transmasculine youth aged 13 to 25. They found that youth who had not undergone MCS had chest dysphoria scores nearly 10-fold higher than post-MCS youth. Much, however, remains unknown about transmasculine youths' overall experiences with chest dysphoria and MCS, information that is critical to guiding providers and policy makers to address the needs of this vulnerable population. Therefore we aimed to (1) describe the physical and emotional experience of chest dysphoria in transmasculine youth aged 13 to 21 and (2) explore transmasculine youths' perceptions of MCS, their decision-making process for whether to pursue MCS, and (for postsurgical youth) their experiences of MCS and its impact on quality of life.

METHODS

Participants and Recruitment

Study participants were recruited from a large US pediatric hospital-based gender clinic. Participants were eligible if they were aged 13 to 21 years, assigned female sex at birth, identified their gender as male or along the masculine spectrum, endorsed having had discomfort or distress about their chest, had experienced notable breast development (as indicated by electronic health record [EHR] documentation revealing a previous breast sexual maturity rating of 4 to 5 or by being postmenarcheal), and received care at the Children's Hospital of Philadelphia Gender and Sexuality Development Clinic, Youth were ineligible if (1) they had undergone MCS within the past 90 days (so that post-MCS youth would be able to reflect on the impacts of the procedure on their life beyond the recovery period) or (2) their primary gender-affirming care provider was the lead investigator.

Potentially eligible youth were identified by the clinical team, and a limited EHR review was performed to ensure appropriateness for study inclusion. Youth were purposefully sampled in an effort to recruit a sample of both non-MCS and post-MCS youth that was diverse in age, race, ethnicity, and insurance status. Youth were approached either in person during a clinic visit, by phone, or by e-mail. Recruitment continued until thematic saturation was achieved.

Procedures

The study was approved by the Children's Hospital of Philadelphia Institutional Review Board. Written informed consent was obtained either from youth (≥18 years) or from guardians of minors who provided their assent. Study visits were conducted in person or via video conference on the basis of youth preference. A one-on-one semistructured interview was conducted with each youth to explore their experiences with chest dysphoria and their thoughts about or experiences with MCS (see the Supplemental Information for interview questions). Youth also

completed a brief demographic survey. The participant's EHR was reviewed post study visit. Participants received a \$40 gift card after interview completion.

Analysis

All interviews were audio recorded, transcribed, deidentified, and entered into NVivo software (version 12; QSR International Pty Ltd, Doncaster, Australia). Key themes and patterns were identified by using a modified grounded theory approach.20 The team developed a codebook by reading each transcript independently and identifying key ideas and also included a priori codes derived from the study questions. Key ideas became codes with definitions. A team of 3 coders triple-coded the first 14 interviews. Discrepancies were reviewed and discussed, and the codebook was revised iteratively. The remaining 16 interviews were double-coded. Interrater reliability was calculated by using Cohen's k, with a median across all codes of 0.92 (range 0.80-0.99). The contents of each code were summarized and examined for patterns and themes. Bivariate analyses of sociodemographic and clinical variables were conducted by using χ^2 tests for categorical variables and ttests for comparison of means.

RESULTS

Demographics

Of 35 youth approached for recruitment, 30 youth enrolled and completed the study visit: 16 had not had MCS (non-MCS) and 14 had undergone MCS (post-MCS). Descriptive characteristics of each group are shown in Table 1. There was no significant difference in age, race, ethnicity, or insurance status between the 2 groups. Youth overall had a mean age of 17.5 years (range 14–21 years) and were predominantly white, non-Hispanic, and privately insured. The post-MCS

TABLE 1 Descriptive Characteristics of Youth Participants

	0verall	Non-MCS	Post-MCS	Р
	(N = 30)	(n = 16)	(n = 14)	
Age, y, mean (range)	17.5 (14-21)	17.1 (14-20)	17.9 (14-21)	.29
Race, a n (%)				.52
White	22 (73)	11 (69)	12 (86)	
Black or African American	5 (17)	2 (13)	3 (21)	
Asian	2 (7)	1 (6)	1 (7)	
Other	2 (7)	2 (13)	0	
Hispanic or Latinx ethnicity, n (%)	3 (10)	3 (19)	0	.09
Insurance, n (%)				.35
Private	26 (87)	13 (81)	13 (93)	
Public	4 (13)	3 (19)	1 (7)	
Testosterone				
On treatment, n (%)	25 (83)	11 (69)	14 (100)	.02
Duration of treatment, mo, mean (range)	21.9 (8-60)	14.5 (9-24)	27.7 (8-60)	0.009^*
MCS, mean (range)				
Age at MCS, y	_	_	16.4 (14–18) ^b	_
Time since MCS, mo	_	_	19 (6-48)	_
Payer of MCS, n (%)				
Insurer	_	_	4 (29)	_
Patient or family	_	_	10 (71)	_
Surgical technique, n (%)				
Periareolar or keyhole surgery	_	_	4 (29)	_
DI/FNG or inverted-T	_	_	10 (71)	_

DI/FNG, double incision with free nipple graft; ---, not applicable

youth were more likely to be receiving testosterone therapy than the non-MCS group and were more likely to be on testosterone for a longer time. Additional information about the post-MCS group may be found in Table 1. All participants met Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria for gender dysphoria. Five youth were approached for recruitment and did not enroll: 4 met eligibility criteria but declined to participate (2 declined because of time constraints, 1 declined because of discomfort with audio recording, 1 gave no reason), and 1 did not respond to the recruitment call and e-mail.

Qualitative Results

Eight major themes emerged, which are presented with example quotes in the text below with randomly assigned initials for confidentiality. Additional illustrative quotes are presented in Tables 2 and 3. In general we did not find major differences in themes by

demographics, nor between the nonand post-MCS groups, regarding experiences before MCS, so results are reported in aggregate unless otherwise specified.

Theme 1: Chest Dysphoria Causes Strong Negative Emotions and Can Trigger Suicidal Ideation

All youth described how chest dysphoria triggered strong negative emotions; the most commonly cited emotions included sadness, depression, anxiety, anger or frustration, a subjective feeling of heaviness or burden, self-loathing, disgust, annoyance, and envy or jealousy: "I was really self-loathing the chest dysphoria—it just ate away at me" (E.P.).

Many youth noted that chest dysphoria made them emotionally dysregulated: "[Chest dysphoria] would influence how I would interact with the world that day, just on a baseline more anxious, more

⁸ More than 1 race could be selected.

b n = 10 underwent MCS before age 18 у

^{*} P ≤ .05.

TABLE 2 Themes 1-5 and Additional Example Quotes

Theme	Example Quotes
Theme 1: chest dysphoria causes strong negative emotions and can trigger suicidal ideation	
Strong negative emotions	
	"I get tingly and stuff and it kind of makes me want to punch something." (I.B.) "There's a feeling of hopelessness, of desperation, of—almost makes me feel physically sick." (I.S.) "It felt like there was this burden that I was just constantly carrying around with me and this sort of insecuritylike I had a secret that I was trying to hidethis constant feeling of being uneasy and sort of on edge." (J.L.)
Suicidal ideation	With the sharp and a second of the ship has sharp be and a second of the
	"[My chest dysphoria] made me feel like shit, honestly. It made me suicidal. I would have breakdowns." (F.J.) "I've been suicidal quite a few times over just looking at myself in the mirror and seeing [my chest]. That's not something that I should have been born with." (Q.Y.)
Theme 2: youth feel helpless and unable to escape chest dysphoria	anough make net contacting that i cheard have been been with figure
	"It feels like a burden on my life that's kinda like always there and it always makes me feel bad and I can't really do anything about it." (V.S.) "It's a really invasive feeling that I can't do anything about It feels like this is something that's
Theme 3: chest dysphoria is an intrinsic phenomenon and is not limited to social settings	holding me back. It's like my own body's discriminating against me." (Z.P.)
<u></u>	"Not even to outsiders—just inside, to yourself, you're embarrassed If I'm getting ready to shower—you have to strip in order to take a showerthere's nothing that I can hear or someone can tell me or I can even tell myself that will make it better." (N.C.)
Theme 4: chest dysphoria causes functional impairments	
Social avoidance, impaired interpersonal relationships	"I became more isolated I was really self-conscious, so it was kind of like if I don't go outside then I don't really have to think about what people think or what people perceive." (X.B.) "I would have a lot of days where I would just feel too dysphoric to even really leave my room or just interact with anybody." (E.P.)
	"I sometimes feel like I'm really on edge because I wonder how they are perceiving me and if they're noticing my chest a lot more and stuff like that." (T.Q.) "I didn't want people to touch me or get too close, because I didn't want them to notice [my chest]."
	(S.U.)
Interference with school or work	"Comptimes I'm short duscharial would manifest into assist, and I would not be able to assist
	"Sometimes [my chest dysphoria] would manifest into anxiety and I would not be able to even get out of bed in the morning, it would be so bad." (G.N.) "Little things would definitely tip me off to the edge where I would feel too overwhelmed—I couldn't
Impact on personal hygiene and posture	manage very simple tasks like just doing schoolwork." (H.G.)
impact on porconal riggions and poetars	"I wouldn't use public restroomseven though that's—it's not a place you're taking off your shirt, but it's still vulnerable to me During classes and stuff, I would always be hunched over I'd never walk with my head up." (L.S.)
Avoidance or limitations in physical activity and sports participation	
	"I don't really do any physical activities really because I'd have to bind if I did them in public, and I really cannot do that safely I can't really do intense physical activity with this [binder] on, and I don't want to not have it on." (I.S.)
	"I'm a freshman next year and I want to pursue sports. Some of them I can't pursue because of the chest dysphoria and because [my chest] could target me out to the other people." (A.O.)
Theme 5: chest binding is a trade-off between physical and psychological discomfort	
	"Binding's really uncomfortable I don't like doing it, but at the same time, I have no other option. I don't really leave my room unless I have a binder on" (K.C.)

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twitchy, ready to be reactive sort of to just things, in general" (D.V.).

Some reported that chest dysphoria induced thoughts of suicide and self-harm: "Suicidal ideation definitely stemmed from that—from chest dysphoria and the feelings that it gave me" (X.B.).

Theme 2: Youth Feel Helpless and Unable to Escape Chest Dysphoria

Nearly all youth reported feeling helpless and unable to escape chest dysphoria, and many reported constant intrusive thoughts: "[Chest dysphoria] was just like always on my mind no matter what I was doing" (A.C.).

Theme 3: Chest Dysphoria Is an Intrinsic Phenomenon and Is Not Limited to Social Settings

Many youth described that their chest dysphoria was not confined to social settings. They explained that chest dysphoria caused distress even when they were alone, not just at times when their chest might be in view of others: "[My chest dysphoria is worse] when I'm in the shower...when I'm by myself it's an issue because I'm like, wow. That's there right now." (L.E.).

Theme 4: Chest Dysphoria Causes Functional Impairments

Every youth reported experiencing functional impairments from chest dysphoria. Many avoided social interactions because of anxiety or shame about their chest, fear of being outed as transgender if others noticed their chest contour, or not wanting to endure the discomfort of binding their chest (often viewed as a requisite when leaving the home because of dysphoria): "I don't really want to be outside. I don't want people to see me...because I feel gross and just like icky all around" (T.Q.).

Chest dysphoria interfered with interpersonal interactions, causing difficulty in engaging with others because of intense anxiety, shame, or intrusive thoughts.

[I]n social settings...I'm always thinking about [my chest], so it feels

like they're looking at me. And it's just anxiety inducing... It just makes it hard to get to know people and kind of communicate and establish a connection, because I feel like they're noticing something that I don't like about myself.

R.P.

Many explained that they adopted a hunched or closed body posture and would avoid hugs or physical contact as strategies to help hide their chest; however, these strategies would often inadvertently drive others away: "I'm kind of hunched over or I push my shoulders forward...and I just kind of feel like I have to keep hiding myself or just trying to deflect the focus" (Z.P.).

Youth also reported that chest dysphoria interfered with school or work.

It was really hard every day waking up and having to go to school.... For me at least it was impossible to feel like a man especially in an environment like school – with a very large chest. And I didn't wanna be seen...I would miss a lotta school sometimes because I just couldn't get myself together.

H.G.

Chest dysphoria led many to avoid sports and exercise, citing pain or breathing difficulties from chest binding or inability to keep their chest hidden from others. For some youth, chest dysphoria led to avoidance of bathing and public restrooms, making it challenging to address personal hygiene.

Theme 5: Chest Binding Is a Trade-off Between Physical and Psychological Discomfort

All youth engaged in chest binding before MCS, with most doing so on a daily basis. Binding was unanimously viewed as a useful coping strategy, and many reported that it was essential to helping them leave home and get through the day: "The binder helped me at least get out of my room more because at least I could go out in public and I knew I looked pretty flat, and I could pass." (L.S.).

However, although binding helped to alleviate psychological distress, this came at a cost. All youth reported binding to be physically uncomfortable, and many reported adverse health effects, such as pain (in the chest, ribs, back, or shoulders), difficulty breathing, skin rashes or irritation, overheating, and decreased endurance: "[My binder] was incredibly restricting with my breathing. And if I wasn't wearing my binder, I wouldn't go out and do things. So I'd wear it even if I was unable to breathe" (D.V.).

As one participant noted, there was a constant balancing act between physical and mental well-being: "I'd rather be in physical pain than in mental pain. So I'd rather just wear the binder than just deal with it" (A.C.).

Theme 6: MCS Is Viewed as Critical to Gender Affirmation; However, There Are Many Barriers to Accessing It

Every youth in the non-MCS group intended to undergo MCS in the future. All acknowledged the risks and irreversibility of MCS yet expressed confidence in their decision to pursue it, feeling that MCS would be critical to improving their quality of life and functioning: "Even if it's not the prettiest surgery, I will be comfortable.... [I won't] have to limit my activities or limit the most ridiculous things because of my breasts. More freedom. I'll get to live. I'm not living now...I feel like I'm just getting by" (N.C.).

Many barriers to obtaining MCS were identified, the most common of which were lack of insurance coverage for the procedure and high burden of out-of-pocket costs. Most families of post-MCS youth paid for MCS out of pocket because of insurance denial due to age. Other barriers to MCS included lack of family support for MCS, difficulty accessing a skilled surgeon, and challenges with scheduling surgery around school and/or work.

TABLE 3 Themes 6-8 and Additional Example Quotes

Theme	Example Quotes
Theme 6: MCS is viewed as critical to quality of life and functioning; however, there are many barriers to accessing it	
Critical role of MCS	
	"It's just something I've always wanted. And it was never kind of a decision for me Top surgery was kind of what I always envisioned, so it wasn't really like a decision. It was more like a need." (R.P.) "I'm not de
	"I'm not going to love the scars, but I'm going to be happy and grateful for themI'll be able to live my life the way I've always envisioned itI can do everything I've liked to do and wanted to do for the last couple of years that I just couldn't bring myself to do or physically couldn't do." (Q.Y.)
Barriers to accessing MCS	
	"Seven days before I was scheduled to go in for my top surgery, I got a phone call from my surgeon's office telling me that my insurance wouldn't cover it. And it devastated me It's a slap in the face. I cried. I cried because it's like why is that a thing? It's not my fault that I'm trans. I just want to be comfortable. So it's hurtful." (N.C.) "My main barriers were probably getting my parents to agree to it[their] concerns were just that I was gonna regret it." (F.J.)
Theme 7: youth experience resolution of chest dysphoria and improved quality of life and functioning after MCS	
Resolution of chest dysphoria and improved quality of life	
	"I'm happy with what it is. I don't care about the scars. I think they look cool." (D.V.) "[MCS] just makes everything a million times betterI can't even describe how much. I is amazing. That's about the only words that are coming to my brain—because it doesn't just help with the chest dysphoria—but it's also just like you're so much more confident in yourself after you have it I'm happy with itjust like having—like closes to the body that I am supposed to have." (S.M.)
Improved functioning	to the body that I am supposed to have. (o.w.)
	"It was liberating, because I just could finally live a normal life like the rest of kids my age [It's] a lot easier to talk to people because I'm not as uptight, or I don't come of as rigid as I was. So, it's made me a lot more relatable to people because I could actually — I don't have to worry about my chest dysphoria." (A.C.) "It's been a relief Now that the problem is basically solvedI can basically focus the energy that I was focusing on [my chest] and redirect it somewhere way more productive I can now do actual exercise for the first time in my life." (D.V.)
Theme 8: chest dysphoria is a large component of gender dysphoria	,
and is not adequately addressed by testosterone alone	Whitelester and a second and a second and a second at a second
	"I think that a lot of my dysphoria, just general dysphoria, comes from my chest! wan top surgery first and then I wanna decide if I still wanna go on [testosterone] So [my chest dysphoria's] just a lot more prominent." (V.S.)
	"I've looked forward to [MCS] more than I have, to be honest, for the testosterone." (A.O. "I think [testosterone] kind of made [my chest dysphoria] a little worse, because I saw al of these other things changing, but then my body really still kind of stayed the same. (E.P.)
	"Over the past, I want to say year or so, [my chest dysphoria]'s dropped slightly. And I think that's because I'm on testosterone. So there are parts of my body that I like now But there are still days where it's really bad." (J.S.)

Improved Quality of Life and Functioning After MCS

All post-MCS youth reported complete or near-complete resolution of their chest dysphoria after MCS. They were unanimously satisfied with their MCS results and had no regrets, regardless of the surgical technique used.

be absolutely perfect. And now, looking at my chest, I know it's not perfect...but honestly- it's such a breath of fresh air just being able to see it in the mirror and see it be flat.... It's great. I'm just super, super satisfied.

F.J.

All post-MCS youth experienced improvements in quality of life and self-esteem, and interpersonal relationships; decreased anxiety; increased social engagement and physical activity; and relief from the cognitive load of chest dysphoria, enabling them to direct their attention to other endeavors.

I think I really didn't realize how much it was affecting my life until I

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was able to start going out and doing things again without that constant worry and fear. I just felt more confident as a person. I was able to talk to people.... A lot of things that I wasn't able to do because that was holding me back.

H.G.

Theme 8: Chest Dysphoria Is a Large Component of Gender Dysphoria and Is Not Adequately Addressed With Testosterone Alone

Several youth expressed that chest dysphoria was the most prominent or most distressing aspect of their overall gender dysphoria. All youth had access to testosterone earlier than MCS, yet some viewed MCS as the more vital component of their treatment: "I honestly think that [MCS] would help like 95 percent of my issues with dysphoria just solely because for me my chest is the most dysphoric thing about me" (I.B.).

Youth undergoing testosterone therapy noted it had variable effects on their chest dysphoria, with similar numbers of youth commenting that testosterone made their chest dysphoria worse, unchanged, or only slightly better. Of those who felt that their dysphoria had worsened while they were on testosterone, some theorized that their chest dysphoria appeared to worsen because of improvement in other dimensions of dysphoria (ie, voice, menstruation) due to the testosterone therapy.

When I started [testosterone, my chest dysphoria] got worse, because other things that were causing me dysphoria lessened...so it made my chest dysphoria feel worse in comparison...it probably was the same, but the fact that everything else, like...voice dysphoria was getting a bit better-it made my chest dysphoria more prominent in comparison.

I.S.

DISCUSSION

Overall, our study reveals that chest dysphoria is a critical component of gender dysphoria, leading to marked suffering and functional impairments, and can contribute to suicidality. Youth in the post-MCS cohort experienced tremendous benefits, including resolution of chest dysphoria and improvements in mood, confidence, quality of life, and functioning, mirroring what has been described in the adult literature. ^{9–15} In addition, the 10 youth who had MCS as minors were satisfied with their surgical outcomes and reported similar benefits to what has been seen in the adult literature.

Although it is common for pediatric and adolescent gender-affirming medical care to be thought of as limited to pubertal blockers and gender-affirming hormones, postpubertal transmasculine youth reported that testosterone did little to alleviate their chest dysphoria. Olson-Kennedy et al19 observed a positive correlation between their measure of chest dysphoria and time on testosterone therapy. However, several of the youth in our study who reported worsening chest dysphoria after starting testosterone therapy reflected that this was not due to testosterone directly worsening their chest dysphoria but rather due to testosterone resolving other aspects of dysphoria and no longer drawing attention away from the chest. In addition, some insurers and surgeons require testosterone therapy for a requisite amount of time before MCS, 18 but our data suggest that such requirements may potentially cause harm by restricting or delaying access to MCS.

These data suggest that MCS is a critical component of gender-affirming care for many transmasculine youth with chest dysphoria and that MCS should be considered whenever it is clinically indicated, even if the youth is a minor, to alleviate suffering. Recently, legislation has been proposed in 14 US states to prohibit gender-affirming medical and surgical care for minors, 21-34 conflicting with best practice guidelines 16,17 and the official position of the American Academy of Pediatrics.35 Our results suggest that such age-based bans for clinically indicated care are misguided. Withholding clinically indicated MCS purely on the basis of age may needlessly prolong suffering, as

unanimously described in our study, resulting in heightened risk of negative health outcomes, including suicidality.

Our study has several limitations, including a sample from a single clinical site that was predominantly white and privately insured, which reflects the population receiving gender-affirming care in our clinic and across the United States³⁶ but limits generalizability to youth in other locations or youth who lack access to care. In addition, we focused on transmasculine youth and did not include nonbinary youth assigned female sex at birth who do not identify along the masculine spectrum, so our findings cannot be generalized to that population, and is an area for future work.

CONCLUSIONS

This study is one of the first studies to describe transmasculine youths' experiences of chest dysphoria and the impact that MCS can have in alleviating suffering and improving function. These findings lend support for current clinical practice guidelines,16,17 which support MCS in minors when clinically and developmentally appropriate, and underscore the importance of insurance coverage not being restricted by age. Future research is needed to develop and assess patient-reported outcomes of MCS across a broad age range of adolescents, with the hope that it will lead to improved health outcomes in this vulnerable population.

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ABBREVIATIONS

EHR: electronic health record MCS: masculinizing chest surgery

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Breast augmentation in male-to-female transgender patients: Technical considerations and outcomes

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ABSTRACT

Introduction: Gender-affirmation surgery is essential in the management of gender dysphoria. For male-to-female transgender women (transwomen), feminization of the chest is a component in this process. There is minimal literature describing effective and safe techniques for breast augmentation in transwomen. Here we describe our operative techniques and considerations.

Methods: A retrospective review of a single surgeon experience was performed for transwomen who underwent primary breast augmentation between October 1, 2014, and February 1, 2017. Surgical outcomes and complications were analyzed.

Results: Thirty-four patients with an average age of 34.4 years were included in this series (range 19–59 years). Surgical approach was through an inframammary incision with a submuscular pocket and either silicone smooth round (24%) or textured anatomic implants (76%). Six patients experienced postoperative complications (17.6%). Two patients underwent reoperation for implant extrusion

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(5.9%). Higher BMI and longer preoperative hormonal therapy duration were significantly associated with complications (p=0.008; p=0.039, respectively). Feedback from the respondents was overall positive. Most of patients (92.7%) reported being happier and feeling more satisfied with their chest than before their operation. All respondents (100%) reported improvement in their gender dysphoria and would undergo the operation again. Patient dissatisfaction was significantly associated with longer time on preoperative hormones (p=0.008) and had a trend toward association with higher implant volume (p=0.083).

Conclusions: Breast augmentation in transwomen is safe and typically leads to high patient satisfaction with improvement of gender dysphoria. Larger, longer term studies are needed to appropriately delineate complication risks and contributing factors.

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Introduction

Gender dysphoria, or the emotional and social distress due to discrepancy between an individual's gender identity and their assigned sex at birth, requires a multidisciplinary approach.¹⁻³ As such, many individuals benefit from both hormonal and gender-affirmation surgery. Although not all patients with gender dysphoria require surgical intervention, gender-affirmation surgery continues to be recognized as one of the optimal treatments for this patient population.^{2,4-6}

For male-to-female transgender patients (transwomen), the acquisition of a female appearance is essential to ameliorate the incongruity between gender identity and assigned sex. There are marked differences between the male and female chest. These include differences in the quantity of glandular tissue, as well as a broader breast base diameters and shorter nipple to inframammary fold (IMF) distance in males. In addition, the male nipple-areolar complex (NAC) is smaller, wider spaced, and more ovoid than the female NAC.^{7,8} A feminized chest is one way for transwomen to present their desired gender in public and private life; it is not surprising that breast augmentation is generally the first, and sometimes only, surgical procedure that transwomen pursue.

Although transwomen typically initiate hormonal therapy before surgical evaluation, there is a wide response range to estrogen therapy. Ultimately, the majority of individuals choose to pursue surgical intervention, with breast augmentation rates reported up to 67% in the transwomen population. Importantly, studies have confirmed the positive impact breast augmentation can have for transwomen. Such studies support breast augmentation as a quality-of-life operation and not simply a cosmetic procedure. 10,11

There are many techniques described for primary breast augmentation and implant-based breast reconstruction for the cis-gender population. There is far less literature available describing breast augmentation for transwomen. The purpose of this study is to describe the senior author's preoperative assessment, surgical technique, and surgical limitations of breast augmentation when specifically performed for transwomen along with surgical and patient-reported outcomes.

Methods

The study design was approved by an institutional review board. A retrospective, single-institution, single-surgeon experience was performed for primary breast augmentations that occurred between October 1, 2014, and February 1, 2017. Inclusion criteria for the study were a diagnosis of gender dysphoria, age 18 years or older, and capacity to make informed consent for treatment.

Rank your agreement with the following statements: (Completely Agree, Agree, Disagree, Completely Disagree, I Don't Know)

I feel positively about my chest.

I am satisfied with the appearance of my chest.

I feel comfortable letting a sexual partner look at my chest.

I feel comfortable letting a healthcare provider examine my chest.

I am not embarrassed about my chest.

I am now happier after my operation than before my operation.

I am more satisfied with the appearance of my chest after my operation than before my operation.

My gender dysphoria is improved.

My gender dysphoria is resolved.

My physical appearance adequately expresses my gender identify.

I am generally comfortable about how others perceive my gender identity when they look at me.

I would do this operation again.

I would recommend this operation to a friend.

Answer the following questions:

(Yes or No)

Did you have any complications from surgery?

Will you or have you had corrective surgery for your chest feminization?

Are you currently employed?

Have you had a history of sexual abuse?

Have you had a history of physical abuse?

Have you had a history of suicide attempt?

Figure 1. Patient-reported outcome measures were assessed using a 19-item inventory developed by our study team.

Patient demographic data were compiled, including age, height, weight, body mass index, comorbidities, and pertinent social history. Surgical details including implant characteristics, incision location, and pocket position were reviewed. Surgical outcomes and complications were analyzed. Analysis was performed using Fisher's exact test and Student's unpaired *t*-test (MedCalc Software, Ostend, Belgium).

Patient-reported outcome measures (PROMs) were evaluated with a 19-item inventory adapted from previous transgender studies that was delivered electronically (Figure 1). To date, there have been no validated PROMs for breast augmentation in transwomen. Thus, our inventory attempted to assess not only patient satisfaction but also changes in quality-of-life, psychosocial well-being, and gender dysphoria postoperatively.

Technique

Preoperative assessment

A complete history is obtained and physical examination is made with careful assessment for comorbidities. Patients are instructed to avoid aspirin and other antiplatelet medications if not medically contraindicated. Patients are also instructed to abstain from nicotine products for four weeks before surgery and four weeks after surgery.

The majority of patients are treated with hormonal therapy before undergoing breast augmentation, but this is not mandatory. There is evidence to suggest an increased risk of deep venous thrombosis in transgender women receiving hormonal therapy.¹⁴ While we did not routinely

ask our patients to stop taking these medications in the perioperative period due to the potential negative emotional and physiological changes experienced by the patient, it was important for the patient to be educated and to understand these risks before proceeding with breast augmentation.

Unlike traditional breast augmentation, the World Professional Association for Transgender Health Standards of Care (WPATH SOC) recommends at least one referral letter from a mental health professional before chest/breast surgery. While some argue this may place undue strain on this patient population, it is important to adhere to current WPATH SOC guidelines and request appropriate medical-legal documentation. 16,17

The breast augmentations were performed in the submuscular plane with textured anatomic or smooth round breast implants. We prefer this technique due to the lack of overlying glandular tissue and to provide naturally shaped feminine breasts without the appearance of overly full superior pole. Implant size is determined using a combination of patient preference and surgeon experience in conjunction with patient characteristics including breast base width, height, weight, soft tissue thickness, and preoperative asymmetries. Although described for cis-patients, the authors have found Tebbett's methodology in determining planned implant size and new IMF placement a helpful guide in the trans population.¹⁸

Special considerations

As previously mentioned, there are notable anatomic differences between male and female chests, many of which cannot be overcome completely with current reconstructive procedures and devices. Males tend to have wider chests with laterally displaced NACs. When placing an implant, it can be placed either directly behind the NAC (which allows for only limited cleavage) or placed slightly more medial (which will ultimately lead to nipples located more lateral on the breast mound). Fat grafting can help to smooth or fill the medial breast, but it is often difficult to obtain sufficiently feminine cleavage. In addition, we have found that the differences in male and female NAC size and shape tend to be ameliorated when the tissue is placed on stretch from the underlying device. Overall, individuals must be counseled on these differences to offer realistic expectations and discuss the aforementioned tradeoffs before proceeding with surgery.

Preoperative markings and operative technique

Before surgery, the midline and IMF are marked. Breast diameters are then confirmed. A 3-cm zone between the breasts is marked to avoid undermining in an effort to prevent medial implant migration. The new IMF can be planned according to the desired implant size as noted above. (Figure 2A) In determining the new IMF placement, the authors advocate erring on the incision possibly riding up slightly onto the breast rather than onto the chest; patients tolerate scars on the inferior breast mound better than one visible in a bathing suit or brassiere.

The procedure is then performed in similar fashion to that of an inframammary, submuscular augmentation in a cis patient (Figure 2B). Notably, the access incision in most circumstances needs to be significantly below the native IMF. In contrast to a cis patient, however, pocket location must be predetermined based on the desire for optimized cleavage vs. nipple position. Care must be taken to dissect a pocket to the exact dimensions of the chosen implant to avoid possible implant migration or rotation. The authors prefer to utilize triple antibiotic solution for irrigation when the pocket has been established.¹⁹

Preferably, the implant should be chosen during preoperative consultation. If there is some degree of uncertainty intraoperatively, especially of the overlying skin envelope, saline sizers can be used. These devices should be used with caution to prevent overdissection of the pocket. In rare instances, lateral relaxing incisions may be required.

An implant insertion funnel is typically used for larger implants. (Figure 2C) If there is concern for downward migration, a three-point fixation stitch is used to tack Scarpa's fashion down to the chest wall. The incision is closed in a layered fashion, and a sterile dressing is placed. Immediate



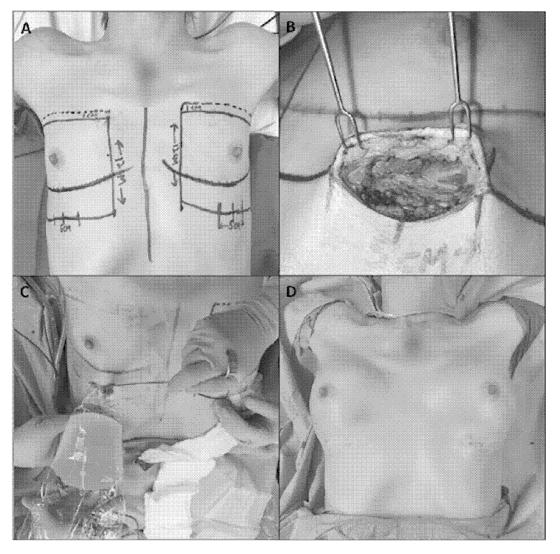


Figure 2. Preoperative markings (A), surgical plane (B), implant insertion (C), on table result (D).

postoperative results are shown in Fig. 2D. Preoperative and 1-year postoperative results are shown in Figures 3 and 4.

Postoperative care

At the conclusion of the procedure, a circumferentially placed elastic wrap is used for compression. When not medically contraindicated, these procedures are performed as outpatient surgery. At follow-up, the patient is instructed to wear a sports bra for four weeks and to avoid strenuous activities to prevent implant migration.

Additional approaches and adjunctive procedures

While our results have been promising using a single-stage augmentation, there may be utility for a two-stage approach with tissue expansion in select patients. In addition, fat grafting can be performed as an adjunct procedure, especially to the medial and superior poles of the breast to help camouflage widely spaced breasts. Further, NACs that are not sufficiently large can be tattooed to increase the apparent size.

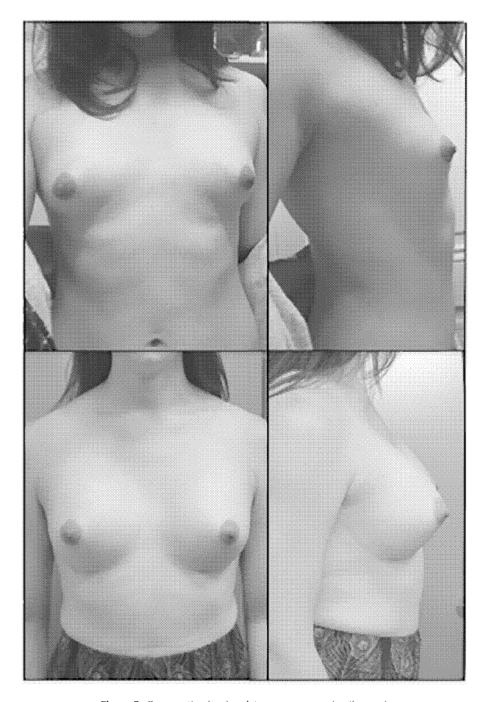


Figure 3. Preoperative (top) and 1-year postoperative (bottom).

Results

A total of 34 patients who met inclusion criteria for the study were identified. Representative postoperative results are shown in Figures 3 and 4. Patient demographics and implant characteristics are detailed in Table 1. Patient age ranged from 19 to 59 years at the time of operation, with an average age of 34.4 years old. The average follow-up period since time of surgery was 15.9 months (range 0.5–38.7 months). Two patients were lost to follow-up postoperatively. Over one quarter of patients (26.5%) had documented medical comorbidities at the time of operation, and over half (55.9%) had a

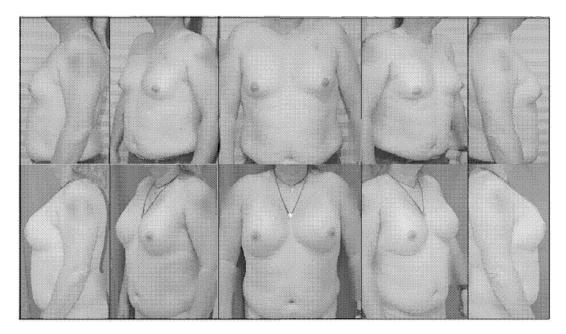


Figure 4. Preoperative (top) and 1-year postoperative (bottom).

history of a mental health diagnosis. All implants used were silicone based. The average implant size was 520 cc with a range of 350 to 700 cc. The majority of implants were textured, anatomic devices.

Our patients experienced an overall complication rate of 17.6%. Complications included hematoma (n=1), infection (n=1), extrusion (n=2), excessive scarring (n=1), asymmetry (n=1), hypersensitivity (n=1), and numbness (n=1). (Table 2) Two patients underwent reoperation for implant extrusion. Four patients expressed dissatisfaction with their postoperative result.

On univariate analysis correlating surgical complications with comorbidities (Table 3), patients with comorbid conditions were not found to be at higher risk of complication (OR=0.5, p=0.55). Similarly, smoking (OR 2.3, p=0.40), implant type (OR 0.57, p=0.63), and age (p=0.86) were not found to be statistically significant predictors of complications. Interestingly, higher BMI and longer preoperative hormonal therapy were significant predictors of complications in this series (p=0.008; p=0.039, respectively). Increased implant size did trend toward significance for higher rates of complication (p=0.058).

When stratifying results by satisfied versus dissatisfied patients (Table 4), comorbidities, smoking, implant type, mental health history, history of abuse, history of suicide attempt, age, and BMI were not significant between the two groups. However, time of hormonal therapy was significant between satisfied and unsatisfied patients (p = 0.008), with longer preoperative hormonal therapy associated with patient dissatisfaction. Increased implant size again appeared to trend toward significance (p = 0.083), with higher implant size associated with patient dissatisfaction.

A total of twelve patients (35.3%) responded to the postoperative survey. Feedback from the respondents was overall positive. Most patients (92.7%) reported being happier and feeling more satisfied with their chest after their operation than before their operation. All patients (100%) reported improvement in their gender dysphoria and expressed they would choose to undergo the operation again. Some patients (25%) reported they would seek revisionary surgery after their chest feminization. (Table 5)

Discussion

Despite a large body of literature dedicated to esthetic breast augmentation, there is a paucity of data dedicated specifically to breast augmentation in transwomen. Further, the majority of literature dates back to the 1990s or earlier. 10,20-22 A more recent study has offered data showing improvement

Table 1 Patient demographics and implant characteristics.

Demographics	Count
Patients	34
	Average (Range)
Age (years)	34.4 (19–59)
Patient Weight (lbs)	182.2 (120–275)
Patient Height (in)	70 (64–76)
BMI	26.1 (19.4–39.5)
Hormone Therapy Period (years)	3.1 (0-18)
Follow-Up Time (months)	15.9 (0.43–48.7)
	Count (%)
Medical comorbidities	9 (26.5)
Mental health history	19 (55.9)
Prior chest surgery	3 (8.8)
Tobacco use	7 (20.6)
Illegal drug use	7 (20.6)
Comorbidity Type	Count
Diabetes	3
HIV infection	4
Hypertension	4
Heart disease	1
Implant Characteristics	
	Average (Range)
Size (cc)	520 (350-700)
	Count (%)
Smooth, round	16 (24%)
Textured, anatomic	52 (76%)

Table 2 Surgical outcomes.

	Count (%)
Patients with complications	6 (17.6%)
Specific complications	
Hematoma	1
Infection	1
Extrusion	2
Scarring	1
Asymmetry	1
Hypersensitivity	1
Numbness	1
Patients undergoing reoperation	2 (5.9%)

Table 3 Analysis of characteristics associated with surgical complications,

Complications				
Patient Factor	Odds ratio (p-va	lue)		
Medical Comorbidity	0.5 (0.55)			
Smoker	2.3 (0.40)			
Prior chest surgery	0.75 (0.75)			
Mental health history	0.56 (0.71)			
Factor	Complication	No Complication	<i>p</i> -value	
Age (yrs)	34.3	33.7	0.86	
BMI	29.3	25.4	0.008	
Hormonal Therapy Period (mo)	74.1	29.4	0.039	
Implant size (cc)	601	504	0.058	

Table 4Analysis of characteristics associated with patient dissatisfaction.

Patient Factor	Odds ratio (p-value)		
Medical comorbidity	0.29 (0.42)		
Smoker	0.34 (0.5	5)	
Implant type	0.26 (0.3	22)	
Mental health history	0.56 (0.7	71)	
History of physical abuse	2.18 (0.65)		
History of sexual Abuse	2.18 (0.65)		
History of suicide attempt	6.7 (0.3	5)	
Factor	Satisfied	Dissatisfied	p-value
Age (yrs)	34.2	34.75	0.93
BMI	25.7	29	0.3
Hormonal Therapy Period (mo)	29.5	96	0.008
Implant size (cc)	509	614	0.083

Table 5Patient-reported outcomes after breast augmentation in transwomen.

Survey statement (%)	CA	Α	D	CD	IDK
I feel positively about my chest.	66.7	25	0	8.3	0
I am satisfied with the appearance of my chest.	66.7	16.7	8.3	8.3	0
I feel comfortable letting a sexual partner look at my chest.	83.3	8.3	0	0	8.3
I feel comfortable letting a healthcare provider examine my chest.	83.3	16,7	0	0	0
I am not embarrassed about my chest.	66.7	25	0	8.3	0
I am happier now after my operation than before my operation.	66.7	25	8.3	0	0
I am more satisfied with the appearance of my chest now after my operation than before my operation.	83.3	8.3	8.3	0	0
My gender dysphoria is improved.	58.3	41.7	0	0	0
My gender dysphoria is resolved.	33.3	8.3	50	0	0
My physical appearance adequately expresses my gender identity.	50	41.7	8.3	0	0
I am generally comfortable with how others perceive my when they look at me.	50	50	0	0	0
I would do this operation again.	83.3	16.7	0	0	0
I would recommend this operation to a friend.	66.7	33.3	0	0	0
Survey question (%)		Y	es/es		No
Will you or have you had corrective surgery for your chest feminization. Are you currently employed?	on?		25 66.7		75 33.3
Have you had a history of sexual abuse?		1	6.7		83.3
Have you had a history of physical abuse?		2	25		75
Have you had a history of suicide attempt?		2	!5		75

CA = "Completely Agree,", A = "Agree," D = "Disagree," CD = "Completely Disagree," IDK = "I Don't Know".

in breast satisfaction and psychosocial and sexual well-being for transwomen who have undergone breast augmentation, highlighting the medical necessity of this procedure. ¹¹

In our experience, we encountered distinct technical challenges related to differences in male and female anatomy when performing breast augmentation in transwomen. As previously mentioned, there are differences in quantity of glandular tissue, shape and size of chest sternum and chest wall, nipple to IMF distances, and shape and size of NACs.^{7,8} Further training in the care of transgender patients and gender-affirming surgeries may allow providers to more effectively address the technical challenges in these procedures.^{23–27}

Despite the fact that the majority of our patients had been taking hormonal therapy for greater than 12 months before undergoing breast augmentation, there was infrequently enough subcutaneous tissue in both the superior and inferior pole to safely support an implant. For that reason, all of our reconstructions required a submuscular plane. This is in contrast to some of the findings of previous studies; Kanhai and colleagues document a preference for the subglandular approach to better "fill"

the breast as opposed to a submuscular or dual plane approach.²⁸ Of note, the aforementioned study reported a trend toward larger implants with an average prosthesis volume of 165 cc in 1979 and 287 cc in 1996 ²⁸. The apparent trend toward larger implants continues, as our study had an average size of 520 cc, which also favors our preference for a submuscular rather than subglandular approach.

Based on our experience, we have noted a distinct limitation related to chest wall and NAC position. Males tend to have wider chests with laterally displaced NACs. When planning the operation, a decision must be made regarding implant placement relative to the NAC. In our experience, patients prefer to have their nipples centered on their breast mound, often making it difficult to obtain sufficient feminine cleavage, even with adjunctive procedures like fat grafting. This balance needs to be underscored at the preoperative consultation to allow the patient to make the decision regarding these tradeoffs.

While our results were relatively favorable, our group did experience complications in 6 of the 34 patients (17.6%). Specifically, we experienced hematoma (n=1), infection (n=1), poor scarring (n=1), asymmetry (n=1), hypersensitivity (n=1), and numbness (n=1). Further, we had two patients who experienced implant extrusion: one who developed a hematoma with superimposed infection and one who was diagnosed with Ehlers-Danlos syndrome postoperatively. In our analysis, we found that BMI and length of hormone therapy beore operation were significantly higher in individuals who experienced complications. BMI has been correlated with adverse surgical outcomes in many fields, and thus,s this is not surprising. Our group is uncertain why the length of hormonal therapy was correlated with complications, but we do note that there were several outliers who had been on hormonal therapy for greater than a decade, potentially confounding results.

Additionally, longer time on hormonal therapy preoperatively was associated with higher dissatisfaction. Once again, the reason is unknown. One could speculate that patients who have been on hormonal therapy for a longer time may have been living in their desired gender role for longer, with potentially a higher degree of dysphoria and higher preoperative expectations. In addition, patients who may have been on hormonal therapy longer preoperatively may have more breast development, and thus, surgical breast augmentation may not seem as dramatic as compared to patients who had minimal breast tissue. This highlights one shortcoming in this study that preoperative breast volumes were not assessed in our patients. Additionally, endocrine therapy also may stimulate the growth of axillary breast tissue, and this may be contributory to dissatisfaction in appearance, although none of the patients in the study expressed this as a concern. Axillary liposuction/lipectomy was not performed in this patient cohort.

In this series, four patients were found to be dissatisfied with their size with 50% wanting to be larger. Interestingly, the two patients who wished to have larger implants were initially augmented with 600cc implants, which was the higher end of the range of this study and the upper limit of what their breast pocket could tolerate at the time of surgery. Although not statistically significant in our study, we found that larger implant sizes trended toward a higher rate of complications and patient dissatisfaction. Given this finding, our group has continued to stress the size limitations to our patients during preoperative counseling and education. There may be a role for a staged procedure with a tissue expander for patients who desire a size that far exceeds their available breast pocket.

Based on our PROMs data, we found a high level of satisfaction and improvement in our patients' quality of life following breast augmentation. (Table 5) In addition, 100% of respondents either completely agreed or agreed that their gender dysphoria was improved following breast augmentation. Complete resolution of gender dysphoria following breast augmentation was minimal. This is not surprising, as there are many aspects of gender-affirmation beyond chest appearance. Yet, these are valuable data supporting the efficacy of this procedure. Further studies are needed to determine validated, standardized patient-reported outcome measures for gender-affirming surgery, and these data will continue to alter considerations in these procedures.³³⁻³⁵

Despite these promising early results, our study has several limitations. First, this is a single-institution, single-surgeon experience. While different types of implants were used, a similar submuscular technique was employed for all patients. We understand that there are several ways to perform this operation, but in the senior author's hands, this technique offers safe, reliable, and replicable results. Additionally, this study is limited by the relatively small sample size and variable follow-up

times. To date, few surgeons offer dedicated care to transgender patients; hence, a significant portion of the senior author's practice is made up of patients who travel long distances for care. Thus, it is not surprising that several of the patients in this study were lost to follow-up or were unable to be contacted to perform the PROM inventory. Finally, the PROM inventory was not completed by any of the six patients who experienced a complication. This may lead to some level of response bias in our PROM data but unlikely to negate the overall positive responses from patients who participated in this portion of our study. Despite these limitations, this study offers insight into the preoperative planning, intraoperative strategy, postoperative complications, overall limitations, and the clinical value and efficacy of breast augmentation in transwomen.

Conclusions

Breast augmentation in transwomen poses technical challenges unique to this patient population. While there are strategies to cope with the anatomic differences between male and female chests and NACs, certain characteristics are difficult to overcome and hence should be discussed with patients before proceeding with surgery. Overall, this operation is clinically meaningful, and additional research is needed to continue to offer this population optimal and reliable results.

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The authors have no financial interest to declare in relation to the content of this work.

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Guiding the conversation—types of regret after gender-affirming surgery and their associated etiologies

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Background: A rare, but consequential, risk of gender affirming surgery (GAS) is post-operative regret resulting in a request for surgical reversal. Studies on regret and surgical reversal are scarce, and there is no standard terminology regarding either etiology and/or classification of the various forms of regret. This study includes a survey of surgeons' experience with patient regret and requests for reversal surgery, a literature review on the topic of regret, and expert, consensus opinion designed to establish a classification system for the etiology and types of regret experienced by some patients.

Methods: This anonymous survey was sent to the 154 surgeons who registered for the 2016 World Professional Association for Transgender Health (WPATH) conference and the 2017 USPATH conference. Responses were analyzed using descriptive statistics. A MeSH search of the gender-affirming outcomes literature was performed on PubMed for relevant studies pertaining to regret. Original research and review studies that were thought to discuss regret were included for full text review.

Results: The literature is inconsistent regarding etiology and classification of regret following GAS. Of the 154 surgeons queried, 30% responded to our survey. Cumulatively, these respondents treated between 18,125 and 27,325 individuals. Fifty-seven percent of surgeons encountered at least one patient who expressed regret, with a total of 62 patients expressing regret (0.2–0.3%). Etiologies of regret were varied and classified as either: (I) true gender-related regret (42%), (II) social regret (37%), and (III) medical regret (8%). The surgeons' experience with patient regret and request for reversal was consistent with the existing literature.

Conclusions: In this study, regret following GAS was rare and was consistent with the existing literature. Regret can be classified as true gender-related regret, social regret and medical regret resulting from complications, function, pre-intervention decision making. Guidelines in transgender health should offer preventive strategies as well as treatment recommendations, should a patient experience regret. Future studies and scientific discourse are encouraged on this important topic.

Keywords: Transgender surgery; transgender regret; detransition; reversal surgery; retransition; gender-affirming surgery

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Introduction

Over the past several years, there has been sustained growth in institutional and social support for transgender and gender non-conforming (TGNC) care, including genderaffirming surgery (GAS) (1). The American Society of Plastic Surgeons (ASPS) estimates that in 2016, no less than 3,200 gender-affirming surgeries were performed by ASPS surgeons. This represents a 20% increase over 2015 (2) and may be partially attributable to an increase in third party coverage (3,4). A rare, but consequential, risk of GAS is post-operative regret that could lead to requests for surgical reversal. As the number of patients seeking surgery increases, the absolute number of patients who experience regret is also likely to increase. While access to genderaffirming health care has expanded, these gains are under continued threat by various independent organizations, religious, and political groups that are questioning the legitimacy of this aspect of healthcare despite an evergrowing body of scientific literature supporting the medical necessity of many surgical and non-surgical affirming interventions. It is therefore not surprising that studies on regret and surgical reversal are scarce compared to studies on satisfaction and patient-reported outcomes. The transgender community rightfully fears that studies on this topic can be miscited to undermine the right to access to healthcare.

The goal of this study is to assist patients, professionals, and policy makers regarding this important, albeit rare, occurrence. We do so by addressing the following:

- The current literature regarding the etiology of regret following gender-affirming surgery;
- (II) The experience of surgeons regarding requests for surgical reversal.

Based on these results, the authors propose a classification system for both type and etiology of regret.

It is important to acknowledge that the authors identify along the gender spectrum and are experts in the field of transgender health (mental health, primary care, and surgery). We hope to facilitate discussion regarding this multifaceted and complex topic to provide a stepping-stone for future scientific discussion and guideline development. Our ultimate goal is to reduce the possibility of regret and provide clinical support to patients suffering from the sequelae of regret. We present the following article in accordance with the SURGE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-6204).

Methods

Survey

A 16-question survey (see Table S1) was developed and uploaded to the online survey platform SurveyMonkey (SurveyMonkey, Inc., San Mateo, CA, USA). This anonymous survey was e-mailed by the senior author to the 154 surgeons who registered for the 2016 World Professional Association for Transgender Health (WPATH) conference and the 2017 USPATH conference. There were no incentives offered for completing this survey. One reminder e-mail was sent after the initial invitation.

Respondents were asked to describe their practices, including: country of practice, years in practice, a range estimate of the total number of TGNC patients surgically treated, and the number of TGNC patients seen in consultation who expressed regret and a desire to reverse or remove the gendered aspects of a previous gender-affirming surgery. We limited the questions to breast and genital procedures only. Facial surgery was excluded as there are no associated WPATH criteria, so there is less standardization of patient selection for surgery. Thus, we did not feel that those patients should be pooled with those who were subject to WPATH criteria in our calculation for prevalence of regret. We did not define the term "regret" in order to capture a wide range of responses. Respondents were asked about their patients' gender-identification, the patient's surgical transition history, and the patient's reasons for requesting reversal surgery. If the respondents had experience with patients seeking reversal surgery, the number of such interventions were queried to include: the initial genderaffirming procedure and the patients' reason(s) for requesting reversal procedures. The respondents were also asked about the number of reversal procedures they had performed, and what requirements, if any, they would/did have prior to performing such procedures. Finally, respondents were asked whether they believed that the WPATH Standards of Care 8 should address this topic.

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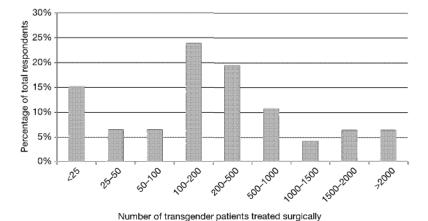


Figure 1 Distribution of transgender surgery experiences among respondents.

Statistical analysis

Response rate was calculated from the total number of respondents as compared to the number of unique survey invitations sent. Responses to the survey were analyzed using descriptive statistics. When survey questions offered ranges, (i.e., estimating the number of patients surgically treated), the minimum and maximum values of each of the selected answers were independently summed to report a more comprehensible view of the data. Partially completed surveys were identified individually and accounted for in analysis. Any missing or incomplete data items from the survey were excluded from the results with the denominator adjusted accordingly.

Narrative literature review

A MeSH search of the gender-affirming outcomes literature was performed on PubMed for relevant studies pertaining to regret and satisfaction. Terms included (regret) and (transgender) and (surgery) or (satisfaction) and (transgender) and (surgery). These terms included their permutations according to the PubMed search methodology. Original research and review studies whose abstracts addressed the following topics were included for full-text review: gender-affirming surgery, sex reassignment, patient satisfaction, detransition, regret. A total of 163 abstracts were reviewed and a total of 21 articles were closely read for the relevant discussion of regret and satisfaction.

Ethical statement

This study was approved by the Oregon Health & Science

Institutional Review Board #17450 and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Subjects were physicians and so gave consent through their participation in the survey. The patients who were captured in the study were not individually consented for this research as the IRB felt it to be unnecessary given the degree of separation of the study and lack of identifiers. None of the study outcomes affect future management of the patients' care.

Results

Survey results

Of the 154 surgeons who received the survey between December 2017 and February 2018, 46 (30%) surgeons completed the survey. The survey, including its results, can be found in Table S1. Thirty respondents (65%) were in practice for greater than 10 years, and most (67%) practice in the United States, followed by Europe (22%). The respondents treated between 18,125 and 27,325 TGNC or gender non-conforming (TGNC) patients. Most of the respondents (72%) surgically treated over 100 TGNC patients (see Figure 1). Of the 46 respondents, 61% of respondents encountered either at least one patient with regret regarding their surgical transition or a patient who sought a reversal procedure-irrespective of whether their initial surgery was performed by the respondent or another surgeon. Twelve respondents (26%) encountered one patient with regret, and the remaining 12 (26%) encountered two or more patients with regret. One respondent indicated that they encountered between 10 and

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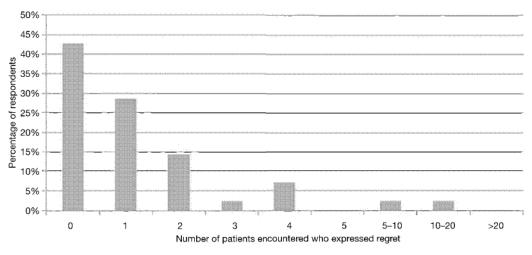


Figure 2 Number of transgender patients encountered who expressed regret.

Table 1 Regretful patients encountered and surgeries performed

Table 1 Regrettar patients encountered and stars	erres perr	ormea .
Results regarding regret and reversal	N	%
Total regretful patients encountered	62	100.0
Type of procedure patient sought to reverse		
Chest surgery	13	21.0
Genital surgery	45	72.6
Reversal procedures performed		
Reversal of mastectomy	0	0
Reversal of breast augmentation	6	9.7
Reversal of phalloplasty	16	25.8
Reversal of vaginoplasty	1	1.6
Regretful patients encountered, per surgeon re	sponden	t
0	18	39.1
1	12	26.1
2	6	13.0
3	1	2.2
4	3	6.5
5	0	0.00
5–10	1	2.2
10–20	1	2.2
>20	0	0.0

Totals do not add to 100 due to incomplete responses.

20 patients who regretted their surgical gender transition. No respondent encountered more than 20 such patients (see *Figure 2*). This amounted to a total of 62 patients with regret regarding surgical transition, or a 0.2% to 0.3% rate of regret. Of these 62 patients, 13 (21%) involved chest/breast surgery and 45 (73%) involved genital surgery (see *Table 1*).

Of the 62 patients who sought surgical reversal procedures, at the time of their initial gender-affirming surgery, 19 patients identified as trans-men, 37 identified as trans women, and 6 identified as non-binary. The reasons for pursuing surgical reversal were provided for 46 patients (74%) and included: change in gender identity or misdiagnosis (26 patients, 42%), rejection or alienation from family or social support (9 patients, 15%), and difficulty in romantic relationships (7 patients, 11%). In some patients, surgical complications or social factors were cited as a reason for regret and request for reversal of genital surgery—no change in the patient's gender identity was elucidated (see Table 2, etiologies of regret). Of the 37 trans-women seeking reversal procedures, complaints at the time of secondary surgical consultation included: vaginal stenosis (7 patients), rectovaginal fistulae (2 patients), and chronic genital pain (3 patients). Of the 19 trans-men seeking reversal procedures, complaints at the time of secondary surgical consultation included: urethral fistulae (2 patients) and urethral stricture (1 patient). A total of 36 reversal procedures were reported, with supplemental

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Table 2 Etiologies of regret as seen in our survey

Regret type	Reason cited by surgeon	N	%
-	Reason unknown or no response	16	25.8
True gender-related	Change in gender identity	22	35.5
regret	Misdiagnosis	4	6.5
	Total	26	41.9
Social regret	Fear for safety due to societal judgment	1	1.6
	Difficulty in marriage or romantic/sexual relationships	7	11.3
	Rejection or alienation from family, emotional, or social supports	9	14.5
	Problems associated with employment or professional life	1	1.6
	Spiritual or religious conflict or pressure	5	8.1
	Total	23	37.1
Medical regret	Concern for health	1	1.6
	Complications due to surgery	1	1.6
	Change in sexual response	1	1.6
	Desired pregnancy	1	1.6
	Missed their natal genitals	1	1.6
	Total	5	8.1

Totals exceed 100 as respondents could select multiple options.

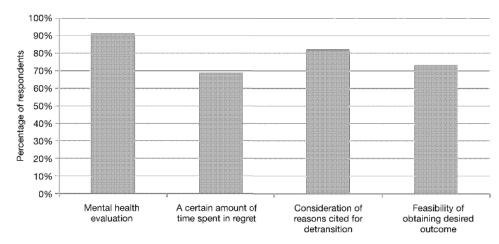


Figure 3 Respondent's requirements to proceed with surgical reversal.

qualitative descriptions provided for only 23 procedures. The distribution of the 23 reversal procedures is found in *Table 1*.

Most respondents (91%) indicated that new mental health evaluations would be required prior to performing surgical reversal procedures. Eighty-eight percent of respondents indicated that WPATH SOC 8 should include a chapter on reversal procedures (see *Figure 3*).

Literature review

Overall, the incidence of regret following gender-affirming

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surgery has been reported to be consistently very low (5-26). Wiepjes et al. (27) reported an overall incidence of surgical regret in the literature in transgender men as <1% and transgender women as <2%. Landen et al. comment that outcomes following gender-affirming surgery have improved due to preoperative patient assessment, more restrictive inclusion criteria, improved surgical techniques, and attention to postoperative psychosocial guidance (28). Although retrospective, the Wiepjes et al. study is the largest series to date and included 6,793 patients over 43 years. In this study, only 14 patients were classified as regretful, and only 10 of these patients pursued procedures consistent with intent to detransition. Perhaps most importantly, the Amsterdam team categorized regret into three main subtypes: "social regret, true regret, and feeling non-binary".

Many of the reviewed studies aimed to identify various variables or risk factors that may identify patients that are at risk or that may predict future postoperative regret.

Earlier studies focused on patient characteristics and identified several variables that were associated with regret in their patient populations. These variables include psychological variables (11,22,23), such as previous history of depression (15,26), character pathology (26) or personality disorder (5,15), history of psychotic disorder (15,28), overactive temperament (26), negative self-image (26) or other psychopathology (15,19,26), as well as various social or familial factors that include history of family trauma (19,29), poor family support (5,11,15,28), belonging to a non-core group (28), previous marriage (15,19), and biological parenthood (15,19). Landen et al. identified poor family support as the most important variable predicting future postoperative regret in transgender men and women undergoing gender-affirming surgery in Sweden between 1972-1992 (28). Defined as subsequent application for reversal surgery, the authors found that 3.8% of their study population regretted their surgery. Other factors previously associated with regret include: sexual orientation (5,7,15,19), impaired postoperative sexual function [most notably in transgender women; (29)], previous military service (29), a physically strenuous job (29), history of criminality (5), age at time of surgery and transition [>30 year increased risk; (5,6,11,15,19,29)], asexual or hyposexual status preoperatively (15,29), too much or too little ambivalence regarding prospect of surgery (29), and/ or an absence of gender nonconformity in childhood (15).

Studies examining transgender women have identified postoperative sexual function to be a significant factor contributing to possible surgical regret (15,29). A literature

review by Hadj-Moussa et al. (11) (2018) identified poor sexual function as a factor that may contribute to postoperative regret in transgender women after vaginoplasty. Lindemalm et al. (29) (1986) previously reported a rate of 30% regret in their study examining 13 transgender women in Sweden after vaginoplasty. This rate of regret is the highest reported and appears to be an outlier. In their patient population, they found that only one third had a surgically-created vagina capable of sexual intercourse. This was consistent with patientreported poor postoperative sexual function and highlights the importance of discussing sexual function following vaginoplasty. Similarly, Lawrence et al. (15) (2003) found that occasional regret was reported in 6% of transgender women after vaginoplasty, with 8 of the 15 regretful patients identifying disappointing physical and functional outcomes after their surgery. These findings are consistent with literature reviews that have found that regret is related to unsatisfactory surgical outcomes and poor postoperative function (19,30).

Transgender men have been found to manifest more favorable psychosocial outcomes following surgery and are less likely to report post-surgical regret (26). These findings highlight the importance of surgical results, and their influence on surgical regret. Despite this difference between transgender men and women, overall regret continues to remain low.

While the rate of surgical regret is low, many patients can suffer from many forms of "minor regret" after surgery. Although this could skew the outcomes data (30), this is considered temporary and can be overcome with counseling. As such, this should not be calculated in assessments of true regret (30). Alternatively, lasting regret is attributed to gender dysphoria and is explicitly expressed through patient postoperative behaviors (30). Factors that have been found to contribute to "minor regret" after gender-affirming surgery include postsurgical factors such as pain during and after surgery, surgical complications, poor surgical results, loss of partners, loss of job, conflict with family, and disappointments that various expectations linked to surgery were not fulfilled (19). Previous reviews further underline the importance of following the contemporaneous WPATH Standards of Care. This is especially important regarding patient education pertaining to surgical expectations and outcomes (11,26). Patient education programs are thought to identify those individuals who would most benefit from surgery (20). Other issues reported to decrease postoperative regret include appropriate preoperative

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diagnosis (19,20,26), consistent administration of hormone therapy (15), adequate psychotherapy (15), and the extent to which a patient undergoes a preoperative "real-life test" living in their desired gender role (15,19,20,26).

Discussion

As compared to the volume of literature regarding postoperative satisfaction following gender-affirming surgery, the literature on regret is still relatively small. However, the literature (and anecdotal surgeon reports) consistently shows low rates of regret. We juxtaposed these findings to the surgeons' experience with patients seeking reversal surgery or verbalizing regret. We found a rate of regret between 0.2–0.3%. This is consistent with the most recent data from Wiepjes *et al.* who reported rates of regret of 0.3% for trans-masculine and 0.6% for trans-feminine patients (27). The question of prevalence seems relatively well-answered by the current literature.

Perhaps the most striking finding is the heterogeneity of etiologies and risk factors associated with regret. Within this context, establishing consistent definitions for both regret and its underlying etiology is essential. Furthermore, as our understanding of gender identity evolves, our definitions and understanding become more precise. We highlight the Wiepjes et al. classification as an example of how narrower definitions may preclude an understanding of evolving gender theory. This predominantly single-institution study included 6,793 individuals, and the authors classified regret into three subtypes: social regret, true regret, and feeling non-binary. They categorized patients as either trans-female or trans-male. Conversely, in the 2015 US Transgender Survey, 35% of the nearly 28,000 respondents reported a non-binary identification (31). The classification by Wiepjes et al. is important in that it recognizes that individuals may not regret "transitioning", but rather regret specific aspects of their medical treatment. More specifically, if these individuals request a reversal procedure, they are not necessarily requesting a "reversal" of their gender identity. However, the Wiepjes et al. study does not elaborate on this topic.

Case example: a trans-masculine, non-binary individual after testosterone therapy and chest masculinization regrets having secondary sex characteristics from hormonal therapy but is highly satisfied following chest masculinization. This should be considered true gender-related regret as the individual desires, at least in part, to return to the phenotype of the sex assigned at birth (e.g., hair removal). However,

the etiology regarding this type of regret can be varied. For example, the etiology may include: insufficient exploration of the individual's gender identity [by the individual and/or mental health professional (misdiagnosis)], lack of knowledge of professionals regarding surgical options for non-binary individuals, insurance carrier mandate to undergo hormonal therapy prior to chest masculinization (healthcare stigma), etc.

Based on the reviewed literature and our consensus expert opinion, we propose the following classification of regret, examples of etiology pertaining to regret (*Table 3*), and an overview of associated terminology regarding regret (*Table 4*).

Regret is a general term that describes an emotional state wherein a previous decision now feels incorrect. This can be temporary (fleeting ambivalence) or permanent. Permanent regret can be divided into three forms: true gender-related regret, social regret, and medical regret.

True gender-related regret involves a person having undergone a transition in gender whether by social, medical, or surgical means, indicating a formal change in gender identity, who then desires to return to their assigned sex at birth or a different gender identity. True genderrelated regret differs from other types of regret in that it implies a misdiagnosis or misinterpretation of gender incongruence at the time of transition. Based on the case example, true gender-related regret need not be related to all medical treatments, but instead may be focused on specific treatments for which the individual seeks reversal. True gender-related regret constituted 42% of the requests for surgical reversal in our study. Etiology may include: misdiagnosis, insufficient exploration of gender identity, or barriers to access for options to transition to non-binary gender expression.

Social regret refers to one's desire to return to their sex assigned at birth to alleviate the repercussions of transitioning on their social life. The etiologies can vary widely and include feeling unsafe in public, losing partnership, feeling unable to partake in one's community, and encountering professional barriers. An additional reason identified in this study included religious conflict, mentioned in 9% of individuals. Social regret was cited in 37.1% of the requests for surgical reversal.

Medical regret includes regret originating from a direct outcome of a surgery or an irreversible consequence thereof. This area is particularly important for the medical community as it is preventable and may increase as access to care expands. Medical regret can be further subdivided

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Table 3 Categorizing the etiology of regret. Regret is a general term that describes an emotional state wherein a previous decision now feels incorrect

Regret type	Definition	Potential etiology	Percent citing this in request for reversal	
True gender- related regret Involves a person having undergone a transition in gender whether by social, medical, or surgical means, indicating a formal change in gender identity, who then desires to return to their assigned sex at birth or a different gender identity		Misdiagnosis, insufficient exploration of gender identity, barriers to access for non-binary transition	42%	
Social regret	Refers to one's desire to return to their sex assigned at birth so as to ease the repercussions of transitioning on their societal life	Feeling unsafe in public, loss of partnership, religious conflict, inability to partake in one's community, encountering professional barriers	37%	
Medical regret	Includes regret originating from a direct outcome of a surgery or an irreversible consequence thereof	Medical complications, dissatisfaction with functional outcome, pre-operative decision making (e.g., inadequate/incomplete counseling, change in life goals)	8%	

Table 4 Definitions associated with regret

Term	Definitions
Gender fluidity	An inclusive term describing gender along a spectrum rather than a binary construct. A gender fluid individual may identify differently at various time points in their lives
Continued transition	Treatments following initial gender-affirming procedure(s) that may relate to an evolving gender identity or request further surgical consolidation of their identity. Continued transition need not be accompanied by regret for previous transition
Detransition	A change in gender role and/or the cessation of medical transition. This term should only be utilized for those who self-identify with this experience, rather than to describe the process of surgical reversal
Retransition	A phenomenon where a patient, following surgical reversal procedures, later feels that this reversal was wrong and seeks to re-affirm their previously expressed gender identity
Fleeting ambivalence	A short term or temporary regret, often related to societal stigma or medical complications in the post-operative period

into regret secondary to medical complications, long-term functional outcomes (i.e., sexual), and preoperative decision-making.

Medical regret due to inadequate preoperative decisionmaking is directly related to a medical intervention, but it is not due to a change in gender identity, medical complication, functional outcome, or social stigma. Examples include choosing a simple-release metoidioplasty rather than a phalloplasty or regretting gonadal sterilization later in life (32). In these situations, individuals may not have appreciated the long-term implications at the time they underwent the procedure, may have received incomplete or inaccurate counseling, may have had a change in life goals, or may have not had access to technologies that are currently available. This form of regret may be mitigated by employing a multidisciplinary approach which includes discussions beyond surgical risks (i.e., fertility preservation, sexuality, etc.) (33,34). Medical regret was cited in 8% of requests for reversal, however 24% of patients were separately noted to have experienced post-operative complications.

Associated definitions

Gender fluidity is an inclusive term describing gender along a spectrum rather than a binary construct. When

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applied to identity, gender fluidity, sometimes called "genderqueer" (35,36) describes an individual who remains flexible regarding their identity and may identify differently at different times in their lives. Surgeons should work collaboratively with their mental health colleagues to help the patient understand the impact of surgery and how surgery may influence/affect future life goals. Non-identified gender fluidity can be one etiology for true gender-related regret.

Continued transition medically recognizes the concept of gender fluidity and the gender spectrum. This patient seeks additional medical treatment following their initial genderaffirming procedure(s) and may express an evolving gender identity or request further surgical consolidation of their identity. The patient need not express regret over their initial transition. An example is a patient assigned maleat-birth who takes feminizing hormones and undergoes breast augmentation. Subsequently, the patient returns to the surgeon indicating they identify as non-binary and requests implant removal. With decreased stigmatization of non-binary gender identity and ability to access non-binary affirming surgical options, this type of regret may be less common in the future.

Detransition refers to a change in gender role and/or the cessation of medical transition (e.g., hormonal treatment). This term has been used controversially and disparagingly with regards to surgical transition and fails to honor the spectrum of reasons why patients may undergo reversal surgery. However, some patients utilize this term to self-identify and to describe their experiences. This term should not be used to describe the process of surgical reversal.

Retransition is a phenomenon where a patient, following surgical reversal procedures, later feels that this reversal was wrong and seeks to re-affirm their previously expressed gender identity. A reason for retransition may include a change in societal structure that has provided a safer environment for transition. The need to distinguish continued transition from retransition results from a clash between increasing societal perception of a gender spectrum and the Western culture's binary gender construct (35).

Fleeting ambivalence (considered short-term regret) over one's transition is common, especially if the patient experiences initial surgical complications or loss of their support communities. The normal grief experienced as a result of trauma should not be pathologized, and the patient should be encouraged to trust in their long-standing gender identification. Some patients may desire a change in gender identify as a result of feeling unsafe due to severe

social stigma. Knowing this, healthcare teams should counsel patients regarding the implications of transitioning within a given societal structure prior to surgery. This may include discussions regarding the effect of transitioning on relationships, careers, personal safety in public, sexuality, etc. These discussions are often facilitated by the patient's mental health professional and/or primary care provider.

Special considerations

We recognize that regret and surgical reversal are complex, multifaceted phenomena without an easy treatment path. While both regret and requests for surgical reversal are rare, the need for guideline development is critical in providing high-quality care for this patient population, regardless of prevalence.

A concern expressed by both providers and patients is that discussions regarding regret and surgical reversal may be used to restrict access to affirming care. The authors believe that research including feelings of grief and regret will not only help individuals who experience severe forms of regret but will also help to refine surgical indications and procedures to minimize this already rare occurrence. Finally, and perhaps most importantly, failure to study regret and surgical reversal procedures will allow these topics to be left up to interpretation and may not reflect the actual experience of patients.

Limitations

The literature review was not performed systematically and as such is subject to selection bias. Our survey involved a survey of gender surgeons but did not include other medical or mental health professionals who may evaluate patients requesting surgical reversal. In addition, the study findings are limited by its design. Because survey studies are prone to recall bias, response bias, and selection bias, they are not well-suited for calculating the prevalence of a particular condition. For example, 89% of the respondents practice in the United States and Europe. This leaves significant areas of the world underrepresented and so does not represent the experiences or desires of all international surgeons. Furthermore, the survey was distributed in English only, as it was circulated to surgeons who attended conferences in the United States. Most notably, patients may have sought consultation from multiple surgeons resulting in an overestimation of the prevalence of regret. Conversely, patients seeking surgical reversal may not have had access

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to additional surgical care, causing an underestimate in the prevalence of regret. While our study findings are strengthened by external validation from other studies, the true prevalence of regret remains an estimate.

Conclusions

Regret after gender-affirming surgery was found to be rare, both in the literature as well as in our survey of surgeons' experiences with this topic. Regret can be classified as true gender-related regret, social regret and medical regret from complications, function, pre-intervention decision making. Guidelines in transgender health should include both preventive strategies as well as treatment guidelines if regret occurs. Future studies and scientific discourse are encouraged on this important topic.

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ORIGINAL RESEARCH & REVIEWS

TRANSGENDER HEALTH

Individual Treatment Progress Predicts Satisfaction With Transition-Related Care for Youth With Gender Dysphoria: A Prospective Clinical Cohort Study



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ABSTRACT

Background: The number of adolescents presenting with gender dysphoria (GD) in healthcare services has increased significantly, yet specialized services offering transition-related care (TRC) for trans youth is lacking.

Aim: To investigate satisfaction with TRC, regret, and reasons for (dis)satisfaction with transition-related medical interventions (TRMIs) in trans adolescents who had presented to the Hamburg Gender Identity Service for children and adolescents (Hamburg GIS).

Methods: Data were collected from a clinical cohort sample of 75 adolescents and young adults diagnosed with GD (81% assigned female at birth) aged 11 to 21 years (M = 17.4) at baseline and follow-up (on a spectrum of ongoing care, on average 2 years after initial consultation). To determine progress of the youth's medical transitions, an individual treatment progress score (ITPS) was calculated based on number of desired vs received TRMIs.

Outcomes: Main outcome measures were satisfaction with TRC at the time of follow-up, ITPS, social support, reasons for regret and termination of TRC, and (dis)satisfaction with TRMIs.

Results: Participants underwent different stages of TRMIs, such as gender-affirming hormone treatment or surgeries, and showed overall high satisfaction with TRC received at the Hamburg GIS. Regression analysis indicated that a higher ITPS (an advanced transition treatment stage) was predictive of higher satisfaction with TRC. Sex assigned at birth, age, and time since initial consultation at the clinic showed no significant effects for satisfaction with TRC, while degree of social support showed a trend. No adolescents regretted undergoing treatment at follow-up. Additional analysis of free-text answers highlighted satisfaction mostly with the physical results of TRMI.

Clinical Implications: Because youth were more satisfied with TRC when their individual transition (ITPS) was more progressed, treatment should start in a timely manner to avoid distress from puberty or long waiting lists.

Strengths and Limitations: This study is one of the first to report on treatment satisfaction among youth with GD from Europe. The ITPS allowed for a more detailed evaluation of TRMI wishes and experiences in relation to satisfaction with TRC and may close a gap in research on these treatments in adolescent populations. However, all participants were from the same clinic, and strict treatment eligibility criteria may have excluded certain trans adolescents from the study. Low identification rates with non-binary identities prevented comparisons between non-binary and binary genders.

Conclusion: The study highlights the role of TRMI and individual treatment or transition progress for youth's overall high satisfaction with TRC received at the Hamburg GIS. Nieder TO, Mayer TK, Hinz S, et al. Individual Treatment Progress Predicts Satisfaction With Transition-Related Care for Youth With Gender Dysphoria: A Prospective Clinical Cohort Study. J Sex Med 2021;18:632—645.

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Key Words: Transgender; Gender Dysphoria; Individual Treatment Progress; Health Care; Treatment Satisfaction; Gender-Affirming Treatment

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INTRODUCTION

Transgender (or trans) adolescents, like their adult counterparts, experience an incongruence between their sex assigned at birth and their gender identity. This experienced incongruence is often accompanied by psychological distress and a persistent strong desire for social and physical gender changes, at which point they can be diagnosed with gender dysphoria (GD), as per the diagnostic and statistical manual of mental disorders.

Trans youth, being underage, cannot legally consent alone to gender-affirming treatments (transition-related medical interventions [TRMI]), resulting in involvement of parents/ guardians, who also have limited decision-making authority.4 This places unique prerequisites on client self-determination and high demands on health care professionals (HCPs) working in specialized services aiming at reducing GD in children and adolescents,⁵ as it must be ensured that youth are cognitively and emotionally capable of understanding decisions regarding transition steps.⁶ As such, a 4-step framework for pediatric shared decision-making has been suggested to balance the youth's client autonomy and the parents'/guardians' choices and values⁷; both must work together with HCPs to agree on where the youth's best interests lie.4 In each step, the HCP weighs treatment options and approaches parents/guardians for decision-making at the point in which there are multiple options or when certain treatments have particular benefits/burdens. As adolescents mature, modifications to the framework can be made to include the youth more actively in shared decision-making. Taking such an approach to health-related decisions in childhood and adolescence can help ensure that biomedical ethical principles are respected for trans youth.7,8

Thus, treatment decisions are a staggered process that do not always follow certain strict criteria but rather are age-dependent and influenced by the developmental and psychosocial situation.^{9,10} Younger children may undergo social transition, highlighted by use of gender-affirming name, pronoun, and clothing. 10 Adolescents undergoing medical transition often start treatment with hormone blockers gonadotropin-releasing hormone agonists (GnRHa) to suppress secondary sex characteristics at the start of puberty to allow more time for identity development, 9,10 which can minimize risks of false decisions and quell worries of treatment regrets from parents and HCPs. 11,12 Treatment with genderaffirming hormones (GAH; estrogen or testosterone) and surgeries (GAS; usually after reaching legal age) can follow. 9,10,13,14 Adolescents and young adults rarely regret or stop TRMIs, provided they fulfill the criteria for a GD diagnosis and their readiness for treatment is sufficiently assessed.^{6,15}

Recent research points to gender affirmation being the appropriate care for youth GD, when indicated by a thorough assessment process, as trans adolescents are likely to experience improvements to general mental well-being through social 16 and/or medical transition. 15,17,18 However, with few specialized centers dedicated to transition-related care (TRC)

existing in Germany¹⁹ and a steady rise of children and adolescents with GD presenting clinically in recent years, ^{6,20–22} including more diverse gender presentations, variant gender experiences and non-binary youth, ^{2,23} the specific examination of the quality of TRC for youth becomes increasingly relevant.

In the German health system, health insurances largely cover TRMIs, such as hormone treatment and most surgical interventions being relevant to TRC.²⁴ However, with the exception of hormone treatment, each cost reimbursement is based on an individual case decision by the medical service of the insurance companies.²⁵ In general, physicians working for the medical services of the insurance companies are not specialized in TRC but decide on reimbursement based on various requirements (eg, to undergo psychotherapy of at least 6 months before starting hormone treatment). However, with regard to the reduction of GD, the effectiveness of these requirements is not evidence-based. To increase the quality of TRC in Germany, an evidence-based guideline for adults was developed by the German Society for Sex Research (Deutsche Gesellschaft für Sexualforschung, DGfS) in collaboration with related professional societies following methodologies proposed by the Association of the Scientific Medical Societies in Germany (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., AWMF). The treatment recommendations of this guideline are evidence-based, researched, and evaluated systematically. In a structured consensus process, the guideline development group, representative of the target group, and a stakeholder group of trans people in Germany agreed on 100 recommendations.²⁴ The guideline aims to individualize and deregulate TRC in Germany. Based on empirical and clinical evidence, a procedure is recommended that is tailored to the individual conditions of treatment and encompasses the full range of TRC. However, the guideline is aimed at trans adults, a comparable guideline for children and adolescents is still being developed.26

Satisfaction with received health care is often used as an indicator of health care quality and a springboard for identifying potential areas of improvement.²⁷ The few studies investigating adolescents' experiences with TRC from specialized gender clinics or doctors specializing in transgender health care (THC) generally show high levels of satisfaction. Specifically, receiving care from respectful, affirming HCPs with specialized knowledge on THC and open client-clinician communication were identified as key elements for satisfaction, 28,29 as well as the effects of TRMI (GAH). 28,30 These findings are encouraging, as youth may not seek out or continue treatment relevant to their transitions³¹⁻³³ owing to poor treatment experiences. However, long wait times³⁴ or treatment delays, especially to start GAH treatment, 28-30 as well as low frequency of appointments 34 and lengthy assessment processes³⁰ or gatekeeping,²⁹ may lead to decreased satisfaction with TRC. Negative experiences or barriers to TRC are more common among non-binary youth, 31,35,36 as many clinicians approach THC from a binary understanding.

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Studies examining treatment regret or effects on mental wellbeing also hint at further potential factors for satisfaction with TRC in trans adolescents. Age may play a role; in one prospective follow-up study exploring puberty suppression in 70 youth gender clinic clients, younger individuals were more likely to react negatively to long wait times, while older youth started treatment feeling more dissatisfied with their bodies. 15 Studies of (young) trans adults determined social support³⁷ and being further along in transition 15,37 predicted improved mental wellbeing after receiving TRMI. Finally, trans individuals may also undergo different pathways of medical procedures based on the sex assigned at birth/gender identity, 10,38,39 therefore having different encounters with TRC. Thus, experiences of slow treatment or transition progress, social support, age, and birth sex may influence experiences of, and satisfaction with, the process of TRC and it's results.

Use of transition measurement tools such as the Individual Treatment Progress Score (ITPS)^{37,38} may help to assess and compare individual treatment progress across trans individuals, without assuming a fixed end of a medical transition. By dividing the number of received interventions by the number of planned and received interventions for each participant, the ITPS emphasizes the individual approach in TRC. Because of the variability as a coherent part of adolescence in general, this approach appears to be particularly relevant for adolescents with GD.

Longitudinal data on the impact of TRC in youth are lacking. 40 To close a gap in the research on health care for GD received in Germany during adolescence, the present study aims to investigate satisfaction with TRC and the relationships with the individual transition process.

MATERIAL AND METHODS

Study Design

The present study was based on the first cross-sectional evaluation of a clinical cohort sample from the Hamburg Gender Identity Service for children and adolescents (Hamburg GIS) at the Department of Child and Adolescent Psychiatry, which is part of the Interdisciplinary Transgender Health Care Centre at the University Medical Center Hamburg-Eppendorf (UKE). Participants were assessed individually at 2 time points: at intake/initial consultation (baseline) and at follow-up (at least 6 months after initial consultation and up to 4 years later, with an average of 2 years). At baseline, none of the participants had received TRC. Follow-up refers to a second measurement point in which participants found themselves on a spectrum of care; all had received some form of TRC (including mental health care) and were considered eligible for TRMI. However, while some had not yet undergone any kind of TRMI, others had reached their transition goals or were at a later stage of their transition at the Hamburg GIS.

Adolescents and young adults who had participated in the baseline data collection (between September 2013 and June 2017) and who were considered eligible for further TRMI were

invited by the principal investigator (IBH) to participate in the follow-up study. Participation in both studies was voluntary and independent of the care received at the Hamburg GIS, but the follow-up was rewarded with a 20 € voucher. Participants who did not respond after 1 month were sent a reminder. Informed consent from the adolescents (and their guardians) was obtained at both time points. Follow-up data collection took place between November 2017 and March 2018 using a similar set of standardized self-report questionnaires as used at baseline. Only the social support scale and satisfaction with TRC scales were added to an adjusted version of the baseline questionnaire at follow-up. The study was approved by the local ethics committee. ¹⁷

The specialized Hamburg GIS provides TRC for children and adolescents questioning their gender or sex, including referral to a specialized pediatric endocrinologist for GAH.^{17,19,41} The diagnostic procedures and further treatments are oriented on the 7th version of standards of care, published by the World Professional Association for Transgender Health (WPATH). 10 After a comprehensive diagnostic evaluation over multiple sessions, TRC is currently recommended at the Hamburg GIS if adolescents present the following criteria: (i) maintaining persistent GD over at least 6 months (without strict onset criteria of first GD presentation) and first attempts at living in the preferred gender role; (ii) increased distress because of the incongruent body characteristics (after the onset of first pubertal changes) and a request for TRC; (iii) a mental health assessment revealing the absence of severe mental health problems that may interfere with the diagnostic workup (such as acute suicidality, psychosis, or other severe mental health problems that need to be addressed through psychotherapy first); (iv) adequate local mental health care (close to home) and social support (via the family or others) during the course of TRMI; and (v) a demonstration of thorough understanding and knowledge about the effects of puberty suppression (via GnRHa), GAH, GAS, and the social impacts of a transition. 10,13,14,42 This entails that in some cases, diagnostics may take longer as treatment referral follows individual developmental pathways instead of strict criteria checklists. For more details regarding the sample, study design, and treatment approaches, refer to Becker-Hebly et al. (2020). 17

Sample Characteristics

The original study sample consisted of 434 children and adolescents with gender-variant behaviors and/or experiences who presented at the Hamburg GIS. Of these 434 children and adolescents, 230 individuals had to be excluded from the study for various reasons (see Figure 1),¹⁷ resulting in 204 adolescents whose responses in the baseline study were viable and who were then contacted to complete the follow-up survey. The follow-up response rate was 37%, resulting in a final sample size of 75 adolescents and young adults. Responders did not significantly differ in their sociodemographic characteristics from non-responders. ¹⁷

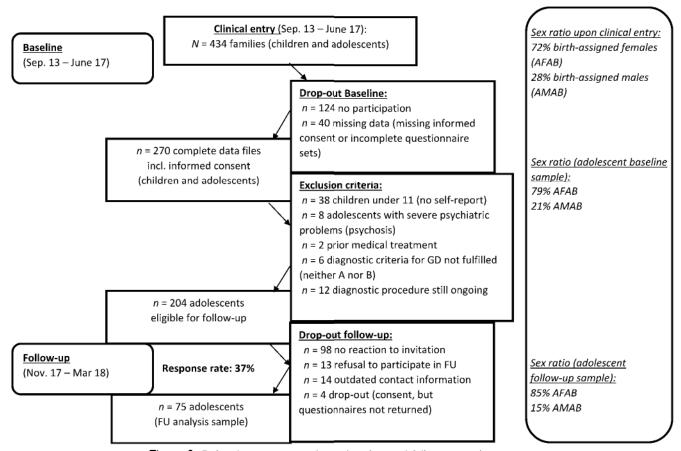


Figure 1. Referrals, participants during baseline and follow-up, and sex ratios.

Within the final sample, 64 (85%) participants were assigned female sex at birth (AFAB) and 11(15%) were assigned male sex at birth (AMAB). When asked at follow-up, all 11 AMAB participants identified as female/trans girl, while 59 AFAB participants identified as male/trans boy. The remaining 5 AFAB participants identified with non-binary identities at follow-up ("in between," "non-binary," or "other"). Their ages ranged from 12 to 21 years (M = 17.4, SD = 1.7) at the time of follow-up. Youth were in treatment at the Hamburg GIS for a length between seven and 47 months (M = 21.4, SD = 12.2).

Of the 75 adolescents and young adults at follow-up, 54 participants had already received TRMI. A smaller group of 21 participants had not yet undergone any medical interventions; this group was either still in the diagnostic/psychosocial treatment phase, but assessed as eligible for these interventions, or was receiving mental health support without GnRHa or GAH.

At baseline, 99% of the adolescents had indicated a desire for GAH hormone treatment. At follow-up, 11 youth had received GnRHa and 32 adolescents had received GAH, while the other 32 (43% of sample) had desired GAH but had not yet begun this form of treatment. Furthermore, 91% of the adolescents had indicated a desire for GAS at baseline. At follow-up, 11 adolescents and young adults had received both GAH and (at least 1) GAS,

while the other 72 youth (96% of sample) desired GAS but had not received this form of treatment (or additional desired surgeries). Table 1 provides a detailed description of each treatment groups, including sex assigned at birth, age, time since initial consultation and average ITPS scores.

Measures and Operationalization

Sociodemographic and Clinical Data (Diagnosis, TRMI History, Treatment Desires, Reasons for Regret or Termination of TRC, and [Dis]satisfaction with TRMI).

Sociodemographic data (age, sex assigned at birth) and self-report data regarding completed TRMI history, (further) treatment desires, reasons for treatment regrets or termination, and (dis)satisfaction with TRMI were collected with the help of (free-text) survey questions. Data regarding diagnosis and time since initial consultation were added from the adolescents' clinical records provided by HCPs working at the Hamburg GIS.

Satisfaction with TRC

Youth's satisfaction with TRC received at the Hamburg GIS was measured using the Client Satisfaction Questionnaire 43 (ZUF-8). The ZUF-8 captures the general satisfaction at the

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Table 1. Sample characteristics based on treatment group

		Sex assigned at birth ^a	Age at follow-up (y)	Treatment length ^b (mo)	ITPS ^c	
Treatment group n (%)		n (%)	M (SD) Range	M (SD) Range	M (SD) Range	
No TRMI	21 (18)	18 (85.7) AFAB 3 (14.3) AMAB	16.7 (1.5) 14.6–20.9	13.9 (6.9) 7–35	.25 (.00) .25–.25	
GnRHa	11 (14.7)	8 (72.7) AFAB 3 (27.3) AMAB	16.6 (2.0) 11.9–18.8	12.6 (4.8) 8–23	.52 (.05) .50–.67	
GAH	32 (42.7)	28 (87.5) AFAB 4 (12.5) AMAB	17.5 (1.2) 14.6–20.4	23.5 (10.3) 7–47	.75 (.00) .75–.75	
GAH + GAS	11 (14.7)	10 (90.9) AFAB 1 (9.1) AMAB	19.2 (1.5) 16.2–21.0	38.0 (11.2) 23–49	.84 (.08) .80–1.0	
Total	75 (100)	75 (100)	17.4 (1.7)	21.4 (12.2)	.59 (.23) .25–1.0	

^aAFAB = sex assigned female at birth; AMAB = sex assigned male at birth

end of a clinical treatment. The questionnaire consists of 8 items rated on a four-point scale (with 4 representing the highest degree of satisfaction). Adding the scores of the 8 questions together, a final sum score with a range between 8 and 32 can be reached. A cutoff value of < 24 was used to classify treatment experiences as (un)satisfactory. Table 2 presents the questionnaire items and corresponding scores.

Individual Treatment Progress

The individual progress with regard to completion of a medical transition with the help of TRMIs was calculated using the ITPS. The ITPS is a metric score with a continuous value between 0% and 100%, calculated for each adolescent based on the number of received treatments divided by the number of received treatments plus treatments still desired (but not yet received) at follow-up. For the participant group without TRMI, the desires for hormonal treatment (GnRHa and GAH) were doubled when calculating the ITPS because both types of hormonal treatment were considered individual steps in the care of adolescents with GD on a spectrum toward a "complete" transition at the Hamburg GIS. For more information on the ITPS, see Koehler et al. 38

Social Support

The adolescents' perceived social support was measured using the short-form version of the Perceived Social Support Questionnaire (F-SozU). The F-SozU consists of 14 items on a five-point scale that captures the degree of agreement to various aspects of perceived support in one's social environment. 46

Statistical Analysis

Data on received and desired treatments at both baseline and follow-up were analyzed descriptively. Four treatment groups were created (see Table 1), to which participants were assigned based on their received TRC at follow-up: no TRMI, GnRHa, GAH, and GAH and GAS. The treatment groups were also used along with their treatment desires at follow-up to calculate their ITPS³⁸ as well as to examine treatment satisfaction (global satisfaction based on ZUF-8 scores).⁴⁵

Table 2. ZUF-8 items

- 1. How would you rate the quality of the care/consultation you received?
 - Excellent (4)/good (3)/satisfactory (2)/bad (1)
- Did you receive the type of care/consultation that you wanted?
 Definitely not (1)/no, not really (2)/yes, in general (3)/yes, definitely (4)
- To what extent did our clinic meet your needs?
 Almost all my needs (4)/most of my needs (3)/only a few of my needs (2)/none of my needs (1)
- 4. Would you recommend our clinic to a friend if s/he requires similar help?
 - Definitely not (1)/no, I don't think so (2)/yes, I think so (3)/yes, definitely (4)
- 5. How satisfied are you with the extent of the help which you received here?
 - Very unsatisfied (1)/unsatisfied (2)/satisfied (3)/very satisfied (4)
- 6. Did the care that you received here help you to deal more appropriately with your problems/questions?
 - Yes, it helped a lot (4)/yes, it helped a bit (3)/no, it did not help (2)/no, it made things worse (1)
- 7. How satisfied are you overall with the care you received?

 Very satisfied (4)/satisfied (3)/unsatisfied (2)/very unsatisfied

 (1)
- Would you come to our clinic again if you needed help?
 Definitely not (1)/no, I don't think so (2)/yes, I think so (3)/yes, definitely (4)

Values in brackets refer to the number of points awarded to each answer to calculate final ZUF-8 score. 44,45

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^bTreatment length = time in months since initial consultation at the GIS.

clindividual Treatment Progress Score, sum of received treatments divided by sum of received and desired treatments, *M*-values also as percentage. GAH = gender-affirming hormone treatment; GAS = gender-affirming surgery; TRMI = transition-related medical intervention.

In the second part of analysis, a multiple linear regression with block-wise factor inclusion was performed to analyze the relationship between treatment-dependent factors (such as time since initial consultation and ITPS), treatment-independent factors (such as age, sex assigned at birth, and social support) and the outcome, satisfaction with TRC. For the analysis of the role of social support on satisfaction with TRC in the multiple linear regression, the total sum score in the F-SozU was calculated for each participant and then divided by the number of completed items. SPSS 22 was used for all analyses.

Finally, free-text answers addressing reasons for termination/ suspension of TRC and/or possible treatment regrets, as well as (dis)satisfaction with TRMI, were used to add individual qualitative insights to the quantitative findings.

RESULTS

Individual Treatment Progress Score

The ITPS showed that the sample of adolescents and young adults had completed 59% of their desired TRMIs on average at the time of follow-up, although ITPS values varied between treatment groups. For example, youth who had not yet received any TRMI at follow-up had completed on average only 25% of their treatment, while those who had received GAH and GAS were of course further along in transition, with an average ITPS of 84%. Table 1 describes the ITPS across treatment groups in detail.

Satisfaction with TRC

Based on the scores on the ZUF-8, 75% of all participants indicated that they were overall satisfied with the TRC received at the Hamburg GIS and thus scored higher than the cutoff score of < 24. Analysis of the ZUF-8 mean scores also indicated that

youth were generally satisfied with the care received (M = 3.29 of a possible score of M = 4.00). The mean scores further show a tendency of increased satisfaction with TRC with advanced treatment stages. However, the differences in mean scores across groups were not statistically significant (F[3,71] = 1.76, p = .16). Table 3 shows the ZUF-8 scores for all treatment groups.

Factors Influencing Satisfaction with TRC

The final model 2 of the multiple linear regression, with all factors included, explained approximately 11% of the variance. The ITPS was the only factor with a statistically significant impact on satisfaction with TRC (P = .012 in model 2). The factor social support showed a trend towards predicting satisfaction with TRC (P = .055). Model 2 had an adjusted $R^2 = 0.114$ and as such, a weak goodness of fit (see Table 4). The Durbin-Watson test for potential autocorrelation had a value of 1.614 and therefore showed a trend of positive correlation. Multicollinearity could be ruled out (variance inflation factor values between 1.043 and 2.516). In a multiple regression with a final sample size of n = 75 (valid completed study questionnaires) and 5 predictors, a moderate effect ($f^2 = 0.15$; α error = 0.05) with a power of 95% (0.951) could be tested (power analysis using G*Power program; $\delta = 3.33$; critical tvalue = 1.67; df = 68).

Reasons for Termination of TRC, Regret, and (Dis) Satisfaction with TRMI

Table 5 provides details of the n=9 free-text responses on reasons for termination of TRC or regret. At follow-up, none of the adolescents and young adults in the sample indicated that they regretted transition so far. In total, 13 participants (of which 4 were AMAB) indicated at follow-up that they had either

Table 3. ZUF-8 scores

	ZUF-8 cutoff sco	ore ^a < 24	ZUF-8 mean sc	ZUF-8 total scores ^c	
Treatment group	Dissatisfied n (%)	Satisfied n (%)	M (SD) Range	95% CI	M (SD) Range
No TRMI	9 (12)	12 (16)	3.08 (.63) 1.88–4.00	2.79-3.37	24.67 (5.06) 15–32
GnRHa	3 (4)	8 (11)	3.17 (.85) 1.25*–4.00	2.59-3.74	25.36 (6.83) 10—32
GAH	6 (8)	26 (35)	3.41 (.57) 1.88–4.00	3.21–3.62	27.31 (4.55) 15–32
GAH + GAS	1(1)	10 (13)	3.49 (.37) 2.75–4.00	3.24-3.74	27.37 (2.95) 22–32
Total	19 (25)	56 (75)	3.29 (.62) 1.25–4.00	3.15-3.44	26.37 (4.98) 10-32

^aCutoff Score by Hannöver et al. ⁴⁵ A score higher than 24 indicates satisfaction with treatment.

^bZUF-8 mean score value between 0 and 4.

[°]ZUF-8 total score value between 0 and 32.

GAH = gender-affirming hormone treatment; GAS = gender-affirming surgery; TRMI = transition-related medical intervention.

^{*}One adolescent's treatment satisfaction score of M = 1.25 was an outlier. However, this data point was kept in all following calculations as its removal did not indicate any significant changes in test results.

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Table 4. Multiple linear regression (model 2)

	Non-standardized coefficients		Standardized o	coefficients	
	В	SE	β	t	р
(Constants)	3.771	.991		4.141	.000
ITPS*	.918	.356	.346	2.582	.012*
Treatment Length ^b	007	.009	− .138	− . 797	.428
Age	043	.058	—. 1 118	–.747	.458
Assigned sex at birth	.211	.198	.121	1.068	.289
Social Support	– 201	.103		-1.950	.055

alndividual Treatment Progress Score.

suspended or terminated their TRC at the Hamburg GIS. Nine participants did so while in the no-TRMI group, while three individuals did so at the GAH stage. One AFAB individual in the GAH group indicated that treatment was terminated after successful GAH administration; however, this individual had previously indicated desire for mastectomy and potentially other surgical procedures. Only one participant terminated/suspended treatment at the GAS stage. Reasons related to mental health issues were most often listed as a cause for suspension/termination, followed by reasons unrelated to direct treatment experience (eg, long distance to Hamburg). Only one participant (trans boy in the no-TRMI group) indicated poor TRC experience (subjective lack of understanding from HCPs) as cause for treatment termination.

Table 6 provides details of the free-text responses on (dis) satisfaction specifically with TRMI for the three treatment groups that had received TRMI. The free-text responses of the 21 adolescents and young adults who had not yet undergone TRMI were excluded from analysis as these participants could not yet evaluate medical treatment experiences and/or results. Of the 54 youth who had received TRMI, 38 individuals (33 AFAB and 5 AMAB participants) provided free-text responses. The positive and negative physical effects of TRMI were highlighted by participants as reasons for both treatment satisfaction (eg, praised suppression of primary sex characteristics or surgery results) and dissatisfaction (eg, criticism of GAH side effects or slow physical changes).

DISCUSSION

The present prospective clinical cohort study following up 75 adolescents and young adults with GD aged 12 to 21 years aimed to assess satisfaction with TRC received at the Hamburg GIS, individual treatment progress (ITPS), regret, and reasons for (dis) satisfaction with TRMI. Most youth had desired TRMIs at baseline and had undergone GAH treatment at follow-up, as well as some surgical procedure(s). However, the treatment pathways, including time since initial consultation and number/order of procedures, varied; therefore, the ITPS in the sample also ranged

from 25 to 100%. The sample reported overall high satisfaction with TRC. Considering that trans youth are still an underserved population and specialized clinics for GD are rare, not only in Germany, ^{5,19} participants may have simply been happy to (be able to) receive any TRC at all, thus explaining the determined overall high satisfaction with TRC. More likely, however, is that the high satisfaction rates reflected the high quality of TRC offered, as the results mirror findings of other studies investigating treatment satisfaction. ^{28,30,34}

Table 5. Free-text responses of reasons for TRC termination/ suspension

Reason	n (%)
Mental Health Issues	5 (38)
"I should first get my depression treated"	
"Clinic stay and therapy pause"	
"I have to go to a clinic, but I'm back at the GIS since summer 2017"	
"Personal reasons (psychological), desire for re-admission [to the Hamburg GIS]"	
"Psychological treatment"	
Long Distance to GIS	3 (23)
"Moving away" "Distance from Nuremberg to Hamburg too big, too expensive long term"	
"Save the way to Hamburg (from Hannover), appointments when needed"	
Other Reasons "I did not feel understood"	1 (8)

^aListed as reason by 1 trans boy in the no-TRMI group.

GIS = Gender Identity Service; TRC = transition-related care; TRMI = transition-related medical intervention.

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^bTime in months since initial consultation at GIS.

^{**}P < .05; adjusted $R^2 = 0.114$.

Table 6. Free-text responses of reasons for TRMI (dis)satisfaction

Treatment group	Satisfied with:	n (%)	Unsatisfied with:	n (%)
Hormone blockers, GnRHa (n = 14)	Menstruation suppression	7 (50.0)	Insufficient menstruation suppression	3 (21.4)
	"lack of period"		"that I have spotting"	
	"living without my period!"		"menstruation did not stop"	
	"that I don't have my period anymore"		"menstruation returned"	
	"good suppression" "no period"			
	"end of menstruation"			
	"suppression, especially of menstruation"			
	Breast tissue shrinkage	2 (14.3)	Hot flashes	4 (28.6)
	"chest becoming smaller"		"hot flashes"	
	"breasts getting smaller"		"temperature fluctuations/hot flashes"	
	Improved skin "less acne"	1 (7.1)	Libido suppression "decrease in sex drive"	2 (14.3)
			"less libido"	
	Libido suppression	1 (7.1)		
	"reduced libido"			
	Other responses	4 (28.6)	Other responses	2 (14.3)
	"the effects"		"mood swings"	
	"everything (especially my beard growth)"		"voice cannot be undone"	
	"no male puberty"			
Gender-affirming hormones ($n = 31$)	Voice change	11 (35.5)	Skin appearance	5 (16.1)
	"voice"		"acne"	
	"voice breaking"		"pimples"	
	"change in voice"		"side effects (such as acne and so on)"	
	"changes in body (voice, and so on.)"		VIII	
	Hair growth	7 (22.6)	Mood swings	2 (6.5)
	", hair,"		"mood swings sometimes"	2
	"body hair (especially beard)" "body hair"		"irritability"	
	"hair coverage"			
Treatment group	Satisfied with:	n (%)	Unsatisfied with:	n (%)
Treatment group Gender-affirming hormones ($n = 31$)	Other physical changes	8 (25.8)	Too slow/little	9 (29.0)
Serial diffining normones (7 — 21)			changes	ری.رے ر
	"breast growth, skin,,facial features"		"takes a long time, I take hormones as gel for almost 5 months and notice little"	

(continued)

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Table 6. Continued

Treatment group	Satisfied with:	n (%)	Unsatisfied with:	n (%)
	"light breast growth"		"through the low dosage (25 mg) it takes a bit too long"	
	"more weight, small breasts"		"could be more"	
	"face"		"long wait for change"	
	"fat distribution, muscle growth"		"the hormones take effect very slowly"	
	"muscle mass"		"otherwise little effect"	
	"changes, body"		"too little beard growth, change in physique"	
	"body changes"		"too little change to genitals"	
	0.1	77 (51 0)	"too little change"	
	Other responses "everything"	17 (54.8)	Other responses "libido,"	2 (6.5)
	"the onset of the proper puberty"		", that the hormones have not completely suppressed my period"	
	"the changes" "the effects" "total treatment" "complete change" "otherwise everything" "Testosterone gel" "Testosterone"			
Gender-affirming surgery ($n = 8$)	Breast reduction "the flat chest" "the right breast"	4 (50.0)	Scars "the scars don't heal that well" "big, thick scars"	2 (25.0)
	"mastectomy" "abovementioned operations"		sig, there sea s	
	Other responses "entire picture" "small scars, natural appearance"	3 (37.5)	General result "Form (a little bit)" "the lefta lot of tissue is still inside"	2 (25.0)
	"scars, result"			

 ${\sf GnRHa} = {\sf gonadotropin-releasing\ hormone\ agonists;\ TRMI = transition-related\ medical\ intervention.}$

The study also showed that overall satisfaction with TRC for adolescents in the GnRHa group, although still quite high, was slightly lower than satisfaction with care found in the GAH and GAS groups. While studies show favorable results for GnRHa to treat GD in adolescents, 6.42 another recent study from Germany only reported moderately better scores at

follow-up. ¹⁷ As satisfaction with psychiatric treatment has been shown to be influenced by intrapersonal factors such as trust in treatment or prior treatment experiences, ⁴⁷ it is unclear if the satisfaction rates between groups is influenced by expectations based on previous treatment experiences or subjective perception of GnRHa effectiveness, for example.

A higher ITPS (advanced individual medical transition stage or more desired TRMIs) predicted higher satisfaction with care outcomes. This finding, that advanced individual treatment progress proved significant for overall satisfation with TRC, mirrors findings that show many trans individuals do not feel like their transition has fully begun with mental health care/psychotherapy, which was captured in a lower ITPS score/earlier transition stages. Rather, it is at the earliest with GAH and/or GAS, that trans individuals feel like their identified gender and feel like they are recognized by others as such and report sufficiently diminished GD. 6,50

The significance of the ITPS emphasizes the importance of integrating individual desires and individual treatment pathways into TRC plans. 10-12,17 Although most adolescents came to their initial consultation with the goal to receive most types of TRMI, some had individual desires for specific medical interventions. Results showed that satisfaction with TRC was higher when more of these desires were fulfilled, even for those still within the treatment process. This result has also been found in non-trans populations: a similar study determined an effect between the implementation of individual desires and expectations of psychiatric clients and their experienced treatment.⁵¹ In general, it is recommended to consider individual treatment desires instead of following criteria-based checklists, if decisions must be made in which several equivalent and ideally evidencebased treatment options are available (so-called equipoise), if decisions on how to deal with life-changing situations are preference-sensitive, and if the consequences of the decision are potentially significant for the further life of the person concerned.52

In addition, this individualized approach ensures client autonomy, as reflected in pediatric shared decision-making ^{4,7}; input from adolescents themselves can reduce the gatekeeping function of the HCPs, improving the client and HCP relationship ⁵³ and increasing treatment satisfaction. ^{29,54} As such, participants further along in their transition (higher ITPS) had more subjective positive experiences of receiving TRC which reflected and respected their treatment desires.

Although previous studies found effects for age on psychiatric treatment satisfaction, ⁵⁵ for example, or that younger adolescents reacted particularly frustrated to waiting for TRC, ⁶ no influence of age on satisfaction with TRC was found in this study. This finding is not only relevant as it contradicts previous research, it indicates that younger trans adolescents do not react significantly differently to TRC than older youth, demonstrating they may possess (cognitive and emotional) maturity needed for treatment. However, the present sample was relatively "old" on average. Even though there were no strict age criteria for the start of TRMI, youth received TRMIs at approximately age 16 on average, with the youngest participants being 11.8 years old at the start of GnRHa administration and 14.5 years at the start of GAH.

Similarly, time since initial consultation did not prove significant. However, this could be owing to the operationalization; the often long waiting period up until the initial consultation was not incorporated, and many studies show it to be criticized by trans youth. 6,34 Social support only demonstrated a slight trend (P=.055), which may be owing to low variance in the sample; most adolescents from the same baseline sample reported high levels of support from family. 41 As adolescents are dependent on guardians for accessing TRC and subsequent decision-making, this factor may be particularly important, and further research is needed.

When it comes to satisfaction with TRMI, the physical effects, particularly as a result of GAH or GAS, seemed to be of paramount importance for adolescents. This is in line with studies showing that medical transition has positive effects on young trans individuals who began transition in adolescence, including decreases in GD and improvements in psychosocial functioning (ie, decrease in depression and anxiety). ^{6,15,17,42}

Results indicate that adolescents have high expectations and specific visions for (the outcomes of) TRMI. Youth desire their body to physically reflect their experienced gender identity²³ and, as such, may be disappointed by less than ideal treatment results. Indeed, treatment side effects (such as scarring) or slow progress/lack of physical changes were most often listed as reasons for dissatisfaction with TRMIs, which is in line with other studies revealing that cosmetic outcomes of (surgical) TRMI in adulthood were criticized,⁵⁶ including the results of mastectomy.⁵⁷ With this in mind, the high satisfaction rates should be weighed against the overall low rate (14.7%) of surgical interventions undergone in the sample.

With respect to prevailing uncertainties when it comes to treatment of trans youth and desires of HCPs to avoid misdiagnoses, ^{5,11,12} an important finding is that no adolescents and young adults in the present study regretted TRC at the time of follow-up, mirroring other studies that determined no regret of GnRHa administration or GAH and GAS. ^{15,18,58} It can be assumed that the sample selection (of only adolescents who were considered generally eligible for further TRMI) and value placed on the individual treatment desires played a role in this outcome.

However, a small percentage of youth indicated they had terminated or delayed treatment, among others, because of mental health concerns. Good mental health and psychosocial functioning important aspect for consideration TRC. 6.9,10,13-15,17,19 While many adolescents may have mental health concerns which do not interfere with TRC when they are stable in treatment or on medication, it is in the interest of the adolescents and young adults to receive mental health care first for issues which may put successful TRC at jeopardy (ie, acute suicidality) followed by - if needed - a medical transition. While this may seem sensible, it does have its drawbacks (eg, a delay in transition because of mental health care in line with increased frustration).6 Other participants indicated treatment termination

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owing to long distance to the Hamburg GIS. This result is not surprising given the poor THC provider situation for trans youth in Germany. ¹⁹ For many individuals, a specialized clinic such as the Hamburg GIS is too far away, and they must rely on local (potentially unspecialized) HCPs. It is therefore essential that more clinics provide specialized care for youth with GD, including in rural or suburban areas or offer e-health approaches.

Clinical Implications

HCPs should get bidirectional feedback from adolescents/guardians throughout the TRC process to ensure treatment desires and needs are adequately captured and integrated into TRC. As changes in desires can occur throughout the treatment process, ⁵⁹ this may also help not to ignore changing transition pathways.

Treatment expectations and what TRMI can accomplish, side effects (eg, acne), cosmetic outcomes (eg, scarring), complications, and so on should be discussed to avoid dissatisfaction with physical outcomes or side effects of TRMI, as much emphasis is placed on these aspects by youth. As also recommended by the WPATH, ¹⁰ this can help empower adolescents in making fully informed decisions on what TRMI are right for them. Satisfaction may thereby increase because treatments will best suit transition goals ¹⁰ and youth could be mentally prepared for potentially less-than-ideal side effects or outcomes.

Since youth were more satisfied with TRC when their transition was more progressed and effects of puberty were "paused" or "reversed," TRC should start in a timely fashion and HCPs should mind the distress that some of the puberty-related changes of the body may cause for adolescents. 3,60

Mental HCPs can help young people deal with feelings of impatience during the process toward a medical transition (ie, with slow physical changes). In addition, HCPs should expect treatment satisfaction to increase as adolescents and young adults get closer to their individual transition goals; dissatisfaction with TRC in earlier stages should not necessarily be interpreted as a sign that the treatment is wrong or will be regretted.

Limitations and Future Research Directions

Results must be interpreted cautiously as participants came from the same clinic, and there was no randomized control group owing to ethical considerations. The strict internal diagnostic requirements for the selection of the follow-up sample as well as treatment eligibility criteria at the Hamburg GIS for children and adolescents may have led to a biased sample selection; while all study participants had been deemed eligible for further TRMI, individuals presenting with certain gender expressions or experiences (eg, non-binary) may have been excluded from the data collection.

Furthermore, the high level of desired/underwent TRMI may not be representative for the total sample of referred adolescents or all trans youth who do not consult with a specialized service such as the Hamburg GIS. Many adult trans individuals report satisfactory decreases in GD with only social transition, ^{10,61} with some explicitly refusing TRMI. ⁶² These individuals would most likely not seek TRC from a specialized service, and thus, their treatment desires are not included in clinical cohort samples.

The low number of adolescents and young adults who participated in the follow-up survey (37%) could indicate that the survey had low priority for those finished transitioning or that only those who experienced positive course of treatment were motivated to participate. In addition, the large number of participants in the GAH group could indicate that youth currently in treatment were worried a lack of participation could have negative consequences for their further treatment and may have even rated treatment more positively than actually experienced. However, this can be considered unlikely, as participants were aware that their HCPs had no access to study data.

The low follow-up participation may have also increased the already disproportionate sex ratio, with only 15% of the participants who were AMAB; however, non-responder analysis determined no significant differences in sex assigned at birth between the follow-up group and those who only participated in baseline. This sex ratio also reflects findings in other studies on prevalence rates of gender-incongruent experiences and behaviors. Nonetheless, the sex ratio meant analyses of the 'GAH + GAS' group could only explore satisfaction with mastectomy for AFAB participants.

Finally, only 5 participants identified with non-binary identities at follow-up. This is particularly relevant, as previous studies show that between 11%23 and 41%63 of youth and young adults under the age of 25 years identify with non-binary gender identities, meaning the percentage (7%) of non-binary youth in the current sample is lower than average prevalence rates. However, all non-binary participants in the sample were AFAB, mirroring results of other studies showing non-binary youth³⁵ and adults³⁸ more likely to be AFAB. Recent studies showed that non-binary youth are less likely to undergo GAH to reach transition goals³⁵ and may face barriers regarding access to hormones when they do desire this type of TRMI, 31,35 making it essential to critically examine the lack of non-binary participants in the present study. Nonetheless, the small sample size means additional analyses based on gender binarity would have most likely been severely limited anyway.

In sum, sampling limitations imply that the results cannot be transferable to all other trans populations, particularly non-Western countries or people of color, or youth identifying with non-binary genders, but also to AMAB youth or those undergoing other types of TRMI, such as genital surgeries. Future research should thus explicitly capture the TRC experiences of non-binary and racially diverse adolescents, in particular. Furthermore, while the present study was performed over a period of several years, this early data regarding satisfaction with TRC cannot be extrapolated to assume long-term TRC success as many adolescents continue to grow and

evolve their identities throughout the years. Future research should aim to follow up the developmental pathways of trans youth long term into their adult years.

On a different note, results provide suggestions for improvement in measurement tools to be used with trans adolescents. The ITPS was an interesting measurement tool for capturing individual transition progress in the present adolescent population and future research should consider its application, as existing tools for understanding GD and transition needs have limitations. 40 With regard to measuring satisfaction using the ZUF-8, high satisfaction must be interpreted cautiously as it may simply be caused by a ceiling effect. 45,47 To make a valid assessment of treatment satisfaction, high satisfaction values should be classified with the help of further information, such as free-text answers. Furthermore, the ZUF-8 only reflected overall satisfaction with general health care instead of satisfaction with the specialized nature of TRC. Analysis of the free-text responses suggest that future research should also include specific questionnaires to capture aspects that other studies have shown to be relevant to satisfaction with TRC: wait times, TRMI side effects and outcomes, relationships with HCPs, psychotherapy and assessment requirements, and so on. 6,30,34,5

CONCLUSION

This study was one of the first in Germany to assess satisfaction with TRC within a prospective sample of clinically referred trans adolescents and young adults. It builds on the few studies in this^{28,30,34} and related areas, such as effects of TRC on adolescent mental well-being. ^{15,17,42} Overall, satisfaction with TRC was high in this population of trans youth, and no participants regretted treatment, reflecting high quality of care at the Hamburg GIS. Participants' focus on physical results of treatment as reason for (dis) satisfaction with TRMI adds to the literature supporting the use of TRMI on adolescent populations. A progressed transition (higher ITPS) significantly predicted higher satisfaction with TRC, providing insight into the usefulness of measuring individual treatment progress and incorporating individual desires in TRC in younger populations.

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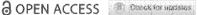
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Sexual Experiences in Transgender People: The Role of Desire for Gender-Confirming Interventions, Psychological Well-Being, and **Body Satisfaction**

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ABSTRACT

We examined the role of gender-confirming treatment (GCT; i.e., hormonal treatment and genital surgery), psychological well-being, and body satisfaction in the sexual feelings and behaviors of transgender adults. A survey was conducted among a nonclinical sample of 325 male-to-female (MtF) and 251 female-to-male (FtM) Dutch adults (17–76 years, $M_{\rm age} = 41.87$), divided into those with no GCT desire, those who desired (more) GCT, and those who completed GCT. Findings indicated that whereas GCT may positively affect sexual feelings, particularly in MtF persons, body satisfaction may play an even bigger role. Those without a GCT desire may experience particular difficulties in their sexual experiences.

Being able to enjoy sex is, to many people, an important aspect of their general well-being. Transgender people¹ (i.e., people who do not identify with their birth-assigned sex) may face considerable challenges to their sexual experiences, such as their sexual behavior (i.e., type and frequency of sexual activities) and sexual feelings (e.g., their sexual pleasure). After all, the experience of being transgender is closely related to (sexual) identity and body image. Further, some transgender persons choose to undergo hormonal therapy and/or surgery, which alter the endocrine system and sex characteristics. These aspects are likely to influence the sexual experiences of transgender persons, which in turn may affect their quality of life (Rolle, Ceruti, Timpano, Falcone, & Frea, 2015).

Research on the sexual experiences of transgender persons has thus far focused predominantly on the impact of gender-confirming treatment (i.e., hormonal treatment or genital surgery to change one's sex characteristics; hereafter referred to as "GCT") on several aspects of sexuality. This is not surprising given that sexual experiences, such as masturbation frequency and the ability to reach an orgasm, are seen as indicators of treatment success (De Cuypere et al., 2005). There has been great variability in studies on sexual experiences in transgender people following GCT, both in terms of the outcomes under study and the study findings, which hinder comparisons across studies (for reviews, see Klein & Gorzalka, 2009; Murad et al., 2010). Nevertheless, some general observations can be made. Concerning sexual behavior, empirical research has typically focused on frequency of sex and masturbation. For trans women (male-assigned at birth), studies have generally shown increased frequency of sex after GCT, but

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¹ We are using the term transgender people to refer to all individuals who do not (fully) identify with their birth-assigned sex. These individuals do not necessarily meet criteria for a formal DSM-5 diagnosis of gender dysphoria. Thus, we are referring to a broader spectrum of individuals.

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either decreased, increased, or unchanged frequency of masturbation (Klein & Gorzalka, 2009). Studies among trans men (female-assigned at birth) have shown either unchanged or increased frequency of sex and masturbation (Costantino et al., 2013; Klein & Gorzalka, 2009; Wierckx et al., 2011). Studies on sexual feelings after GCT have mainly focused on general measures of sexual satisfaction, as opposed to more specific measures like sexual pleasure and esteem. In general, studies have indicated increased sexual satisfaction in the majority of both trans women and trans men following GCT (Murad et al., 2010; Weigert, Frison, Sessiecq, Mutairi, & Casoli, 2013).

Most of the existing studies on the impact of GCT have been retrospective in nature (Klein & Gorzalka, 2009; Murad et al., 2010) and may therefore suffer from recall bias. Further, these studies may suffer from a cognitive dissonance effect, whereby respondents may evaluate the effect of the treatments as more positive. A pre- and post-measure of a behavior (e.g., masturbation frequency) may have given a more realistic representation. Few studies have assessed the sexual experiences of transgender persons who wish to, but did not yet receive treatment (for some exceptions, see Cerwenka, Nieder, Briken, et al., 2014; Cerwenka, Nieder, Cohen-Kettenis, et al., 2014). This group of transgender persons may have particular negative sexual experiences due to their yet unfulfilled desire for treatment (Cerwenka, Nieder, Briken et al., 2014). Similarly, little research has focused on transgender persons who do not wish to undergo GCT (for a similar observation, see Bauer & Hammond, 2015), thereby ignoring a substantial subgroup of transgender people. For example, a recent study in Canada showed that 3% of male-to-female (MtF) transgender adults and 6% of female-to-male (FtM) transgender adults did not plan to undergo medical treatment, 13% of MtF and 6% of FtM transgender persons were not sure, and 11% of MtF and 9% of FtM transgender persons felt that the concept of "medical transition" did not apply to them (Scheim & Bauer, 2015). Although these transgender people do not have the intention to undergo GCT, they may still experience problems with identity development and body image, which may negatively influence their sexual behavior and feelings. The difficulties they face, however, may be particularly different from those of transgender people who have a yet unfulfilled treatment desire and those who have already had treatment. Our first aim was therefore to examine the sexual behaviors and sexual feelings of these three subgroups of transgender persons.

Aside from differences in treatment desire, two factors that are likely to be associated with sexual experiences of transgender people are their psychological well-being and body satisfaction. There are several indications that dissatisfaction with one's appearance or feelings of gender dysphoria can make it more difficult to enjoy or to be satisfied with sexual experiences (Doorduin & Van Berlo, 2014). Further, although in general transgender people reported improved sexual satisfaction after GCT (De Cuypere et al., 2005; Klein, & Gorzalka, 2009), findings also indicate that satisfaction with one's genitals plays an important role in sexual satisfaction following GCT (De Cuypere et al., 2005). Because psychological well-being and body satisfaction can vary considerably between as well as within groups of transgender persons with different treatment desires, it is essential to explore the role of these factors in their sexual experiences, which was our second aim.

In sum, this study was aimed at gaining more insight into the sexual behavior and sexual feelings of different groups of transgender persons in the Netherlands. Further, it examined the role of psychological well-being and body satisfaction in the sexual behaviors and feelings of transgender people. The study was conducted among a nonclinical convenience sample of transgender adults who were divided into three groups: those who never received any GCT and had no desire to do so, those who had a yet unfulfilled desire to undergo GCT, and those who had received (partial) GCT and have no desire (at the moment) to undergo more GCT.

Method

Sample and procedure

Our study included 576 Dutch trans people, with a mean age of 41.87 (SD = 14.41, range = 17-76 years). Of the total sample, 325 (56.4%) were in the male-to-female (MtF) spectrum, and 251 were in the femaleto-male (FtM) spectrum. Respondents were recruited between July and August 2013 by two means. Most respondents (N = 445) were recruited through transgender organizations and other transgender-specific

Table 1. Descriptive statistics.

		Male-to-Female			Female-to-Male		
	NTD (N = 125)	UTD (N = 133)	FTD (N = 67)	NTD (N = 98)	UTD (N = 108)	FTD (N = 45)	
Age—M (SD)	47.85 ^c (13.08)	43.14 ^d (13.44)	48.30 ^c (12.70)	41.28 ^c (14.64)	31.68 ^d (12.82)	37.84 ^c (11.57)	
Gender identity (%)							
Binary	14 ^a	83 ^b	84 ^b	15 ^a	92 ^b	76 ^b	
Nonbinary	86 ^b	17 ^a	16 ^a	85 ^b	8 ^a	24 ^a	
Registered at gender clinic (% yes)	15 ^a	79 ^b	91 ^b	3ª	92 ^b	91 ^b	
Undergone treatment (% yes)							
Hormones (ever)	n/a	56	99	n/a	57	86	
Chest surgery	n/a	11	49	n/a	32	91	
Hysterectomy/oophorectomy	n/a	n/a	n/a	n/a	28	78	
Vagino-/phallo-/metoidioplasty	n/a	11	73	n/a	9	20	
Treatment desire (% yes)							
Hormones	n/a	38	n/a	n/a	40	n/a	
Chest surgery	n/a	50	n/a	n/a	64	n/a	
Hysterectomy/oophorectomy	n/a	n/a	n/a	n/a	67	n/a	
Vagino-/phallo-/metoidioplasty	n/a	74	n/a	n/a	37	n/a	
In a relationship (% yes)	54	45 ^a	49	47	39	42	
Psychological well-being ^f — M (SD)	3.87 ^{c,d} (0.82)	3.68 ^d (0.84)	4.08 ^c (0.70)	3.57 (0.89)	3.59 (1.05)	3.99 (0.96)	
Body satisfaction —M (SD)	3.13 ^c (0.91)	2.57 ^d (0.80)	4.01 ^e (0.64)	2.94 ^c (0.77)	2.59 ^d (0.87)	3.80 ^e (0.96)	

Note. NTD = no treatment desire; UTD = unfulfilled treatment desire; FTD = fulfilled treatment desire. ^a Significantly lower than among the entire sample, p < .05 and Cramér's V > .10. Significantly higher than among the entire sample, p < .05 and Cramér's V > .10. c,d,e Means with different superscripts are significantly different at p < .05. f Scores ranged from 1–5, with higher scores indicating higher psychological well-being/body satisfaction.

channels, who distributed a call for participation in our survey via their websites, mailing lists, leaflets, social media, and activities. The remainder of the sample (N=131) was recruited through a commercial online panel of a large research institute (Intomart GfK). As part of a monthly screening, all panel members (around 100,000) were asked whether they knew any transgender persons personally. Assuming that respondents who answered yes may have had themselves in mind, those respondents subsequently received a screening survey asking about their own birth-assigned sex and current gender identity (male, female, partly male and partly female, neither male nor female, not sure, or other). If birth-assigned sex and current gender identity did not match, people received an invitation to fill out our survey.

Respondents were classified into three groups, based on whether or not they had ever received treatment (hormonal or surgery) and whether or not they had a desire to undergo (more) treatment (see Table 1 for sample characteristics). In the sample of MtF transgender people, 125 respondents were in the no treatment desire (NTD) group (have never had any treatment and have no desire to do so), 133 were in the unfulfilled treatment desire (UTD) group (may or may not have had any treatment and have a desire to do so or do more), and 67 were in the fulfilled treatment desire (FTD) group (had received some form of treatment but at the moment have no desire for further treatment). In the sample of FtM transgender adults, these numbers were 98 (NTD), 108 (UTD), and 45 (FTD). In both samples, respondents in the NTD group were significantly more likely to identify themselves as neither male nor female or as male and female, whereas respondents in the UTD and FTD subgroups were significantly more likely to identify themselves as either female (in the sample of MtF transgender adults) or male (in the sample of FtM transgender adults). In the sample of MtF transgender adults, those in the UTD subgroup were less likely to be in a relationship. Age significantly differed in both samples, with respondents in the UTD subgroup being younger than both other subgroups.

Measures

Sexual behavior

To measure sexual behaviors, we asked three main questions and two follow-up questions. Respondents were first asked whether they ever had sex, whether they had been sexually active in the past six months, and whether they ever masturbated (all three questions coded as 0 = yes, 1 = no). Sex was defined as fondling (of breasts, penis, or vagina), oral sex, anal sex, or vaginal sex. If respondents answered yes to

either one of the latter two questions, we asked how often respondents had sex in the past six months and/or how often they currently masturbate (both questions coded as 0 = never, 1 = once a month at most, 2 = once a week at most, 3 = more than once a week).

Sexual feelings

We measured respondents' feeling of sexual agency (six items), sexual pleasure (four items), and sexual esteem (four items). In total, respondents filled out 19 statements about how they feel during sex, rated on a 5-point scale, with 1 = completely agree to 5 = completely disagree. Respondents could also indicate "not applicable" in which case the item was not included. An exploratory factor analysis revealed three factors, explaining 48.37% of the variance. Five items were removed because they either had factor loadings < .40 on all three factors or loaded on more than one factor. The first factor, sexual agency, accounted for 18.75% of total variance (e.g., "during sex I have little influence over what happens"). Items were averaged such that higher scores indicated higher sexual agency ($\alpha = .78$). The second factor, sexual pleasure (e.g., "I enjoy sex a lot"), accounted for 18.04% of total variance. Items were reverse-coded and averaged such that higher scores indicated higher sexual pleasure ($\alpha = .81$). The third and final factor, sexual esteem, accounted for 11.59% of total variance (e.g., "I focus more on my sex partner than on myself when having sex"). Items were averaged such that higher scores indicated higher sexual esteem ($\alpha = .66$). In addition to these statements about specific sexual feelings, we asked one question about people's general sexual satisfaction ("How satisfied are you with your sex life in general?"), with 1 = verydissatisfied, 2 = dissatisfied, 3 = not dissatisfied/not satisfied, 4 = satisfied, 5 = very satisfied. The first two and the last two categories were collapsed to create three groups: 1 = (very) dissatisfied, 2 = notdissatisfied/not satisfied, and 3 = (very) satisfied. Finally, we asked respondents how important sex was to them, with 1 = very important, 2 = important, 3 = not important/not unimportant, 4 = unimportant, $5 = very \ unimportant$. The first two and the last two categories were collapsed to create three groups: 1 = (very) important, 2 = not important/not unimportant, and 3 = (very) unimportant).

Psychological well-being

The 10-item Kessler Psychological Distress Scale (K10) was used to assess respondents' psychological well-being (Kessler et al., 2002). This scale asks respondents to indicate how often they experienced certain negative feelings during the previous four weeks (e.g., "Did you feel worthless?"), using a 5-point scale (1 = all of the time to 5 = none of the time). The 10 items were averaged such that higher scores indicated higher levels of psychological well-being ($\alpha = .93$). Means and standard deviations for the different subgroups are displayed in Table 1.

Body satisfaction

To measure body satisfaction, we constructed a scale consisting of 12 statements (e.g., "I dislike my face" and "My body fits me"). Items were answered on a 5-point scale ($1 = completely \ agree$ to 5 = completelydisagree). After reverse-coding positively worded items, items were averaged such that higher scores indicated higher body satisfaction. Cronbach's alpha was .92. Means and standard deviations for the different subgroups are displayed in Table 1.

Statistical analyses

All statistical analyses were conducted in SPSS V23.

Bivariate analyses

For lifetime experience of sex, sexual activity in the past six months, whether or not one masturbates, sexual satisfaction, and importance of sex, between-group differences were tested using chi-square analysis. In case of significant chi-square results, we performed paired comparisons in which we compared the three subgroups with one another in 2×2 chi-square analyses. We used a Bonferroni-adjusted p value of 374 S. W. C. NIKKELEN AND B. P. C. KREUKELS

Table 2. Sexual behavior among transgender people.

	Male-to-Female			Female-to-Male		
	NTD (N = 125)	UTD (N = 133)	FTD (N = 67)	NTD (N = 98)	UTD (N = 108)	FTD (N = 45)
Lifetime experience of sex (% yes)	91	92	88	86	79	93
Sexually active in past 6 months (% yes)	58	44	45	43 ^a	46	67 ^b
Masturbates (% yes)	98ª	78 ^b	82 ^b	87	89	93
Frequency of sex ^c M (SD)	1.01 (1.05)	0.87 (1.11)	0.78 (0.98)	0.73a (0.97)	0.87 ^{a,b} (1.09)	1.24 ^b (1.07)
Frequency of masturbation (SD)	2.37 ^a (0.82)	1.64 ^b (1.13)	1.48 ^b (1.02)	1.71 ^b (0.99)	2.20 ^b (1.07)	2.59 ^b (0.87)

Note. NTD = no treatment desire; UTD = unfulfilled treatment desire; FTD = fulfilled treatment desire; a,b Means with different superscripts are significantly different. CScores ranged from 0 (never) to 3 (more than once a week).

0.017 (0.05/3), correcting for the three separate subtests to evaluate the significance of the paired comparisons. For frequency of sex, frequency of masturbation, sexual agency, sexual pleasure, and sexual esteem, group mean differences between the NTD, UTD, and FTD groups were analyzed using one-way analysis of variance (ANOVA), including post hoc testing with Bonferroni correction.

Multivariate analyses

To analyze the relative contribution of psychological well-being, body satisfaction, and group membership on sexual behaviors and feelings, we used linear regression analysis for continuous dependent variables (sexual agency, sexual pleasure, and sexual esteem) and ordinal regression for ordinal dependent variables (frequency of sex, frequency of masturbation, sexual satisfaction, and importance of sex). Dummy variables were created to analyze subgroup differences, with the UTD group as the reference group. Age, relationship status (0 = no partner, 1 = partner), and gender identity (0 = binary [male or female], 1 = nonbinary [both male and female or neither male nor female]) were included as control variables. Previous studies have shown the importance of relationship status for sexual satisfaction, sexual activity, and sexual functioning (Bouman et al., 2016; Weyers et al., 2009).

Results

Group sizes and means for the different indicators of sexual behavior and sexual feelings are presented in Tables 2 and 3, separated by sample (MtF and FtM) and subgroup (NTD, UTD, or FTD). Regression results for factors correlating with sexual behavior and sexual feelings are presented in Table 4.

Table 3. Sexual feelings among transgender people.

	Male-to-Female			Female-to-Male		
	NTD (N = 125)	UTD (N = 133)	FTD (N = 67)	NTD (N = 98)	UTD (N = 108)	FTD (N = 45)
Sexual agency ^d M (SD)	3.23 ^a (0.74)	3.59 ^b (0.87)	3.98 ^c (0.71)	3.30 ^a (0.84)	3.84 ^b (0.82)	3.79 ^b (0.74)
Sexual pleasure ^d M (SD)	3.55a (0.85)	3.22 ^b (1.00)	3.60a (0.79)	3.13a (0.92)	3.48b (0.95)	3.66 ^b (0.75)
Sexual esteem ^d M (SD)	2.77 ^a (0.84)	2.42 ^b (0.89)	3.34° (0.86)	2.88a (0.79)	2.46 ^b (0.84)	2.95a (0.80)
Sexual satisfaction (%)						
Satisfied	27	28	35	32	39	41
Not satisfied, not dissatisfied	36	33	33	29	22	32
Dissatisfied	38	39	33	39	39	27
Importance of sex (%)						
Important/very important	56	47	46	39	57	62
Not important, not unimportant	31	28	28	35	24	27
Unimportant/very unimportant	13	26	25	27	19	11

Note. NTD = no treatment desire; UTD = unfulfilled treatment desire; FTD = fulfilled treatment desire. a,b,c Means with different superscripts are significantly different. $^{\rm d}$ Scores ranged from 1–5, with higher scores indicating higher agency/pleasure/esteem.

Table 4. Factors correlated with sexual behaviors and feelings.

	Ordinal Logistic Regression—OR					ar Regression	—b*
	Frequency of sex ^b	Frequency of masturbation ^b	Sexual satisfaction	Importance of sex	Sexual agency ^a	Sexual pleasure ^a	Sexual esteem ^a
Male-to-female							
Age	0.97**	0.97**	0.99	1.00	06	— .01	.09
Relationship	10.94***	0.95	2.98***	2.05**	.02	.12*	.07
Gender identity	1.37	4.12***	1.34	1.32	04	.09	.02
NTD (vs. UTD)	0.84	1. <i>7</i> 1	0.46*	0.98	30***	— .05	02
FTD (vs. UTD)	0.42*	0.84	0.38*	0.41*	05	16*	.05
Psych. well-being ^a	1.03	0.97	1.19	1.03	.11	.07	.03
Body satisfaction ^a	1.69**	1.04	2.13***	1.72***	.39***	.54***	.57***
R ² /Pseudo R ^{2 ←}	.15	.09	.09	.05	.25	.29	.39
F/χ^{2c}	118.24***	76.30***	57.98***	35.84***	13.65***	16.33***	25.36***
Female-to-male							
Age	0.97**	0.97**	0.98*	0.99	.01	09	.21**
Relationship	16.61***	0.45**	1.75*	1.69*	.03	— .0 1	.06
Gender identity	1.69	0.90	1.50	0.95	— .15	— .03	.07
NTD (vs. UTD)	0.34*	0.43*	0.55	0.48	— .21*	— .20	.04
FTD (vs. UTD)	1.15	1.68	0.49	0.92	— .15	− .16*	05
Psych. well-being ^a	1.07	1.12	1.37*	1.08	.35***	.17	.17**
Body satisfaction ^a	1.79**	1.93***	2.13***	1.37	.20**	.46***	.46***
R ² /Pseudo R ^{2 c}	.21	.10	.07	.04	.31	.27	.40
F/x ^{2 c}	123.46***	61.50***	34.07***	20.56**	12.64***	10.44***	18.58***

Note. OR = odds ratio; NTD = no treatment desire; UTD = unfulfilled treatment desire; FTD = fulfilled treatment desire. a Scores ranged from 1–5, with higher scores indicating higher psychological well-being/body satisfaction/agency/pleasure/esteem. bScores ranged from 0 (never) to 3 (more than once a week). $^{c}R^{2}$ and F are reported for linear regression; McFadden Pseudo R^{2} and χ^{2} are reported for ordinal logistic regression.

Sexual behavior of MtF transgender people

In the sample of MtF transgender individuals, there were no significant differences between the three groups in whether they ever had sexual intercourse, $\chi 2$ (2, N = 325) = 0.76, p = .683, or whether they had been sexually active in the previous six months, $\chi 2$ (2, N = 325) = 5.72, p = .057. There was a significant difference between groups in whether they masturbate, $\chi 2$ (2, N = 313) = 21.73, p < .001, Cramér's V = .26. Pairwise comparisons showed that respondents in the NTD subgroup were more likely to masturbate (98%) than respondents in the UTD subgroup (78%), $\chi 2$ (1, N = 248) = 21.94, p < .001, and respondents in the FTD subgroup (82%), $\chi 2$ (1, N = 184) = 14.27, p < .001. The UTD and FTD subgroups did not significantly differ from each other. Frequency of sex did not significantly differ between the three groups, F(2, 319) = 1.15, p = .318. Finally, frequency of masturbation, F(2, 310)= 23.16, p < .001), was significantly higher in the NTD subgroup than in the UTD subgroup (p < .001) and in the FTD subgroup (p < .001). The UTD and FTD subgroups did not significantly differ from each other.

Sexual feelings of MtF transgender people

Sexual agency, F(2, 287) = 17.82, p < .001, was lowest among the NTD subgroup MtF transgender people, and was significantly lower than among the UTD (p = .002) and FTD subgroups (p < .001). The UTD subgroup also scored significantly lower than the FTD subgroup (p = .008). Sexual pleasure differed significantly between the groups, F(2, 283) = 5.17, p = .006. Sexual pleasure was higher in the NTD subgroup than in the UTD subgroup (p = .017), but the NTD subgroup did not significantly differ from the FTD subgroup. The UTD subgroup had significantly lower sexual pleasure compared to the FTD subgroup (p = .030). Sexual esteem differed significantly between the groups as well, F(2, 280) = 15.46,

^{***}p < .001; **p < .01; *p < .05.

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p < .001: It was higher in the NTD subgroup than in the UTD subgroup (p = .008), but significantly lower than in the FTD subgroup (p < .001). Sexual esteem was significantly lower in the UTD subgroup than in the FTD subgroup (p < .001). There were no significant differences in sexual satisfaction between the different subgroups, $\chi 2$ (4, N = 298) = 1.51, p = .826, nor in the importance ascribed to sex, $\chi 2$ (4, N = 325) = 7.68, p = .104.

Psychological well-being and body satisfaction in MtF transgender people

After controlling for age, relationship status, gender identity, and subgroup status, psychological well-being was not related to any of the indicators of sexual behavior or feelings in the sample of MtF transgender adults. In contrast, body satisfaction was positively related to all indicators of sexual behavior and feelings (all ps < .01), except frequency of masturbation. Further, the results showed that the relationship between subgroup membership (i.e., NTD, UTD, or FTD) and sexual feelings and behaviors in some cases disappeared (compare Tables 2 and 3 with Table 4). In one case, there was a change in the direction of the relationship when adjusted for body dissatisfaction: The FTD subgroup scored higher on sexual pleasure compared to the UTD subgroup before adjusting for body satisfaction, but lower after adjusting for body satisfaction.

Sexual behavior of FtM transgender people

In the sample of FtM transgender adults, there were no significant differences between the three groups in whether they ever had sexual intercourse, $\chi 2$ (2, N=251) = 5.40, p=.067, nor whether they masturbate, $\chi 2$ (2, N=245) = 1.05, p=.590. There was a significant difference between subgroups in whether they had been sexually active in the past six months, $\chi 2$ (2, N=251) = 7.40, p=.025. Pairwise comparisons showed no significant differences between the NTD and UTD subgroups, but respondents in the NTD subgroup were less likely to have been sexually active in the past six months (43%) than respondents in the FTD subgroup (67%), $\chi 2$ (1, N=143) = 6.99, p=.008. There were no significant differences between the UTD and FTD subgroups. Frequency of sex, F(2, 246) = 3.79, p=.024, did not significantly differ between the NTD and UTD subgroups, but was significantly lower in the NTD subgroup compared to the FTD subgroup (p=.019). There were no significant differences between the UTD and FTD subgroups. Frequency of masturbation, F(2, 242) = 12.98, p<.001, was significantly lower in the NTD subgroup compared to both the UTD subgroup (p=.002) and the FTD subgroup (p<.001). The UTD and FTD subgroups did not differ significantly from each other.

Sexual feelings of FtM transgender people

Sexual agency, F(2, 202) = 10.34, p < .001, was lowest among the NTD subgroup of FtM transgender adults and was significantly lower than in the UTD (p < .001) and FTD (p = .005) subgroups, which did not significantly differ from each other. Sexual pleasure differed significantly between the groups, F(2, 201) = 5.84, p = .003: It was significantly lower in the NTD group than in the UTD (p = .037) and FTD subgroups (p = .006), which did not significantly differ from each other. Sexual esteem differed significantly between the groups as well, F(2, 198) = 7.33, p = .001: It was significantly higher in the NTD subgroup than in the UTD subgroup (p = .004). The NTD subgroup did not significantly differ from the FTD subgroup, but the UTD subgroup scored significantly lower than the FTD subgroup (p = .006). Sexual satisfaction did not significantly differ between subgroups, $\chi 2$ (4, N = 219) = 3.51, p = .476. The chi-square analysis for importance of sex was significant, $\chi 2$ (4, N = 251) = 10.86, p = .028, Cramér's V = .15, but pairwise comparisons did not show significant differences between subgroups.

Psychological well-being and body satisfaction in FtM transgender people

In the sample of FtM transgender adults, after controlling for age, relationship status, gender identity, and subgroup status, psychological well-being was positively associated with sexual satisfaction, sexual

agency, and sexual esteem. Body satisfaction was positively related to all indicators of sexual behavior and feelings (all ps < .01), except importance of sex. As was the case in MtF transgender adults, the relationship between subgroup membership (i.e., NTD, UTD, or FTD) and sexual feelings and behaviors disappeared in some cases (compare Tables 2 and 3 with Table 4). In one instance, there was a change in the direction of the relationship when adjusted for body dissatisfaction: The FTD subgroup scored higher on sexual pleasure compared to the UTD subgroup before adjusting for body satisfaction, but lower after adjusting for body satisfaction.

Discussion

This study aimed to acquire insight into the sexual behavior and sexual feelings of different groups of transgender persons in the Netherlands, distinguished by whether or not they have received some form of GCT and whether or not they have a yet unfulfilled desire for GCT. Further, we examined the role of psychological well-being and body satisfaction in these feelings and behaviors. Overall, this study shows differences in sexual behaviors and feelings between transgender persons based on whether or not they have had GCT and whether or not they have a yet unfulfilled desire to undergo GCT. Further, our study indicates that in addition to GCT status and desire, body satisfaction and, to a lesser degree, psychological well-being play a vital role in the sexual behaviors and feelings of transgender people.

Sexual behaviors

Concerning sexual behaviors, we explored sexual intercourse as well as masturbation behaviors. Regarding the indicators of sexual intercourse, our study showed no significant differences between subgroups of MtF transgender persons in whether or not they ever had sexual intercourse, whether they had sexual intercourse in the past six months, and frequency of sex. In contrast, among FtM transgender persons, those with a fulfilled treatment desire were more likely to have been sexually active in the past six months and had a higher frequency of sex than FtM transgender persons who did not have any treatment and had no desire for treatment. Concerning masturbation behavior, MtF transgender persons who had no desire for any treatment were more likely to masturbate and masturbated more often than the other two subgroups. In contrast, among FtM transgender persons, those who did not want any treatment masturbated less often than the other two subgroups. In sum, there were little differences in the sex and masturbation behaviors between trans people with an unfulfilled and those with a fulfilled treatment desire. There were, however, some differences in the sexual behaviors between transgender persons with no treatment desire and the other two subgroups, which are likely due to differences in testosterone levels. In cisgender people, males have higher testosterone levels, which relates to higher sexual desire and arousal, than females (Meston & Frohlich, 2000). Hormone treatment affects testosterone levels, with decreasing testosterone level in trans women who receive cross-sex hormone treatment and increasing testosterone levels in trans men receiving cross-sex hormone treatment. In our sample of MtF transgender persons without treatment desire, who are not treated with hormones and thus still exposed to endogenous testosterone levels, the frequency of masturbation was higher than in the other two groups. For FtM transgender persons, the majority received hormone treatment (i.e., testosterone) in the UTD and FTD groups, and their frequency of masturbation was higher than in the group without treatment desire not receiving any testosterone. A similar pattern can be seen for frequency of sex, especially in the sample of FtM transgender persons.

These findings are in line with previous studies showing that after gender-confirming interventions, trans women reported low levels of sexual desire and trans men high levels of sexual desire (Elaut et al., 2008; Wierckx et al., 2011; Wierckx et al., 2014). Higher levels of sexual desire will result in more motivation to engage in sexual activities like masturbation and partner sex. In our sample of FtM transgender persons with a fulfilled treatment desire, the percentage that had been sexually active in the past six months was significantly higher than the other two groups. Further, the frequency of sex was higher than the other two groups, although this difference was not statistically significant. Thus, when FtM transgender persons with a fulfilled treatment desire have no treatment wishes anymore (regardless of 378 S. W. C. NIKKELEN AND B. P. C. KREUKELS

whether they had genital surgery or not), they may feel "ready" to engage in sexual activities with a partner, whereas frequency of masturbation is also higher in the group that still desires treatment probably as a result of testosterone treatment.

Sexual feelings

In both samples, there were no significant differences between subgroups on general sexual satisfaction. However, when comparing our groups to general population percentages, it seems that in general in our groups, the percentage of those satisfied with their sex life is lower (27%–41% compared to 46.8% in the general population) and the percentage of those dissatisfied is higher (27%–39% compared to 20.8% in the general population) (Skevington, Lotfy, & O'Connell, 2004). We did find differences between our groups when examining three separate aspects of sexual satisfaction, namely agency (the extent to which one has influence over what happens during sex), pleasure (whether sex is enjoyable), and esteem (whether one feels confident during sex). MtF transgender persons with a fulfilled treatment desire responded most positively: They scored higher on all of these three aspects of sexual satisfaction than those with an unfulfilled treatment desire. Further, they scored higher on sexual agency and esteem than those with no treatment desire. These positive effects may be a result of the alleviation of gender dysphoria by getting rid of the unwanted sex organs and/or having a body congruent with gender identity. This indicates that for those MtF transgender adults, GCT may have a positive influence on these different aspects of sexual satisfaction.

In the sample of FtM transgender persons, individuals with a fulfilled treatment desire scored higher than those with an unfulfilled treatment desire on sexual esteem, but not on sexual agency or pleasure. FtM transgender persons with a fulfilled treatment desire seem to be more confident in their sex life than those with an unfulfilled treatment desire, although only 20% of the FTD group had genital surgery (phalloplasty or metoidioplasty). Chest surgery may be crucial here: In the FTD group, 91% had undergone this surgery as opposed to only 32% in the UTD group, and in the UTD group 64% indicated a desire for chest surgery. Mastectomy has been reported to improve body satisfaction beyond satisfaction with chest appearance only and body satisfaction was associated with higher self-esteem in trans men (van de Grift, Kreukels et al., 2016). For agency and pleasure, however, there was no significant difference between FtM transgender persons with an unfilled and fulfilled treatment desire. These two aspects of sexual feelings may be—like sexual behavior—very much related to the hormonal environment, with also the majority in the UTD group receiving testosterone treatment.

Concerning transgender persons with no treatment desire, we found that this subgroup did not score particularly high on the separate aspects of sexual satisfaction. In the sample of MtF transgender persons, those with no treatment desire scored in between the other two subgroups on pleasure and esteem, but scored lowest on sexual agency. In FtM transgender persons, those with no treatment desire scored lowest on both sexual agency and pleasure. These findings suggest that besides whether or not one undergoes or wants to undergo GCT, the difficulties that come with the experience of being transgender itself can influence aspects of sexual satisfaction. Further, the findings indicate that not having a treatment desire does not necessarily indicate that an individual is satisfied with one's body. One explanation may be that some transgender people without desire for GCT may abstain from treatment because they see a lot of disadvantages to it or may even fear it. Also, they may feel dissatisfied with their body, but may not expect to get something better in return by undergoing GCT. Transgender persons with no treatment desire are often overlooked in research on sexual experiences and therefore deserve specific attention.

Factors correlated with sexual behaviors and feelings

Body incongruence, a key element of gender identity problems, hinders sex and enjoyment of sex (Doorduin & Van Berlo, 2014). Also, gender incongruence is often accompanied by body dissatisfaction that is not confined only to the genitals (van de Grift, Cohen-Kettenis et al., 2016). In both samples, body satisfaction was positively related to almost all of our indicators of sexual behaviors and feelings, underlining the importance that body satisfaction plays in sexual experiences in transgender people. This is



in line with a previous study that showed that MtF transgender persons who indicated a higher degree of satisfaction with their appearance also reported a better sexual functioning (Weyers et al., 2009). Psychological well-being played a role in the sexual feelings of FtM transgender persons only, with higher psychological well-being being related to higher sexual satisfaction, agency, and esteem. Secondary analyses (not shown here) showed that psychological well-being was positively related to these indicators of sexual feelings in MtF transgender persons as well, but this relationship disappeared after including body satisfaction in the analyses. This suggests that psychological well-being and body dissatisfaction in MtF transgender persons are highly related and that sexual feelings are mainly affected by body dissatisfaction. Further, we found that the relationship between subgroup membership (i.e., NTD, UTD, or FTD) and sexual feelings and behaviors in some cases disappeared or showed a change in the direction of the relationship, when adjusted for psychological well-being and body dissatisfaction. This indicates that subgroup differences are partly explained by psychological well-being and body dissatisfaction and that these factors may thus play an even more important role in transgender people's sexual behaviors and feelings than whether or not one has had treatment and desires (further) treatment.

An important strength of this study is that most research thus far has only included transgender people with a diagnosis who are clinically referred or have already been treated (Klein & Gorzalka, 2009; Stephenson et al., 2017). In this way these studies focus on transgender people who seek genderaffirmation therapy. However, these studies do not shed light on the sexual experiences of transgender persons who have no desire for treatment or do not apply at gender identity clinics for other reasons (such as costs or anxiety). The current study did include transgender persons without a treatment desire. In addition, by including this group, our study also better represents experiences of nonbinary identifying transgender persons in comparison to other studies. Around 85% of the respondents in the no treatment desire groups were nonbinary identifying. Another strength is that this was not a clinical study, but a study initiated by an organization that is unrelated to treatment. The respondents may have been more open because they were not questioned by the institute or clinician that provides or has provided their treatment. Further, whereas studies in sexual health of transgender adults have generally focused on sexual functioning (sexual problems, sexual desire, arousal, and the ability to achieve orgasm), our study approached sexual health from a different angle and reports on sexual experiences via sexual behavior and sexual feelings.

Two limitations of this study also deserve attention. For sexual experiences in transgender persons, time since medical interventions may be important. People may have to get used to the new situation. For example, MtF transgender persons may have to get used to a sexual response system in a less androgenic milieu (Wierckx et al., 2014) and trans people after genital surgery have to become familiar with their new genitals (Lawrence, 2006). In the current study, we did not collect information on time since treatment (cross-sex hormones and genital surgery) and therefore could not control for this factor. A second limitation of this study is that sexual orientation of the respondents could not be included in our analyses, due to the manner in which we measured sexual orientation. Because sexual orientation is likely to be relevant for transgender people's sexual feelings and behaviors, we recommend including it in future studies.

Conclusion

By using a survey among a large nonclinical sample of transgender people, this study enabled us to compare the sexual feelings and behaviors of different groups of transgender persons, based on whether or not they received some form of GCT and whether or not they have a yet unfulfilled desire to undergo GCT. We found some differences in the sexual behaviors and feelings of these groups indicating that GCT may have a positive influence on the sexual feelings of MtF transgender persons, which may not necessarily be true for FtM transgender persons, as there were little differences in the sexual feelings of FtM transgender persons with a fulfilled treatment desire compared to those with an unfulfilled treatment desire. Further, transgender persons who do not wish to undergo any treatment still may experience certain difficulties when it comes to their sexual behaviors and feelings. Finally, our study underlines the important role of body satisfaction in the sexual behaviors and feelings of trans people, which may even 380 S. W. C. NIKKELEN AND B. P. C. KREUKELS



be more important than whether or not one has an unfulfilled treatment desire. Efforts to increase body satisfaction in transgender people are therefore warranted, as it can contribute to more positive sexual experiences.

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Quality of life of treatment-seeking transgender adults: A systematic review and meta-analysis

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Abstract

The study aims to systematically extract and analyse data about Quality of Life (QoL) in the transgender population. A systematic literature search and meta-analysis were conducted using the MEDLINE, EMBASE, PubMed, and PsycINFO databases, up to July 2017. Only English language quantitative studies, in adults, which reported the means for validated QoL measures were included. Random-effect meta-analysis was adopted to pool data and estimate the 95% Confidence Intervals (CI). From 94 potentially relevant articles, 29 studies were included within the review and data extraction for meta-analysis was available in 14 studies. The majority of the studies were cross-sectional, lacked controls and displayed moderate risk of bias. Findings from the systematic review suggested that transgender people display poor QoL, independent of the domain investigated. Pooling across studies showed that transgender people report poorer mental health QoL compared to the general population (-0.78, 95% CI = -1.08 to -0.48, 14 studies). However, meta-analysis in a subgroup of studies looking at QoL in participants who were exclusively post-CHT found no difference in mental health QoL between groups (-0.42, 95% CI = -1.15 to 0.31; 7 studies). There was insufficient data for a pre-treatment subgroup. Evidence suggests that transgender people have lower QoL than the general population. Some evidence suggests that QoL improves post-treatment. Better quality studies that include clearly defined transgender populations, divided by stage of gender affirming treatment and with appropriate matched control groups are needed to draw firmer conclusions.

 $\textbf{Keywords} \ \ \text{Transgender} \cdot \text{Quality of life} \cdot \text{Mental health quality of life} \cdot \text{Sex-related quality of life} \cdot \text{Voice-related quality of life} \cdot \text{Body image-related quality of life}$

1 Introduction

The term transgender (or trans) describes people whose gender identity differs from the sex they were assigned at birth based on their sexual characteristics, whilst the appellation cisgender refers to any individual who is not transgender and whose gender identity matches the sex assigned at birth [1]. Due to the mismatch between gender identity and sex assigned at birth, many transgender people experience severe

distress, generally known as gender dysphoria, which tends to ameliorate following transition to the experienced gender [2].

The process of physical transition consists of different stages. Guidelines for the assessment and treatment of transgender and gender non-conforming people have been developed by the World Professional Association of Transgender Health (WPATH) to facilitate this process (Standards of Care, SOC) [2]. The SOC aims to describe the different treatments that transgender people might wish to undergo, known as Gender Affirming Treatments (GAT), which may include puberty suppression, Cross-sex Hormonal Treatment (CHT), Chest Reconstructive Surgery (CRS) and Gender Affirming Genital Surgeries (GAGSs) [2]. Thus, for the present review, the term 'treatment' is also used to describe GAT.

GAT produces bodily changes that impact and alter gender role and its expression by developing secondary sexual characteristics of the experienced gender in order for the body to become more congruent with the gender identity of the individual [2]. These changes might be sufficient to mitigate the gender dysphoric symptoms [2] and hence improve the

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individual's QoL. However, not every transgender person requires gender affirming treatment and the dysphoria may improve through gender social role transition only. Thus, treatment might vary depending on the specific needs of the transgender person seeking treatment [2].

Many transgender people, particularly prior to their physical transition, face considerable challenges. These challenges can be physiological (development of some of the secondary sexual characteristics of the sex assigned at birth), social (lack of social support, rejection, discrimination, victimisation, transphobia) [3–12] and psychological (e.g. anxiety, depression, low self-esteem) [3, 13–16]. All these factors have been found to have a negative impact on the quality of life (QoL) of transgender people [17, 18].

QoL is a complex and broad concept. It has been described in different ways, such as the quality of one's life conditions, one's satisfaction with life conditions, and as a combination of life's conditions and satisfaction [19]. De Vries and colleagues [20] defined QoL as the individuals' perceptions of their life satisfaction and happiness that has an impact on objective and subjective wellbeing. Hence, OoL measures can be considered as a way of quantifying the level of functioning and perceived wellbeing of people's lives [17]. The concept of QoL encompasses a range of different physical and psychosocial domains. Several factors have been shown to affect QoL in transgender populations, such as presence or absence of depression and psychopathology, transitional status (such as the use of cross sex hormone treatment), levels of social support and perceived discrimination [6, 21-29].

The literature regarding QoL in transgender people mainly focuses on four QoL dimensions: voice-related (vQoL); sexrelated QoL; body image-related QoL; and general QoL. Voice-related QoL can be described as the impact that the perception of one's own voice, in terms of femininity and masculinity, has on the QoL of the individual [30]. This dimension is very important for transgender people, as the pitch of the voice is an important aspect of gender expression and perception [31, 32]. Sex-related QoL is a state of social, physical and mental wellbeing related to sexual life [33]. This concept refers to the sexual functioning and general satisfaction with sexual life [34]. Body image-related QoL stems from the notion that experiencing a positive body image is linked with more satisfactory relationships, sexuality, improved well-being and overall general QoL [35]. Thus, transgender people's incongruence between gender identity and bodily characteristics could potentially impact their body satisfaction and as a consequence their QoL [35-38]. Finally, general QoL describes the overall satisfaction with life not linked to specific physical health conditions and which includes subcategories linked to aspects of mental, physical, and social life [39].

There are mixed results regarding the QoL in the transgender population. While most of the literature suggests that transgender people have lower OoL compared to the general population [17], which increases once on CHT or post-GAGS [28, 40, 41], other studies have not replicated such findings [42, 43]. These mixed results may be explained by the lack of homogeneity in the population studies, as well as by the different types of QoL and measurements used. For instance, the effect of CHT and genital surgery on the QoL of transgender people when compared to the general population is unclear, as studies often use mixed samples in terms of treatment status and/or focus onto different states of transition. The review carried out by Murad and colleagues [27] suggested that CHT improves QoL, sexual and psychological functioning as well as gender dysphoria; however these findings are based on low quality evidence and the actual impact of both medical and social transitions upon QoL needs to be better understood [44].

Therefore, the primary aim of this this study is to conduct a critical systematic review and meta-analysis of studies of QoL in transgender populations and to explore the range of QoL assessed. The present research also aims to investigate the impact of CHT by exploring QoL in transgender people at different stages of gender transition.

Additionally, as there is a lack of understanding of the QoL domains most relevant to transgender people and of how demographic, psychosocial and treatment-related factors influence those domains, this review specifically aims to assess the different dimensions of QoL in transgender populations and their associated factors.

1.1 Eligibility criteria

Studies were included if they aimed to measure QoL in transgender populations using validated QoL tools. Articles were eligible for inclusion if they reported a mean QoL score for a transgender population and were either written in the English language or had an available translation into English. Both cross-sectional and longitudinal studies were included and there was no restrictions on settings. Studies were excluded from this systematic review if they investigated QoL in transgender children (<18 years) as QoL vary with age [45]. Additionally, articles were excluded if they had fewer than 20 participants as in small studies there is a high risk of selection bias and a lack of statistical power [46, 47]. Where different articles utilised the same database and same measures, the most recent article was taken into consideration and included within the meta-analysis. Qualitative studies, case studies, conference abstracts and review articles were also excluded. See Table 1 for summary of the review's eligibility process.

1.2 Search strategy

PRISMA guidelines were followed [48] to carry out this review. Ovid (PubMed, EMBASE, PsycINFO) and Medline



Table 1 Criteria for inclusion of studies within the review

Category	Criteria
Study population	Transgender people Gender Dysphoria, Transsexualism as well as previous diagnoses according to DSM or ICD, or self-defined as transgender
	LGBT studies only if describing transgender people as separate category All races, ethnicities, and cultural groups
	Adults
Sample size	At least 20 participants
Study settings	All settings
	No exclusion criteria based on research setting
Time period	Published from 1946 to July 2017
Publication criteria	Articles in English
	Articles in peer reviewed journal
Study design	Observational studies using standardised measure of QoL. Cross-sectional or longitudinal designs

databases were searched from 1946 to July 2017. Terms for transgender people (Transgender, Transsexual, Gender Identity Disorders, and Gender Dysphoria) were searched using the OR function and combined with the terms related to (Quality of Life, QoL, Life Satisfaction) using the "AND" operator. Additionally, the reference lists of pertinent articles were searched to identify any further potential relevant papers.

1.3 Quality assessment

Risk of bias was assessed using an instrument adapted from Ibrahim et al. [49] as this instrument covered the most relevant criteria to assess risk of bias in descriptive studies. Criteria were [1] a clear definition of the target population, [2] adoption of either random, complete or consecutive recruitment or an attempt at recruiting every participant in the sampling frame, [20] sample as representative of the target population or the report presents evidence that results can be generalised to transgender people, acknowledging that most studies included treatment-seeking transgender people attending gender clinics [3] response rate equal or greater than 70%, [4] adequate sample size with a minimum of 300 participants as smaller sample sizes produce large confidence intervals and less precise results [50, 51] and [5] use of validated measures. The chosen criteria were evaluated as providing either a risk of bias (or unclear risk of bias) (1 point) or no risk of bias (0 point). Scores are then summed and an overall risk of bias rating is created where higher scores indicate greater risk of bias. Studies were rated as low risk of bias (++) (when all or most of the criteria were satisfied), moderate risk of bias (+) (when some of the criteria were satisfied) or high risk of bias (-) (when either a few or no criteria were satisfied), as per the NICE [52] guidelines for risk of bias assessment.

1.4 Data extraction

A data extraction table was used to record authors, date of publication, country where the study was conducted, participants' information (sample sizes, mean age of sample at assessments), information on treatment status, study design, control group and follow-up (if applicable), QoL measures used, results, factors associated with QoL and conclusions. Separate tables were constructed differentiating depending on the QoL domain investigated.

1.5 Meta-analysis

Mental health-related QoL was used as the outcome of interest for the meta-analysis, as it was the most widely reported outcome and physical QoL is more sensitive to the effects of age [53]. The most frequently used QoL measures (e.g. SF-36, SF-12) do not calculate a total score but calculate separate composite scores for mental and physical health. Generic (i.e. not condition specific) mental health-QoL scores for all samples with means and Standard Deviations (SDs) reported were eligible for inclusion in the meta-analysis. When the means and SDs for a cisgender group were provided, these were used as the comparison in the meta-analysis. Where these were not available, normative data most applicable to the study country were obtained from the articles providing validation of the specific measures adopted and were used as comparison. Utilisation of normative data as a control might cause methodological concerns, as this might increase effect sizes; however, to not lose valuable data and to be able to carry out the meta-analyses, this method was deemed as the best approach. This approach was adopted for four studies [54–57].

In longitudinal studies, data from the first time point at which the participants met the age criterion for the review were used. Where studies reported incomplete results, values were either manually calculated (e.g. SDs from means) or authors were contacted to provide the missing data.

A second meta-analysis with a sub-group of studies reporting data for samples of participants who were exclusively post-GAGS, and therefore post-CHT, as the big majority of people undergoing gender affirming surgeries are already on hormonal treatment, was conducted. Pre-treatment-QoL was not assessed due to a lack of studies using exclusively pre-treatment samples. RevMan 5 [58] was utilised to conduct the meta-analyses.

It was hypothesised that the results would be heterogeneous because of differences between studies in the stages of transition investigated (e.g. mixed samples, pre-CHT, post-CHT, post-GAGS), in the diverse types of recruitment utilised (e.g. consecutive, snowballing), in the presence of clinical



and/or non-clinical individuals within the samples as well as in the focus onto the different gender identities of the participants (e.g. transman, transwoman, both). Consequently, Random Effects Models (RAM) with 95% confidence interval was used for the analyses as it implies that the selected studies are carried out in diverse populations [59]. I^2 statistics were calculated to examine heterogeneity, which is expressed in percentages suggesting different degrees of heterogeneity with 25% indicating low, 50% moderate and above 75% high [60]. Additionally, Q statistics were calculated to determine the statistical significance of heterogeneity [61].

1.6 QoL measures used in the review

See Table 2 for a description of the measures used in the studies to assess QoL. Voice-related QoL was assessed using the Voice Handicap Inventory (VHI) and the Transgender Self-Evaluation Questionnaire (TSEQ), sex-related QoL using the sexual subdomain of the WHOQOL-100 and the King's Health Questionnaire (KHQ), body image-related QoL using the body image-related subdomain of the WHOQOL-100 as well as the Body Image Quality of Life Inventory (BIQLI), and generic (non-condition specific) QoL was measured using the Short Form 36 Health Survey (SF-36), version 2 of the Short Form 36 Health Survey (SF-36-v2), version 2 of the Short Form 12 Health Survey (SF-36-v2), WHOQOL-100, WHOQOL-BREF, WHOQOL-BREF-TR or the Subjective Quality of Life Analysis (SQUALA). See Table 2 for a description of the measures.

2 Results

A total of 403 studies were identified through database searches, 288 through Ovid and 115 through PubMed. An additional 12 articles were selected for inclusion in the review after screening reference lists of relevant papers. After removing duplicates, 94 abstracts were screened by the first researcher (AN), which resulted in 43 studies that were read in full. Of these, fifteen were excluded due to reasons such as lack of a validated QoL measure (n = 4), of direct measurement of QoL (n = 6), of results reported specifically for transgender people (n = 4) and one study was qualitative. Finally, a sample of 29 papers was discussed, agreed with the other researchers (JA and CG) and included within this review. See Fig. 1 for description of the study's selection process.

2.1 Study characteristics

The earliest articles included within this review were published in 2006 [17, 87] whilst the most recent papers were published in 2017 [31, 32, 55, 57, 64].



The majority of the studies were conducted in European countries (n = 20). Three studies were carried out in Spain [21, 32, 34], in France [22, 23, 66] and in Belgium [43, 65, 83]. Two studies were conducted in Italy [73, 74], UK [69, 70], the Netherlands [20, 35] and Germany [31, 55], whilst one study was carried out in Switzerland [81], one in Sweden [64] and one in Turkey [76]. With regard to non-European countries one study was from Brazil [56], one from China [54] and the remaining articles were from the USA (n = 7).

Out of the 29 included articles; a) four explored vQoL [24, 30, 31, 83], b) four looked at sex-related OoL [34, 73, 74, 81], c) three assessed body image-related QoL [35, 73, 74], and e) 22 studies measured generic (non-condition specific) QoL [2, 17, 21-23, 42, 43, 54-57, 64-66, 68-71, 73, 74, 76, 81]. With regard to vQoL, the study by Mora and colleagues [32] measured vQoL with the aid of a non-validated measure as well as general QoL with a well-validated tool, thus the article was included in the subgroup of general QoL. The study conducted by Parola and colleagues [66] was excluded from the sex-related QoL domain, as it did not employ a validated measure to assess sex-related QoL. Studies reporting generic-QoL that either separated mental and psychological subscales or provided a total QoL score (e.g. Castellano et al. - 71) were included in the systematic review. Of the four papers that measured sex-related QoL, three used the sex-related facet of the WHOQOL-100 [34, 73, 74] whilst one paper measured QoL related to incontinency in transgender women post-GAGS and was included within the sexrelated QoL domain [81]. Finally, with regard to body image-related QoL, one article used a specific body image-related QoL measure (BIQLI) [35] whilst the others used the body image-facet of the WHOQOL-100 [73, 74].

In terms of study design, 22 studies were cross-sectional [17, 21–24, 30, 34, 42, 43, 54, 55, 57, 65, 66, 68–71, 73, 76, 81, 83] and seven were longitudinal [20, 31, 32, 35, 56, 64, 74], although three of the longitudinal studies [20, 31, 32] only reported cross-sectional data for QoL. Of the 29 included studies, eight compared scores of transgender people to normative data [17, 21, 34, 42, 43, 64, 65, 68], and eight compared transgender to cisgender individuals [21, 22, 30, 31, 69, 70, 74, 81] of which four studies used a matched comparison group [22, 69, 70, 74]. However for one matched study [70] the gender identity of the comparison group was unclear. Four articles compared QoL in transgender women to QoL in transgender men [23, 66, 76, 83]. The majority of studies (n = 23) recruited transgender people through clinical services [20-23, 30-32, 34, 35, 43, 55, 56, 64–66, 68–70, 73, 74, 76, 81, 83]. The remaining five studies recruited participants through opportunity sampling, word of mouth, flyers, advertisement and through community outreach [17, 42, 54, 57, 71].

Table 2	Quality	of life	measures	used	in	the review	

Measure Details 1. Short Form 36 Health This tool was developed to measure multiple operational health indicators of QoL [62]. It is Survey a well-validated international measure of health-related QoL consisting of 36-items SF-36 providing scores for two summary components (Physical and Mental), which encompass [62, 63]4 subdomains each. The Physical component includes Physical functioning, Role limitations related to Physical problems, Body pain, whilst the Mental component comprises of Perception of General health, Vitality, Social functioning, Role limitations due to Emotional problems, and Mental health. The scores range from a minimum of 0 until a maximum of 100, where higher scores indicate greater functioning and enhanced perception of QoL. The cut-off for the population norm is around 50. The measure was validated in a wide variety of clinical and non-clinical populations, and it displayed an internal consistency value of .88 when used with Transgender populations [63]. This tool was employed by six studies reported on within this review [43, 54, 55, 64–66]. This measure was developed out of the SF-36. It includes more up-to-date norms and QoL Short Form 36 Health Survey Version 2 SF-36v2 domains. It is a standardised, comprehensive and validated QoL measure assessing two [67] summary scores (Physical and Mental components), which encompass 4 subdomains each. The Physical component includes Physical functioning, Role-physical, Bodily pain, General health, whilst the Mental component comprises of Vitality, Social functioning, Role-emotional, and Mental health, It uses a 5-points Likert-scale ranging from 1 (poor/true) to 5 (excellent/false). Higher scores represent higher perceived QoL levels. This measure has also been used and corroborated in an online sample of transgender men displaying a Cronbach's alpha for reliability ranging from .93 to .95 [17]. This tool was employed by seven studies reported on within this review [17, 22, 42, 68-71]. 3. Short Form 12 Health Survey Version 2 This instrument is a subset of the SF-36. It comprises of two summary component scores SF-12v2 (Physical and Mental), which encompass 4 subdomains each. The former component [72] includes Physical functioning, Role-physical, Bodily pain, General health, whilst the latter component refers to Vitality, Social functioning, Role-emotional, and Mental health. This measure utilises a 5-points Likert-scale ranging from 1 (poor/true) to 5 (excellent/false). Scores range from 1 to 100, with higher perceived QoL represented by higher scores. This measure was validated and showed a good internal consistency, with Cronbach's alphas of .89 for the Physical component summary and of .86 for the Mental component summary [72]. This tool was employed by one study reported on within this review [32]. 4. WHOQOL-100 It is a self-administered, self-rated measure to assess QoL developed by the World Health Organization QoL group. It has been developed cross-culturally and it maintains excel-[39] lent psychometric properties and internal consistency. This tool comprises a total of 100-items; 96 measures 24 specific QoL facets, whilst the remaining 4-items estimate General QoL and Overall QoL. The facets are distributed across 6 domains, such as Physical health, Psychological health, Independence, Social relationships, Environment, and Spirituality/Religion/Personal beliefs. In order to investigate the Sexual QoL the specific Sexual activity facet was measured, whilst to examine Body image-related QoL the body image facet was assessed. Items are rated on a 5-points Likert-scale ranging from 1 (very poor/very dissatisfied/not at all) to 5 (very good/very satisfied/extremely). Higher scores indicate greater reported QoL. The scale's internal consistency values have been found to range between 0.65 and 0.93 [39]. This tool was employed by four studies within this review [34, 56, 73, 74]. WHOQOL-BREF It is a self-rated measure that has been validated in field studies involving approximately 30 [45] languages [27]. It is an abbreviated version of the WHOQOL-100. This tool has 26-items and uses a 5-points Likert-scale measuring 4 domains (Physical, Psychological, Social relationships, and Environment). In addition, there are two questions regarding General QoL and General health. Higher scores indicate greater QoL. Internal consistency values cross-culturally have been found ranging from .51 to .89 [45]. This tool was employed by three studies within this review [20, 21, 57]. The WHOQOL-BREF-TR is a 27-items 5-point Likert-scale measuring four domains 6. WHOQOL-BREF-TR (Physical, Mental, Social and Environmental) in two categories (Perceived QoL in [75] general and perceived health status). It displays acceptable psychometric properties

in this review [76].



when used on the Turkish population (Cronbach's alpha ranging from .53 to .83) [75]. This is the Turkish version of the WHOQOL-BREF and it was used by one study included

Table 2 (continued)					
Measure	Details				
7. Subjective Quality of Life Analysis SQUALA [77]	It is a self-administered, self-rated, multidimensional QoL measure. It covers 23 QoL domains (e.g. Mental well-being, Perceived health, Physical autonomy, Social relations, Environment) as well as general QoL-related concepts (e.g. justice, freedom, truth, beauty and politics), which identify internal and external reality of everyday life [78]. The measures' items need to be rated in importance and satisfaction by the person and higher scores indicate better QoL. Cronbach's alpha was not available. This measure was utilised by one study included within this review [23].				
8. King's Health Questionnaire KHQ [79]	This is a validated measure used to assess QoL, and with the aid of specific questions it is often used to estimate levels of incontinence related-QoL. This is a 29-items Likert-scale assessing ten domains (general health, physical limitations, personal limitations, social limitations, role limitations, personal relationships, emotion, symptom severity, sleep/energy and incontinence) and two categories (QoL and Limitation of daily life). The QoL category is measured with 20-items using a 4-points Likert-scale ranging from 1 (not at all) to 4 (a lot), whilst the incontinence category is measured with 9 items ranging from 1 (a little) to 3 (a lot). A change of 5 points is considered to be significant. It has been validated on a sample of urinary incontinent women with Cronbach's alpha values ranging from .73 to .89 [80]. This tool was employed by one study reported on within this review [81].				
9. Voice Handicap Inventory VHI [82]	This is a validated measure used to self-assess the QoL related to the relative impact of a person's voice upon daily activities. It is also used to measure QoL of transgender people concerning the impact and influence of their voices. The VHI is a 30-items 5-points Likert-scale ranging from 0 (never) to 4 (always). The items are regularly divided within three domains; functional (F), emotional (E) and Physical (P). The total score (T) is achieved by summing up E, F and P, and it ranges from 0 (normal voice) to 120 (severely affected voice). Scores below 40 represent either mild or absent disability, values between 40 and 60 reflect moderate disability, whilst scores above 60 represent disability. Internal consistency value was found to be .95 [82] This measure has been employed by four studies reported on within this review [24, 30, 31, 83].				
9.Transgender Self-Evaluation Questionnaire TSEQ [84]	This is a standardised, subjective measure of voice handicap and vQoL specifically developed for transgender people. It is based on the VHI but adapted to the specific concerns of transgender individuals, such as the impact of masculinity/femininity of voice. It is a 30-items self-reported 5-points Likert-scale ranging from 1 to 5. A total score ranging from 30 to 150 is calculated by adding up the 30 items' scores and lower scores reflect greater vQoL. The TSEQ was found to have good test-retest reliability (r = .97) [85]. Cronbach's alpha was not available. This tool was adopted by two studies reported on within this review [24, 30].				
11. Body Image Quality of Life Inventory BIQLI [86]	This is a 19-items 7-points Likert-scale ranging from -3 (very negative effect) to $+3$ (very positive effect) that assesses body image-related effects onto 19 different areas of life including sexuality and emotional well-being. Higher scores imply better body image-related QoL. Internal consistency was found to be excellent ($\alpha = .95$). This tool was used by one study included in this review [35].				

2.2 Risk of bias

Risk of bias was evaluated for the 29 studies according to the criteria stated in Table 1. Only three studies recruited more than 300 participants [17, 42, 71] and the majority either reported response rates lower than 70% or did not mention this information (n = 21) thus increasing the risk of sampling bias [17, 20, 23, 24, 30–32, 34, 35, 38, 42, 43, 54, 55, 64, 65, 68, 70, 74, 81, 83]. Overall, only two studies were rated having a low risk of bias [22, 69], twenty studies had a moderate risk of bias [17, 20, 21, 23, 34, 35, 42, 54–57, 64, 65, 70, 71, 73, 74, 76, 81, 83] and seven a high risk of bias [24, 30–32, 43, 66,

68]. See Table 3 for details regarding studies' quality assessment and risks of bias.

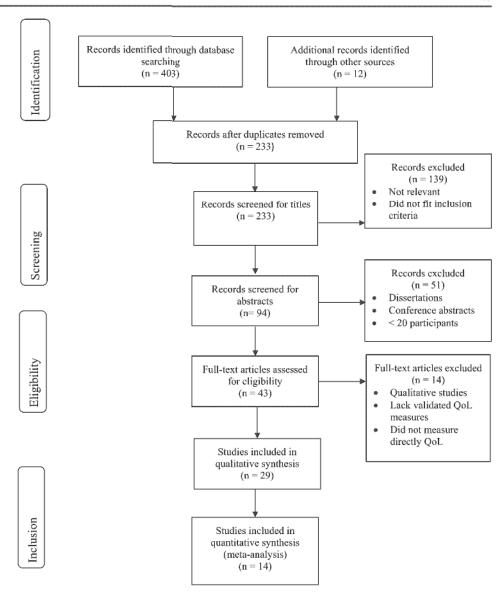
3 Results of the literature review

3.1 Voice-related QoL

Of the four papers describing vQoL, three used a cross-sectional design [24, 30, 83], whilst one article used a longitudinal design with cross-sectional data for vQoL [31]. There were no studies looking at pre-treatment transgender people.



Fig. 1 Process of identification of eligible studies for inclusion within the review



Only one study offered comparisons of transgender people post-treatment with normative data and reported worse vQoL for transgender people when compared to controls [31]. The cross-sectional studies that looked at people post-treatment (GAGS, CHT, Voice Feminisation Treatment -VFT) found transgender people to experience voice-related disability, in that they feel handicapped in everyday life because of their voice [31, 83]. This could be due to the fact that hormone therapy for transgender women had not affected on their voice. Only one study compared people according to their gender identity; this study by T'Sjoen and colleagues [83] found that transgender men report better vQoL compared to transgender women post-GAT. Overall, vQoL appears to be worse in transgender people, particularly in women, even post-GAT. See Table 4 for details.

The few studies investigating predictors of vQoL found increased age of the transgender individual, increased femininity of the voice [24] and low dihydrotestosterone as well as high Luteinising Hormone (LH) in the blood [83] to be factors predictive of a positive vQoL in populations of transgender women.

3.2 Sex-related QoL

Four studies investigated sex-related QoL by adopting a crosssectional design [34, 73, 74, 81]; one offered comparisons with normative data [34], one compared the transgender group with a cisgender group matched for experienced gender [73], one carried out comparisons between transgender men and transgender women as well as between pre- and post-CHT



Table 3 Risk of bias of studies included in the review

Source	Sample definition (Inclusion criteria)	Recruitment (Random, complete, consecutive)	Representativeness of Sample (Exclusion criteria and clinical/non-clinical populations)	Response rate (min 70%)	Sample Size (min 300)	Comparison	Use of validated measures	Quality rating
1,	0	1	0	1	1	1	0	+
Auer et al. (2017) [55] 2. Ainsworth & Spiegel (2010) [68]	1	1	1	1	1	1	0	-
3. Bartolucci et al. (2015) [34]	0	0	1	0	1	1	0	+
4. Başar et al. (2016) [76]	0	0	1	0	1	1	0	+
5. Bouman et al. (2016) [69] UK	0	1	0	0	1	0	0	++
6. Cardoso da Silva et al. (2016) [56]	0	0	1	0	1	1	0	+
7. Castellano et al. (2015) [73]	0	1	1	0	1	0	0	+
8. Colton Meier et al. (2011) [71]	1	1	0	1	0	1	0	+
9. Colton Meier et al. (2013) [42]	1	1	0	1	0	1	0	+
10. Davey et al. (2014) [70]	0	1	1	1	1	0	0	+
11. de Vries et al. (2014) [20]	0	0	1	1	1	1	0	+
12. Gomez-Gil et al. (2014) [21]	0	0	1	0	1	1	0	+
13. Gorin-Lazard et al. (2012) [22]	0	0	1	0	1	0	0	++
14. Gorin-Lazard et al. (2013) [23]	0	0	1	1	1	0	0	+
15. Hancock et al. (2011) [30]	0	1	1	1	1	1	0	-
16. Hancock et al. (2016) [24]	1	1	0	1	1	1	0	-
17. Hoy-Ellis et al. (2017) [57] USA	0	1	1	0	1	1	0	+
18. Kuhn et al. (2009) [81]	0	0	1	1	1	1	0	+
19. Lindqvist et al. (2017) [64] Sweden	1	0	0	1	1	0	0	+
20. Manieri et al. (2014) [74]	0	0	1	1	1	1	0	+



Table 3 (continued)

Source	Sample definition (Inclusion criteria)	Recruitment (Random, complete, consecutive)	Representativeness of Sample (Exclusion criteria and clinical/non- clinical populations)	Response rate (min 70%)	Sample Size (min 300)	Comparison	Use of validated measures	Quality rating
21. Meister et al. (2017) [31]	1	0	1	1	1	1	0	_
Germany 22. Mora et al. (2017) [32]	1	0	1	1	1	1	0	-
Spain 23. Motmans et al.	0	0	1	1	1	1	0	+
(2012) [65] 24. Newfield et al.	1	1	0	1	0	1	0	+
(2006) [17] 25. Parola et al. (2011) [66]	0	1	1	1	1	1	0	-
26. T'Sjoen et al. (2006) [83]	0	0	1	1	1	1	0	+
27. van de Grift et al.	0	0	1	1	1	1	0	+
(2016) [35] 28. Wierckx et al.	0	1	1	1	1	1	0	_
(2011) [43] 29. Yang et al. (2016) [54]	0	1	0	1	1	1	0	+

0 = No risk of Bias; 1 = Risk of Bias; ++ = Low Risk of bias; += Moderate Risk of Bias; -= High Risk of Bias

[74] and the fourth study compared QoL linked to incontinence in transgender people post-GAGS to twenty members of the clinical staff who underwent at least one previous abdominal or pelvic operation [81]. This last study was included within this section as it is linked to surgery outcomes and to satisfaction with sexual life.

Only one study looked at a transgender sample pre-GAGS and found that transgender people report worse sex-related QoL than the general population [34]. Studies including people post-GAGS suggested that transgender people still experienced lower sex-related QoL than their matched controls [73, 81]. When looking at gender differences, Castellano et al. [73] suggested that, at post-GAGS, transgender women did not display significantly different sex-related QoL compared to cisgender women, whilst transgender men showed lower sex-related QoL than cisgender men. Instead, studies comparing transgender people according to gender identity reported a significantly lower sex-related QoL in transgender men when compare to transgender women, independently of the transitional status [34, 73]. Only one study described changes in sex-related OoL using a longitudinal methodology [74]. This study found a significant improvement in sex-related QoL for both transgender men and transgender women post-CHT [74].

Overall, it appears that sex-related QoL improves post-GAT. However, such appears to be poor, particularly in transgender men when compared to cisgender men. See Table 5 for details.

Regarding predictors of sex-related QoL, CHT [34], low LH in the blood [73], having a partner and experiencing less negative mood symptoms [34] have been found to be factors associated with more positive sex-related QoL.

3.3 Body image-related QoL

Three papers described body image-related QoL, however none of these studies investigated QoL pre-GAT [35, 73, 74]. The cross-sectional study conducted by Castellano et al. [73] found no difference in body image-related QoL between the transgender sample post-medical treatments and a matched cisgender sample. The two longitudinal studies reported an improvement in body image-related QoL after treatment, specifically after CHT [74] and mastectomy for transgender men [35]. This suggests that gender affirming treatments are of benefit to body image-related QoL in transgender samples. The limited research in this area shows that body image related QoL improves post-GAT. See Table 6 for details.

Table 4 Studies investigating voice-related quality of life in transgender people (n=4)

Authors (year) Country	Number of Trans participants, mean age at assessment	Treatment status	Study design	Comparative groups, follow-up	Outcome measures	Results	Factors	Conclusions
Hancock et al. (2011) [30] USA	20 TW 48.8 yrs	Post-VFT 100% Post-GAGS 45%	Single centre Clinical group Cross-sectional	CG1 Speakers: 5 cis women (46.8 yrs) 5 cis men (40.8 yrs); CG2 Listeners: 12 cis men (18.8 yrs) 13 cis women (19.65 yrs) (No follow-up)	TSEQ	Self-ratings: Femininity = 529 Likability = 552 Listener ratings: Femininity = 493 Likability = 533	None studied	For TW vQoL moderately correlated with how others perceive their voice. vQoL correlated more strongly with speaker's perception of voice compared with others' perceptions
Hancock (2016) [24] USA	81 TW 43 yrs	VFT 46%	Clinical and non-clinical group Cross-sectional	Online vs. paper Completed VHI vs. completed VHI + TSEQ (No follow-up)	VHI TSEQ	General: VHI = 37.5 TSEQ = 76.5 VHI + TSEQ: VHI = 37.6 TSEO = 76.5	-vQoL.: Increased age Femininity of voice	TW reported a wide range of vQoL; some individuals are severely affected by their voices whilst others are not
Meister et al. (2017) [31] Germany	T0 21 TW 42.1 yrs. T1 18 TW 46 yrs	T0 = Pre-VFT 100% T1 = Post-VFT 100%	Single centre Clinical group Prospective longitudinal with cross-sectional data	T0 vs T1 German control group	АНІ	VHI _{mean} = 32,29 None studied	None studied	Despite the elevation of vocal pitch, elevated VHI scores indicate transwomen feel handicapped in everyday life because of their voice.
T'Sjoen et al. (2006) [83] Belgium	28 TW 20 TM 33 yrs. TW 49 yrs. TM	GAGS 100% CHT 100%	Single centre Clinical group Cross-sectional	TW vs. TM (No follow-up)	VHI	TW: Total = $4(0-10)$ (F = 1, E = 0, P = 3, Phone = 0) TW: Total = 12 (6-31) (F = 1, E = 2, P = 6, Phone = 2)	TM + vQoL: Lower DHT Higher LH	Better vQoL for both TW and TM above the cut-off for disability, meaning that they do experience voice-related disability

CG Control Group, CHT Cross-sex Hormonal Treatment, Cis Cisgender, DHT Dihydrotestosterone, E Emotional, F Functional, FFS Face Feminisation Surgery, GAGS Gender Confirming Genital Surgery, LH Luteinizing Hormone, P Physical, TM Transgender men, TW Transgender women, VFT Voice Feminisation Treatment

limitation than the cis Pre-GAGS about half of perceived sexual QoL as either poor or very poor compared to the QoL is lower for trans people in domains of TW reported significant levels of QoL similar Physical and Personal General health, Role, Trans people reported 15-years post-GAGS sexual and general improvement in to cis controls control group control group trans sample QoL 1 year post-CHT Conclusions Factors associated Having a partner Less negative None studied None studied feelings Lower LH + sQoL: CHT +0°F; KHQ = 27.31sQoL = 62.05sQoL = 50.25poor 48% poor 54% FW = 65.85Good 27% Very good $\Gamma M = 54.21$ Good 23% Very good Poor/very Poor/very 20% 28% Results SOOLSOOLΙM: ΪЩ Σ. WHOQOL-100 WHOQOL-100 WHOQOL-100 measures Outcome KHQ 20 healthy female control sample medical staff, Normative data 60 matched cis Pre- vs. during (No follow-up) (No follow-up) (No follow-up) not matched Comparative follow-up CHT groups, Cross-sectional Cross-sectional Cross-sectional Clinical group Clinical group Clinical group longitudinal Clinical group Single centre Single centre Single centre Study design Single centre Studies investigating sex-related quality of life in transgender people (n = 4)Prospective F0 = initiation of CHT 100% T1 = 3 months post-CHT T2 = 6 months post-CHT Pre-GAGS 100% + 2 years post-GAGS 100% Treatment status Post-CRS 30% GAGS 100% CHT 100% CHT 100% CHT 40% FM 28%) TW 46% (TW 35% (M 19%) Frans participants, 31.46 yrs. TW 28.69 yrs. TM 30.2 yrs. TM 52 TW 32.7 yrs. TW 32.7 yrs. TW 51 yrs. Trans 30.2 yrs. TM DSM-IV-TR mean age at assessment 46 TW 14 TM ML 78 36 TM 26 TW 27 TM 3 TM Kuhn et al. (2009) Castellano et al. Bartolucci et al. Manieri et al. (2015) [73] Switzerland (2015)[34](2014) [74] Table 5 Authors Country <u>~</u> (year) Spain [taly [taly

BI Body Image, CHT Cross-sex Hormonal Treatment, Cis Cisgender, CRS Chest Reconstructive Surgery, GAGS Gender Confirming Genital Surgery, LH Luteinizing Hormone, sQoL Sexual QoL, SR Social Relationships, TM Transgender men, TW Transgender women

14=1 year post-CHT 100%

 $\Gamma 3 = 9$ months post-CHT

100%

Table 6 Studies investigating body image-related quality of life in transgender people (n=3)

Authors (year) Country	Number of Trans Treatment status participants, mean age at assessment	Treatment status	Study design	Comparative groups, follow-up	Outcome measures Results	Results	Factors associated Conclusions	Conclusions
Castellano et al. (2015) [73] Italy	46 TW 14 TM 32.7 yrs. TW 30.2 vrs. TM	+ 2 years post-GAGS 100% CHT 100%	Single centre Clinical group Cross-sectional	60 matched cis control sample WHOQOL-100 (No follow-up)	WHOQOL-100	BodyQoL TW = 64.64 TM = 67.91	+QoL: Lower LH	Trans people reported levels of QoL similar to cis controls
Manieri et al. (2014) [74] Italy	56 TW 27 TM 32.7 yrs. TW 30.2 yrs. TM	T0 = initiation of CHT 100% T1 = 3 months post-CHT 100% T2 = 6 months post-CHT 100% T3 = 9 months post-CHT 100% T4 = 1 year post-CHT 100%	Single centre Clinical group Prospective longitudinal	Pre- vs. during CHT	WHOQOL-100	T4 TW: BI=21.85 TM: BI=68.75	None studied	TW reported significant improvement in sexual and general QoL 1 year post-CHT
van de Grift et al. 26 TM (2016) [34] 26.1 yr The Netherlands	26.1 yrs	T0: CHT 100% T1: CRS 100% CHT 100%	Single centre Clinical group Prospective longitudinal	Single centre Pre- vs. post-CRS Clinical group (T0 = baseline Prospective longitudinal T1 = 6 months after CRS)	відсі	Pro-CRS = 0.32 Post-CRS = 0.38	Pro-CRS = 0.32 +QoL: Post-CRS = 0.38 Body satisfaction Feelings of "passing" in social situations	Body satisfaction and "passing" in social situations are associated with higher QoL and self-esteem in TM

BI Body Image, Body QoL Body image-related quality of life, CHT Cross-sex Hormonal Treatment, Cis Cisgender, CRS Chest Reconstructive Surgery, GAGS Gender Confirming Genital Surgery, LH Lutcinizing Hormone, sQoL Sexual QoL, SR Social Relationships, TM Transgender men, TW Transgender women, VFT Voice Feminisation Treatment

Only one study looked at factors associated to body image quality of life and found low levels of LH in the blood to be associated to a positive body image-related QoL [73].

3.4 General (non-condition specific) QoL

Out of the 22 studies that assessed generic (non-condition specific) QoL, there were no cross-sectional studies looking specifically at people pre-GAT. Five studies investigated post-GAT [20, 43, 66, 68, 73], twelve were mixed in term of treatment status [17, 21–23, 42, 54, 55, 65, 69–71, 76], three were longitudinal [56, 64, 74], one did not report information on treatment status [57] and one study reported only that participants were pre-facial feminisation treatment [32].

There is pre-CHT data available from the longitudinal studies showing that transgender people have lower QoL than the general population [56, 74]. Of the six cross-sectional studies looking specifically at people pre-GAGS [21–23, 54, 68, 71], two studies found transgender people to report poorer QoL than the general population [21, 68] and one found similar scores to their matched cisgender controls [22]. The remaining studies did not include comparisons with the general population but they suggested that transgender people report poor QoL.

Five studies investigated QoL at post-GAGS; four studies found that transgender people at this stage still report lower QoL than the general population [43, 66, 68] whilst two studies suggested transgender people to display similar QoL to the general population [20, 73].

With regard to mixed samples, one study suggested transgender people report worse QoL than their matched cisgender controls [69], two reported poorer QoL than the cisgender non-matched controls [21, 70] and one study suggested worse QoL than the general population [65]. Studies looking at people according to their gender found that some of the results regarding QoL in transgender men were contradictory; one study indicated that they suffer from worse QoL than the general population [17] whilst another study suggested the opposite [42]. Transgender men were also found to report a better QoL when undergoing CHT than when not on hormones [71]. Instead, transgender women displayed high physical healthrelated OoL and poor mental-health related OoL [54]. The remaining three mixed sample studies made comparisons between transgender men and transgender women, and the results are inconsistent. Two studies found that transgender women report better QoL than transgender men [23, 76] and one found no difference between transgender men and transgender women [55]. In another mixed study, Motmans and colleagues [65] found that transgender men had worse QoL than the cisgender population. However the results of the above mixed sample studies need to be interpreted carefully.

Regarding the three longitudinal studies [56, 64, 74], one found an improvement in QoL 1-year post-CHT when compared to pre-CHT levels [74]. A different study also found an

improvement in transgender women 1-year post-GAGS when compare to pre-CHT values [56]. The third study compared QoL pre-GAGS (on CHT) and 1, 3 and 5-years post-GAGS. This study found that although QoL pre-GAGS was lower than the general population it improves 1-year post-GAGS. However the study also found that it reduces 3 years post-GAGS and even more 5 years after genital surgery. This could be explained as the first year post-GAGS is often known as the "honeymoon period" and people tend to report overly enhanced QoL, which are not representative of a long-term picture of patients' psychological status and QoL [43]. When investigating longitudinal results according to gender a study found that transgender women displayed greater improvements in QoL 1-year post-CHT compared to transgender men [74].

Overall, the studies investigating general QoL in transgender people found poorer QoL pre-GAT than the general population, which improve after GAT in the short term. See Table 7 for details.

Medical and surgical treatments (i.e. CHT, CRS, GAGS) [17, 21–23, 56, 66, 68, 71], post-surgical well-being [20] and sexual functioning [43], presence of social and family support [21, 42, 55, 70, 77], decreased depression, anxiety and stress levels [42, 55], lack of chronic pain symptomatology [55], hope and resilience [54], high self-esteem and low levels of interpersonal issues [69], lack of identity stigma [57], having a good body image and good sleep quality [55], low levels of LH in the blood [73] as well as being employed and in a relationship, younger age, higher education, a high household income [65] and having undergone military service [57] were found to be factors predictive of a positive QoL.

4 Results of the meta-analysis

4.1 Meta-analysis – Mental health-related QoL of transgender people compared to the general population

Measurements of QoL provide information regarding physical and mental health-related QoL but only a minority of studies looked at physical health-related QoL; therefore the meta-analysis focused on mental health-related QoL compared to those of the general population. Of the 22 studies assessing general QoL in transgender populations, 14 were considered suitable for inclusion in the meta-analysis [17, 20–22, 43, 54–57, 64, 65, 68–70]. These studies include people pre-GAT, post-GAT and mixed groups at different stages of medical transition. Studies were excluded from meta-analysis due to the absence of the mean, SD and/or sample size [66, 74], mental health quality of life not reported separately [73], insufficient detail about scoring [32, 42, 71] and the lack of access to appropriate normative data [23, 76]. Data at pre-

treatment were utilised for the two longitudinal studies included in the meta-analysis [56, 64]. Additionally, normative data as comparison was obtained for four studies [54–57].

The results of the meta-analysis (14 studies) showed that transgender people report a statistically significantly lower mental health-related QoL than the general population (standard mean difference – 0.78, 95% CI = -1.08 to –0.48, Z = 5.16, p < 0.00001). Heterogeneity was high ($I^2 = 97\%$, p < 0.00001) (see Fig. 2).

4.2 Meta-analysis – Subgroup analysis – Mental health-related QoL post-hormonal treatment of transgender people compared to the general population

A second meta-analysis was conducted with only the 7 studies that included exclusively post-treatment QoL scores [20, 43, 56, 64, 65, 68, 70]. The longitudinal study of Lindqvist et al. [64] investigated QoL post-GAGS but as the first time measurement was pre-GAGS and thus post-CHT, this measure was included in this analysis. Whilst for the longitudinal study of de Vries et al. [20], values at the latest time-point were used, as they measured QoL post-CHT in a sample of individuals older than 17 years of age.

The meta-analysis of 7 studies found that there was no statistically significant difference in mental –health related QoL of transgender people following CHT compared to the general population (standard mean difference = -0.42 CI 95% = -1.15 to 0.31; Z = 1.13; p = 0.26). Heterogeneity was high ($I^2 = 98\%$; p < 0.00001) (see Fig. 3).

5 Discussion

The aim of this study was to systematically and critically review the literature pertaining to quality of life in transgender people, to meta-analytically investigate mental-health related QoL compared to cisgender populations and to investigate the impact of GAT on the QoL of this population. A total of 29 studies met the inclusion criteria and were used for the systematic review and, of these, 14 studies were suitable for including in the meta-analysis. Most papers in this area investigated general QoL and only a few focused on either vQoL, sex-related QoL or body image-related QoL. The majority of these articles displayed either high or moderate risk of bias. Many studies used transgender samples that are not homogeneous in terms of gender affirming medical treatment status, which makes it difficult to draw firm conclusions about the impact of GAT.

Findings from the meta-analysis of mental health-related QoL suggest that the QoL of transgender people is significantly poorer than that of the general population, with a medium to large effect size (standard mean difference = 0.78). The

improved mental health

in TM

CHT is associated with

+0°F;

SF-36-v2

CHT vs. No CHT

(No follow-up)

Cross-sectional

Online

CHT 66% CRS 41%

32.7 yrs. TW 30.2 yrs. TM 369 TM

28 yrs

Colton Meier et al.

(2011) [71]

USA

14 TM

(2015) [73]

control sample

Clinical group Cross-sectional

post-GAGS 100% CHT 100%

(No follow-up)

CHT

No CHT = 53.7

Trans = 61.3CHT = 65.2

TM displayed higher QoL

levels than the norm

Depression

+0oT:

AM = 58.85AW = 64.77

SF-36-v2

AM vs. AW vs. AB

Normative data (No follow-up)

Cross-sectional

Online

CHT 67% CRS 41%

581 TM 27 years

Colton Meier et al.

(2013) [42]

USA

GAGS 4%

AB = 60.81

Anxiety

levels of QoL similar to

Lower LH

cis controls

mQoL compared to the relationships, but 1-year TW have lower QoL than Substantial portion of low OoL in trans is due to physical health and inbetween TW and TM. Trans people have lower Dutch general female psychological aspects post-GAGS TW still report problems with chronic pain in TM Trans people reported poor sleep quality, anxiety in TW and discrimination and of QoL and social statistically differ improvement of OoL levels did not Perceived personal social support predicted QoL GAGS promotes dependence Conclusions population cis group -Chronic pain (TM) +Body image (TW) Interpersonal issues Surgical treatments (too dependent) +Social support -Anxiety (TW) Discrimination +Sleep quality Social support symptoms -Depressive associated Self-esteem Factors mQoL: +0oF: GAGS -----+QoL: -0°F: MCS = 77.66TW = 67.87TM = 69.21CG1 = 50CG2 = 49.3MCS = 70.9CG4 = 39.5T1 = 14.77T2 = 15.52CG3 = 49.2WHOQOL-BREF-TR TW = 15.3 TM = 12.7 Results Outcome measures WHOQOL-100 WHOQOL-100 SF-36-v2 SF-36-v2 SF-36 Pre- vs. post-GAGS CG3 = FFS + GAGS groups, follow-up CG2 = GAGS only $\Gamma 2 = at least 1 year$ CG4 = No surgery control sample TW vs. TM (No follow- up) CG1 = FFS only 140 matched cis population (No follow-up) post-GAGS) (No follow-up) 60 matched cis (No follow-up) CG5 = General (T1 = baseline Comparative Studies investigating general quality of life in transgender people (n = 22)Multicentre (4 sites) Cross-sectional Cross-sectional Cross-sectional longitudinal Study design Clinical group Clinical group Clinical group Clinical group Clinical group Single centre Single centre Single centre Single centre Prospective post-GAGS 100% programme 100% 28 FFS (CHT 86%) 20.8% TM; GAGS: 17.3% Post-GCGS Treatment status Pre-GAGS 79.5% Pre-GAGS 72.2% T2 at least 1 year Assessment 6.7% T1 at enfrance to 47 FFS + GAGS 25 GAGS (CHT 147 no surgery (CHT 27%) Pre-CRS 56.9% (CHI 98%) CHT 79.3% CHT 80.6% CHT 78.8% 54.5% TW 36.4% TW 12.5% TM 100%) CHI Number of Trans participants, mean age at assessment 25 GAGS (50 yrs) 247 TW 28 FFS (51 yrs) 47 FFS + GAGS 28 FFS (51 yrs) 147 No surgery 27.73 yrs. TW 26.82 yrs. TM DMS-IV-TR (49 yrs) (46 yrs) 21.23 yrs. 36.52 yrs DSM-V 64 TW 47 TW 46 TW 72 TM 22 TW 72 TM 40 TM 82 TW Başar et al. (2016) [76] Aucr et al. (2017) [55] Ainsworth & Spicgel et al. (2016) [56] Cardoso da Silva Castellano et al. (2010) [68] Bouman et al. (2016) [69] Germany Table 7 Authors Country (year)

Table 7 (continued)								
Authors (year) Country	Number of Trans participants, mean age at assessment	Treatment status	Study design	Comparative groups, follow-up	Outcome measures	Results	Factors associated	Conclusions
Davey et al. (2014) [70] UK	63 TW 40 TM 56.9 yrs. TW 28.05 yrs. TM	TW: Post-GAGS 17.5% CHT currently 79.4% TM: Post-GAGS 15% CHT currently 70.4%	Single centre Clinical group Cross-sectional	Matched cis control sample No follow-up	SF-36-v2	MCS = 69.31	- Stress + Social Support + MCS, VT, SF QoL: Social support	Trans clinical sample reported lower QoL than matched cis sample
de Vries et al. (2014) [20] The Netherlands	22 TW 33 TM TW: T0 = 13.6 yrs. T1 = 16.5 yrs. T2 = 21 yrs. TM: TM: T0 = 13.7 yrs. T1 = 16.8 yrs.	Chricumony 070 T0 = pre-puberty suppression T1 = post CHT T2 = 1 year post-GAGS	Single centre Clinical group Prospective longitudinal with cross-sectional data re- garding QoL	T0 vs. T1 vs. T2 Participants vs. nonparticipants (T0 = pre-puberty suppression T1 = when CHT introduced T2 = 1 year post-GAGS)	WHOQOL-BREF	T2 pQoL = 14.66	+pQoL: Post-surgical well-being	Well-being in trans same or emhanced compared to same-age general population young adults
Gomcz-Gil et al. (2014) [21] Spain	119 TW 74 TM ICD-10 31.2 yrs. Tans	CHT 62.2% No CHT 37.8%	Single centre Clinical group Cross-sectional	101 cis people (No follow-up)	WHOQOL-BREF	pQoL = 56.09	+QoL: CHT Family support Working/studying	Trans reported lower perceived QoL compared to the cis sample. Additionally, TM reported higher code of the area of the perceived of the area TW.
Gorin-Lazard et al. (2012) [22] France	31 TW 30 TM 39.4 yrs. TW 29.9 yrs. TM	No CHT: TW 19.4% TM 36.7% CHT: TW 80.6%	Multicentre (3 sites) Clinical group Cross-sectional	French age- and sex-matched con- trol Normative data (No follow-up)	SF-36-v2	MCS = 47.92	+ mQoL: CHT - mQoL: Depression	social you usu 1 w Positive effect of CHT on Qol., Trans QoL did not differ from cis matched controls except for RP
Gorin-Lazard et al. (2013) [23] France	36TW 31 TM 35.1 yrs. Trans	IM 05.2% TW 38.9% TM 61.1% CHT: TW 59.2%	Multicentre (3 sites) Clinical group Cross-sectional	TW vs. TM CHT vs. No CHT (No follow-up)	SQUALA	TW = 12.1 TM = 11.34 Total = 11.72	+ pQoL: CHT	CHT predicted positive self-esteem, less severe depression, and greater psychological dimensions of QoL
Hoy-Ellis et al. (2017) [57] USA	84 TW 51 TM 48 Other 46.88 yrs. TW 27.48 yrs. TM 25.64 yrs. Other	None reported	Online and/or paper Non-clinical group Cross-sectional	Military service vs No military service (No follow-up)	WHOQOL-BREF	pQoL = 64.12	-pQoL: Identity stigma +pQoL: Prior military scrvice	Those with prior military service had lower depressive symptomatology and higher pQoL
Lindqvist et al. (2017) [64] Sweden	7.57 yrs. Out. 11 = 108 TW 12 = 64 TW 13 = 43 TW 36 yrs	T0 = pre-GAGS + CHT 100% T1 = 1 yr. post-GAGS 100%	Single centre Clinical group Prospective longitudinal	T0 vs T1 vs T2 vs T3 Swedish normative data	SF-36	MCS: T0 = 73.8 T1 = 74.1 T2 = 71 T3 = 67.6	None studied	TW (both pre and post-GAGS) reported lower QoL than general population; GAGS improves QoL 1 year

Authors (vear)	M1 6.T.	The them can be obtained				n		
Country	number of trans participants, mean age at assessment	reatment status	Study design	Comparative groups, follow-up	Outcome measures	Kesuits	Factors associated	Conclusions
		T2 = 3 yrs. post-GAGS 100% T3 = 5 yrs. post-GAGS						post-GAGS but it tends to gradually diminish over time
Manieri et al. (2014) [74] Italy	56 TW 27 TM 32.7 yrs. TW 30.2 yrs. TM	70 = initiation of CHT 100% T1 = 3 months post CHT 100% T2 = 6 months post-CHT 100% T3 = 9 months post-CHT 100% T4 = 1 year post-CHT 100%	Single centre Clinical group Prospective longitudinal	Pre- vs. during CHT	WHOQOL-100	74 TW: QoL = 63.25 TM: QoL = 72.2	None studied	TW reported significant improvement in sexual and general QoL 1 year post-CHT
Mora et al. (2017) [32] Spain	T0 = 30 TW T1 = 18 TW 30 yrs	Pre-FFS 100%	Single centre Clinical group Prospective longitudinal with cross-sectional data re- gardine SF12v2	None (No follow-up)	SF-12v2	MCS = 48.63	None studied	Trans women suffer poor QoL
Momans et al. (2011) [65] Belgium	63 TW 58 TM 42.26 yrs. TW 37.03 yrs. TM	TW: CHT 94.6% EFS 18.7% GAGS 64% TM: CHT 96.7% GAGS 67.8%	Cinical group Cross-sectional	Normative data (No follow-up)	SF-36	MCS = 72.04	+Qot.: Being Employed Being in a Relationship Young age, Higher Education Higher household	TM reported reduced mQoL than Dutch male sample. Older, low educated, unemployed, with a low household income and single trans people had eimificantly housey Ord
Newfield et al. (2006) [17] USA	376 TM 32.6 yrs	CHT 64% CRS 37% GAGS 11%	Opportunity sampling Cross-sectional	Normative data (No follow-up)	SF-36-v2	MCS = 39.51	+ QoL: Testosterone Usage CRS	Significating towar con- reported significantly lower mental health-related QoL than TS general recondition
Parola et al. (2010) [66] France	32-65 yrs. range	+2 years CHT and GAGS 100%	Single centre Clinical group Cross-sectional	TW vs. TM; Extraversion vs. Introversion; Neuroticism vs. Emotional stability (No follow-up)	SF-36	TW: Better Social QoL = 11/15 people Better Quality of family relationships = 4/15 people TM: Better Social QoL = 10/15 people Better Quality of family relationships =	+QoL: CHT	Os genera population TM reported better social and professional QoL, and friendly lifestyles than TW

Authors Number of Trans Treatment status Study design Comparative Outcome measing groups, follow-up age at assessment	Table 7 (continued)	(par						
	Authors (year) Country	Number of Trans participants, mean age at assessment	Treatment status	Study design	Comparative groups, follow-up	Outcome measures Results	Es Factors associated	Conclusions
						Extrov	Extroverted = 54.28	

	TM have good QoL post-GAGS compared to general Dutch popu- lation but still lower than the normative data	Chinese TW reported high levels of physical QoL but low levels of mental QoL
2 88	QoL: Post-operative sexual functioning	mQoL: Hope Resilience PhQoL: -Lowcr agc
Extroverted = 54.28 Introverted = 52.02 High neuroticism = 53.16 Low neuroticism = 53.16	MCS = 75.8	MCS = 68.28
	lata SF-36	SF-36
	Dutch normative data SF-36 (No follow-up)	None (No follow-up)
	Single centre Clinical group Cross-sectional	Non-clinical group Cross-sectional
	Post-GAGS 100% CHT 100%	FFS 34,93% CHT 17.70%
	49 TM 37 yrs	4] 209 TW 26.7 yrs
	Wierckx et al. (2011) [43] Belgium	Yang et al. (2016) [54] 209 TW China 26.7 yrs

AB Attracted to Both, AM Attracted to Women, BI Body Image, CG Control Group, CHT Cross-sex Hormonal Treatment, Cis Cisgender, CRS Chest Reconstructive Surgery, FFS Face Feminisation Surgery, GAGS Gender Confirming Genital Surgery, hQoL Health-related QoL, LH Luteinizing Hormone, MCS Mental Component Score, mQoL Mental health-related QoL, pQoL Psychological QoL, pAoL Psychological QoL, Physical, SF Social Functioning, sQoL Sexual QoL, SR Social Relationships, TM Transgender men, TW Transgender women, VT Vitality

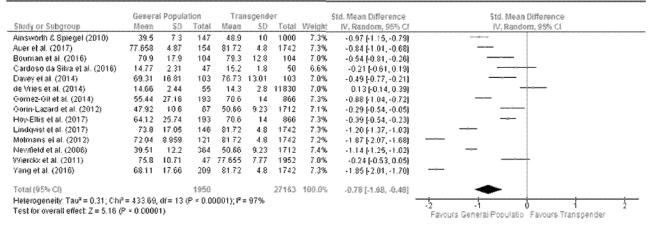


Fig. 2 Meta-analysis on mental health-related QoL of transgender people compared to the general population

subgroup meta-analysis including only the samples of transgender people who were classifiable as post-hormonal treatment found that transgender people post-CHT still had lower mental health-related QoL than the general population. This difference was not significant and the effect size was reduced (standard mean difference = 0.42). The possibility that treatment is associated with improvements in mental wellbeing is supported by the findings from the small number of longitudinal studies in this review. These found that both CHT and GAGS improve QoL [56, 64, 74]. However these results need to be treated with caution, as the only study to employ a longer term follow-up [64] reported that after an initial improvement in QoL at 1-year post-GAGS, scores tend to steadily decrease in the following years until reaching 5-years post-GAGS, when QoL is lower than at pre-treatment [64]. During the first year post-GAGS people tend to report overly enhanced QoL, which may not be representative of a long-term picture of patients' psychological status and QoL [43]. The improvement in QoL experienced by transgender people at shortterm could be attributed to relief at being able to live as the experienced gender. Additionally, as QoL in the general population has been shown to decrease with age [53], a decline in these scores is somewhat expected as time passes.

In contrast, the small number of studies that explore general physical health-related QoL suggest that at post-GAT, transgender people's reported QoL scores either similar to [22] or better than that found in the general population [17, 43].

However, only a minority of studies report findings related to physical health-related QoL and it is difficult to draw accurate conclusions.

5.1 Condition specific QoL

When looking at condition-specific QoL, studies investigating vQoL reported that CHT has been shown to have a positive impact on transgender men. This is not surprising, as testosterone is known to affect voice by thickening vocal chords and by decreasing the pitch [87]. On the other hand, studies in transgender women, including post-voice feminising surgery, found that they still feel handicapped regarding their voice in their everyday life, irrespective of the transitional status. In fact, studies have suggested that the more feminine a transgender person perceives her own voice, the higher the experienced vQoL [30, 31]. However, these studies are limited by focusing on transgender women who transitioned post-puberty. This means that by the time they initiated physical transition, testosterone has already negatively altered their voice. Thus findings from vQoL cannot be generalised to the overall transgender population. Future studies should explore differences in vQoL between those who transitioned pre-puberty and therefore before the breaking of the voice, and those who transitioned post-puberty, when the voice has already been affected.

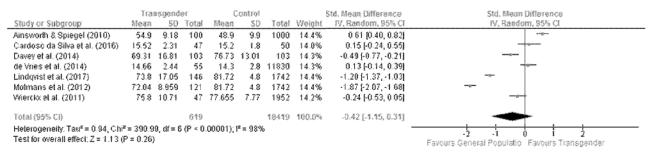


Fig. 3 Meta-analysis on mental health-related QoL transgender people post-hormonal treatment compared to the general population



Regarding sex-related QoL, longitudinal studies suggest that undergoing GAT improves sex-related QoL [74] but the QoL of transgender men post-GAGS is still worse than that of cisgender men. However, the articles investigating sex-related QoL in transgender men did not distinguish whether patients underwent phalloplasty or metoidioplasty. Surgical treatments help the transgender person reach the desired physical changes and lead towards a more congruous body with their gender identity. This may lead to people feeling more comfortable with their own bodies and consequently when being intimate with others.

Longitudinal studies also supported an amelioration in body image-related QoL [35, 74]. In fact, Castellano and colleagues [73] reported no difference between the transgender population and their matched controls. This could be due to the fact that people undergoing GAGS are generally already on CHT and hormonal treatment is known to have a positive effect on body image [10, 36, 88] by aiding in the development of desired secondary sexual characteristics of the experienced gender, whilst helping to alter some of the attributes relative to the sex assigned at birth. Consequently, this leads to an improvement in body image-related QoL. Nonetheless, van de Grift et al. [35] proposed body image-related QoL to be lower for transgender people post-CRS, than for the general population. This might be caused by the fact that following CRS, some people's genital dysphoria may increase. However, caution is still needed when generalising the findings due to the studies' moderate risk of bias as well as their methodological limitations.

5.2 General QoL

Studies regarding general QoL have found that transgender people's QoL is poorer than that of cisgender people, but that it improves post-GAT. The poorer QoL found in the transgender population pre-CHT [56, 74] could be explained by the high degree of mental health problems reported in this population [16, 89] as well as by the difficulties that many have in socialising and living a fulfilling life [10–12, 37]. However, the studies that focus only on people pre-CHT were rare and only included those seeking medical transition, which does not allow for a generalisation of these findings to the general transgender population.

When looking at general QoL post-GAT, only a small number of studies provided control data and none of them had a low risk of bias. Findings of the subgroup meta-analysis at post-treatment showed that there is no difference in general QoL between transgender people and the general population. The improvement in QoL post-GAT could be due to the effect of treatment in the reduction of dysphoria and mental health problems, such as self-harm and depression [13, 90].

Overall, findings support the idea that QoL improves following hormonal treatment [74] as well as post-genital surgeries [43, 56]. As people undergoing surgery are generally already on hormones, the exact role of genital surgery in QoL cannot be extrapolated from these studies. Often, even after an

improvement in QoL post-surgical treatment, transgender people reported lower QoL compared to cisgender individuals [7, 56, 64, 70]. This could be due to the fact that, even if being happier with their own bodies, society is still not ready to accept transgender people; thus work, education or relationships can be affected by being transgender [6, 91, 92]. This is confirmed by the findings of studies investigating factors predictive of QoL in this population, as described in the section below.

Caution is needed while interpreting the results in comparison to cisgender individuals as not all studies have matched controls and sample sizes are generally small. Additionally, as the majority of the studies investigated QoL in transgender clinical populations, generalisation of findings for the general transgender population is hindered.

Studies on differences between transgender men and transgender women advance contrasting results. Two studies seemed to suggest that transgender men display lower QoL compared to transgender women [23, 76], two studies suggested the opposite [21, 66], whilst one study proposed no statistically significant differences between groups [55]. Literature also suggested that at 2-years post-treatment transgender men display higher QoL than transgender women [66], whilst still lower than cisgender people [73]. These findings might be due to baseline differences in QoL scores [65] as well as because of the utilisation of mixed samples in terms of treatment status. Results need to be interpreted with caution as none of the articles displayed a low risk of bias. A possible explanation for transgender men to report higher QoL than transgender women might be due to the wider social acceptance towards masculinity than femininity. This presents itself with transgender men reporting less marked psychopathology, getting involved more easily in society and being employed in more stable jobs, whilst feeling less limitations in daily life related to their physical and emotional state [21, 66]. Additionally, studies that reported transgender women to display higher QoL than transgender men suggested that these findings are unexpected and surprising [76] considering the low social status of and amount of discrimination faced by transgender women in some countries (e.g. Turkey).

5.3 Factors associated with OoL

QoL can be influenced by a wide array of factors, which can predict both its increment, as well as its decline. Literature looking at variables associated with a positive QoL for transgender people suggested that undergoing medical and surgical treatments (i.e. CHT, CRS, GAGS) are the main predictive factors, irrespective of the QoL domain studied [17, 21–23, 34, 66, 68, 71]. These findings were confirmed by longitudinal studies, which indicated an improvement in QoL from preto post-treatment [35, 56, 74].

Additionally, social and family support, being employed, being in a relationship, being younger, having a partner, being highly educated, having a high household income, and the presence of past military service were associated with improved scores on general and sex-related QoL [21, 34, 54, 57, 65].

Instead, anxiety, poor sleep quality, experiencing pain, reduced self-esteem and high interpersonal issues are factors that have been linked to poor QoL in both transgender populations [22, 42, 55, 69, 70, 76] as well as in the general population [93].

6 Conclusion

As all systematic literature reviews, this study is also limited by the amount and quality of the published literature available. Future studies should employ more robust methodologies, which explore QoL in a more homogeneous population and using matched control groups.

Despite the limitations of the published literature, this review concludes that overall transgender people display poorer QoL than the general population, particularly pre-GAT, and that QoL improves once people are on CHT.

When specifically looking at the different dimensions of QoL (vQoL, sex-related QoL, and body image-related QoL), findings of the systematic review suggest that transgender people display poorer QoL than the general population, independent of the QoL domain investigated. As per general QoL, all dimensions of QoL have been shown to improve post-GAT. However, as the effect of GAT is linked to gender, a more positive vQOL was found for transgender men than transgender women at post-GAT, whilst opposite findings were obtained for sex-related QoL.

As long-term follow-up studies are limited in numbers and methodology, more studies are required exploring long-term QoL. This information may aid the development of support and interventions aiming at increasing resilience for those at risk of a poor QoL post-GAT.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

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Research

JAMA Pediatrics | Original Investigation

Chest Reconstruction and Chest Dysphoria in Transmasculine Minors and Young Adults Comparisons of Nonsurgical and Postsurgical Cohorts

Johanna Olson-Kennedy, MD; Jonathan Warus, MD; Vivian Okonta, MPH; Marvin Belzer, MD; Leslie F. Clark, PhD, MPH

IMPORTANCE Transmasculine youth, who are assigned female at birth but have a gender identity along the masculine spectrum, often report considerable distress after breast development (chest dysphoria). Professional guidelines lack clarity regarding referring minors (defined as people younger than 18 years) for chest surgery because there are no data documenting the effect of chest surgery on minors.

OBJECTIVE To examine the amount of chest dysphoria in transmasculine youth who had had chest reconstruction surgery compared with those who had not undergone this surgery.

DESIGN, SETTING, AND PARTICIPANTS Using a novel measure of chest dysphoria, this cohort study at a large, urban, hospital-affiliated ambulatory clinic specializing in transgender youth care collected survey data about testosterone use and chest distress among transmasculine youth and young adults. Additional information about regret and adverse effects was collected from those who had undergone surgery. Eligible youth were 13 to 25 years old, had been assigned female at birth, and had an identified gender as something other than female. Recruitment occurred during clinical visits and via telephone between June 2016 and December 2016. Surveys were collected from participants who had undergone chest surgery at the time of survey collection and an equal number of youth who had not undergone surgery.

MAIN OUTCOMES AND MEASURES Outcomes were chest dysphoria composite score (range O-51, with higher scores indicating greater distress) in all participants; desire for chest surgery in patients who had not had surgery; and regret about surgery and complications of surgery in patients who were postsurgical.

RESULTS Of 136 completed surveys, 68 (50.0%) were from postsurgical participants, and 68 (50.0%) were from nonsurgical participants. At the time of the survey, the mean (SD) age was 19 (2.5) years for postsurgical participants and 17 (2.5) years for nonsurgical participants. Chest dysphoria composite score mean (SD) was 29.6 (10.0) for participants who had not undergone chest reconstruction, which was significantly higher than mean (SD) scores in those who had undergone this procedure (3.3 [3.8]; P < .001). Among the nonsurgical cohort, 64 (94%) perceived chest surgery as very important, and chest dysphoria increased by 0.33 points each month that passed between a youth initiating testosterone therapy and undergoing surgery. Among the postsurgical cohort, the most common complication of surgery was loss of nipple sensation, whether temporary (59%) or permanent (41%). Serious complications were rare and included postoperative hematoma (10%) and complications of anesthesia (7%). Self-reported regret was near 0.

CONCLUSIONS AND RELEVANCE Chest dysphoria was high among presurgical transmasculine youth, and surgical intervention positively affected both minors and young adults. Given these findings, professional guidelines and clinical practice should consider patients for chest surgery based on individual need rather than chronologic age.

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Pl. Trial Ex. 198

Research Original Investigation

Chest Dysphoria and Chest Reconstruction Surgery in Transmasculine Youth

he last decade has seen an unprecedented number of youth presenting for care related to gender dysphoria at gender-specific clinics and centers around the United States, Canada, and Europe. 1,2 Transmasculine youth (those assigned a female sex at birth who have a gender identity along the masculine spectrum) who have undergone an endogenous female puberty and subsequent breast development commonly experience significant discomfort with the presence of breasts (chest dysphoria). Many but not all of these youth desire surgical intervention to achieve a flatter chest contour. This procedure involves a double mastectomy with downsizing and regrafting of the nipple areola complex or a minimally invasive procedure that spares the nipple. 3

As an interim strategy prior to chest surgery, many youth bind their chest in order to achieve a flatter, more masculine appearance. In a recent study of 1800 adults, Peitzmeier et al⁴ report an exhaustive list of negative health outcomes related to the practice of binding. These included pain, rib fractures, light-headedness, weakness, skin infection, and others.

There are no measures that capture the discomfort and subsequent consequences of chest dysphoria. The purpose of this study was to develop a measure that captures the distress associated with having a feminine chest contour (breasts) experienced by minors (persons younger than 18 years) and young adults (those aged 18 to 25 years) with a masculine gender identity, understand the association with chest surgery, and determine if there are differences in this association between young adults and minors. These results may serve to inform the practice of health care professionals with lingering concerns about potential complications, patient regret, and lawsuits, particularly for minors.

Surgical interventions for transgender individuals undergoing phenotypic gender transition have been considered an integral part of the transitioning process from as far back as the 1950s.5 Dissatisfaction with primary and secondary sex characteristics aligned with the chromosomes and gonads one has, rather than one's gender of identity, is a fundamental characteristic of gender dysphoria. 6 While surgical procedures are not desired by all individuals with transgender experience, these procedures are commonly sought in order to bring the physical body into better alignment with the experienced gender.7 Satisfaction rates across studies of adult transmasculine individuals undergoing chest reconstruction are 97%, and regret is present in less than 1% of transmasculine patients.8 Hormone therapy and surgery have been found to be medically necessary to diminish gender dysphoria. 7.9 Few data have been published concerning the outcomes of these procedures among minors, despite the growing numbers of youth presenting for care.1

Most transmasculine youth are accessing care after or near completion of breast development, necessitating surgical intervention for those who wish to have a masculine-appearing chest contour. Because pubertal development of people who are assigned female at birth may begin as early as 8 or 9 years of age, completion of puberty is plausible even as young as 12 years.

National guidelines regarding surgical interventions for minors are outlined in the World Professional Association for Transgender Health Standards of Care, version 7.9 These guidelines recommend that adolescents defer genital surgery until

Key Points

Question Is chest dysphoria (distress about breasts) more common among transmasculine youth who have not had chest reconstruction compared with those who have undergone this surgery?

Findlings In this cohort study, chest dysphoria was significantly higher in the nonsurgical vs postsurgical cohort. Among the nonsurgical cohort, 94% perceived chest surgery as very important; among the postsurgical cohort, serious complications were rare, and 67 of 68 reported an absence of regret.

Meaning Professional guidelines and clinical practice should recommend patients for chest surgery based on individual need rather than chronologic age.

the age of consent, but acknowledge that individual minors might be candidates for chest reconstruction. Despite this acknowledgment, many insurance plans continue to impose a mandatory age requirement of 18 years for chest surgery, as well as the use of testosterone for a full year prior to surgery to ensure the best results. While breast tissue does tend to atrophy with the use of testosterone, this effect is only partial. 10 The adolescent section of the Standards of Care, version 7, recommends 1 year of testosterone use prior to chest surgery, but specifically states elsewhere that "hormone therapy is not a pre-requisite" for surgery. 9(p59) It leaves unclear why the recommendation is in place for adolescents but not for adults. The recommendation to omit the requirement of hormone administration acknowledges that there are individuals who desire chest surgery but do not wish to undergo hormone therapy for phenotypic gender transition.9,11

This study was undertaken to determine if chest reconstruction diminishes chest dysphoria and if it should be considered a medically necessary intervention for both transmasculine minors and young adults. Additionally, in providing data on the experience of youth younger than 18 years, we hope to inform future revisions of existing guideline recommendations regarding transgender minors seeking surgical interventions to help mitigate gender dysphoria.

Methods

Practice Setting

The Center for Transyouth Health and Development at Children's Hospital Los Angeles has been serving the medical and mental health needs of transgender adolescents and young adults since 1993. At the time of this study, the center was serving 818 gender-nonconforming and transgender youth. Of the youth in care, 384 (46.9%) were assigned the female sex at birth; 93 youth (24.2%) had undergone chest reconstruction surgery before the study commenced.

Consent Procedures

The research study was approved by the Children's Hospital Los Angeles institutional review board. One or more parents or legal guardians provided consent for eligible minors. All participants provided verbal consent before completing the survey.

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Chest Dysphoria and Chest Reconstruction Surgery in Transmasculine Youth

Original Investigation Research

Study Eligibility

Youth in the nonsurgical group and the postsurgical group were considered eligible to complete the survey if they were 13 to 25 years old, assigned female at birth, identified their gender as something other than female, were able to read and understand English, and were able to provide consent.

Youth were included in the nonsurgical group if they had not undergone chest reconstruction surgery and had chest tissue consistent with female development. Prepubertal youth and those who had been administered puberty-blocking medications early in development were ineligible.

Youth were included in the postsurgical group if they had undergone chest reconstruction surgery. All participating youth who had undergone chest reconstruction surgery had done so after obtaining referral letters from medical and mental health professionals as required by the surgeons and insurance plans. The process by which individual mental health professionals assess readiness for surgery varies across practices. The common goal of health care professionals is to assure that patients have the capacity to provide consent and are fully informed about the mechanics, recovery, and irreversible nature of the surgery.

Study Recruitment and Data Collection

Participants were recruited from the youth visiting the Center for Transyouth Health and Development for routine genderrelated care between June 2016 and December 2016. A total of 52 patients (13.5%) were ineligible to participate in this study because they did not have chest tissue as a result of being either prepubertal or having taken puberty-blocking medications early in development. The remaining 332 transmasculine youth in active care were considered eligible for the study. All transmasculine youth who met study inclusion criteria and came for visits during this time were approached to participate. Nonsurgical youth outnumbered postsurgical youth in active care at the clinic by a ratio of 3.5:1, and to survey as many postsurgical youth as possible, study staff attempted to contact via telephone all postsurgical youth who had not visited the clinic during the enrollment period. Two postsurgical youth refused the survey, and 24 (26%) could not be contacted. Of those who could not be contacted, 12 had no working phone number, 7 did not respond to 3 messages left, and 5 agreed to participate but could not coordinate a time. Telephone calls and clinic visits during the study period yielded 68 (72%) completed surveys from postsurgical participants.

To obtain a sample of youth without surgery, we recruited until a comparable number of surveys were completed during the window of clinical visits. None of the youth who had not undergone surgery who were approached refused to participate.

The 10-minute survey collected demographic information, characteristics of surgery, and chest dysphoria. No incentive was provided for survey completion. Study data were collected and managed using Research Electronic Data Capture electronic data capture tools, which are hosted at the Southern California Clinical and Translational Science Institute. 12

Development of the Chest Dysphoria Scale

To develop the Chest Dysphoria Scale, 21 survey items were generated that queried multiple aspects of chest dysphoria based on clinical experience of the first author over the past 11 years of delivering clinical care for transgender youth in a large, urban, hospital-based gender clinic. To establish face validity from the community perspective, the scale was reviewed by a small number of transmasculine youth and transmasculine adults who evaluated whether the questions captured elements of chest dysphoria effectively, used appropriate language, and was otherwise generally acceptable. The scale includes items related to physical functioning, including hygiene and exercise, intimate partnerships and dating, being perceived as a member of a gender other than their gender of identity, and disruption of future plans. Items such as "I avoid bathing/showering in order to avoid seeing my chest," and "I avoid seeking medical care because of my chest" were scored using a Likert scale, from 0 (never) to 3 (all the time). The complete Chest Dysphoria Scale is displayed in Table 1.

A principal components extraction method by an oblique (oblimin) rotation yielded a single factor comprised of 17 items (eigenvalue, 11.1). The same factor structure emerged when analyses were conducted with nonsurgical and postsurgical cohorts separately. After imputing the mean of all completed items in place of missing values, the 17 items yielded a composite score ranging from 0 to 51, with higher scores indicating greater chest dysphoria. Missing data were minimal (<5%) for all items. Data with mean imputations were used to calculate the a and also for subsequent analyses involving the Chest Dysphoria Scale. Results of tests for internal consistency suggest high reliability (Cronbach a for postsurgical patients, .79; Cronbach α for nonsurgical patients, .89). See Table 1 for information about the 4 items dropped from the scale.

Statistical Analysis

Descriptive characteristics for both nonsurgical and postsurgical cohorts were summarized. The ages of respondents were stratified by age for binary analyses (<18 years and ≥18 years). In the nonsurgical cohort, the analysis was dichotomized based on age at the time of survey, and in the postsurgical cohort, the analysis was based on age at time of chest surgery. To examine the utility of the 1 year taking testosterone prior to surgery recommended by insurance plans, a simple linear regression model was used to evaluate the relationship between duration of time taking testosterone and chest dysphoria scores in nonsurgical cohort respondents. Results were expressed as regression coefficients with 95% confidence intervals. Analyses were conducted using IBM SPSS Statistics, version 17.0 (IBM Corporation).

Results

Descriptive Characteristics

At the time of survey, the mean (SD) age of postsurgical participants was 19 (2.5) years (range, 14-25 years). The length of time between survey and chest surgery varied from less than 1 year to 5 years (Table 2). The mean (SD) age at chest surgery in this cohort was 17.5 (2.4) years (range, 13-24 years), with 33 (49%) being younger than 18 years. Of the 33 postsurgical participants younger than 18 years at surgery, 16 (48%) were 15

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Table 1. Chest Dysphoria Scale (Final Version)

	Patients Endo No. (%) ^a	rsing Item,
Item	Nonsurgical Patients (n = 68)	Postsurgical Patients (n = 68)
Items included in the final scale		
I like looking at my chest in the mirror	7 (10)	57 (84)
Taking a shower/bath is difficult because I have to see my chest	40 (59)	1 (2)
I avoid going to the beach and/or swimming in public places because of my chest	55 (81)	7 (10)
I get gendered as female because of my chest	24 (35)	1 (2)
Dating/forming intimate partnerships is more difficult because of my chest	34 (50)	1 (2)
Physical intimacy/sexual activity is difficult because of my chest	41 (60)	2 (3)
I have struggled to make future plans because of my chest	39 (57)	1 (2)
I avoid exercise because of my chest	32 (47)	1 (2)
I avoid shopping/buying clothing because of my chest	21 (31)	0 (0)
I avoid seeking medical care because of my chest	9 (13)	1 (2)
I feel like my life hasn't started because of my chest	40 (59)	1 (2)
I avoid swimming in private places because of my chest	44 (65)	2 (3)
I have to buy/wear certain clothes because of my chest	54 (79)	0 (0)
I sleep with a binder on at night	11 (16)	0 (0)
I avoid using locker rooms because of my chest	53 (78)	5 (7)
I worry that people are looking at my chest	57 (84)	7 (10)
I participate in life less than others because of my chest	41 (60)	1 (2)
Additional items not included in final scale		
Thinking about my chest does not get in the way of daily activities	13 (19)	40 (59)
My chest does not get in the way of attending school/work	15 (22)	42 (62)
l avoid bathing/showering in order to avoid seeing my chest	11 (16)	0 (0)
I bind my chest in the daytime	60 (88)	0 (0)

^a Frequencies and corresponding percentages represent combine responses of "frequently" and "all the time."

years or younger (**Figure**). At the time of survey, the mean (SD) age of participants without surgery was 17 (2.5) years (range, 13-23 years), with 39 (57%) being younger than 18 years.

Emotional and Physical Features of Postsurgical Cohort

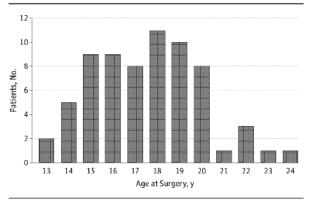
All postsurgical participants (68 of 68; 100%) affirmed the statement, "It was a good decision to undergo chest reconstruction." Sixty-seven of 68 postsurgical respondents reported no regret about undergoing the procedure. Only 1 participant (who was older than 18 years at the time of surgery) reported experiencing regret "sometimes." The most common complications reported following chest surgery were temporary and permanent loss of nipple sensation (40 of 68, or 59%, and 22 of 68, or 32%, respectively; permanency was assessed as continuation of the condition from surgery to the

Table 2. Descriptive Characteristics of Nonsurgical and Postsurgical Cohorts

	No. (%)	
Characteristic	Postsurgical Patients (n = 68)	Nonsurgical Patients (n = 68)
Age range (at time of survey), y	14-25	13-23
Age, mean (SD), y	18.9 (2.5)	16.9 (2.5)
Length of time since surgery, y		
<1	20 (29)	NA
1	20 (29)	NA
2	19 (28)	NA
3	4 (6)	NA
4	4 (6)	NA
5	1 (2)	NA
Hormone related descriptive characteristics		
Currently taking testosterone?	66 (97)	59 (87)
Age at start of testosterone, mean (SD), y	16.3 (2.1)	16.4 (2.0)
Length of time taking testosterone, y		
<0.5	6 (9)	27 (46)
0.50-1	3 (4)	11 (19)
1-2	19 (29)	15 (25)
>2	38 (58)	6 (10)

Abbreviation: NA, not applicable.

Figure. Age at Chest Surgery in the Postsurgical Cohort



Graph includes all study participants who had undergone chest reconstruction (n = 68)

time of survey collection), loss of sensation in other areas of the chest (28 of 68; 41%), and unequal chest appearance (9 of 68; 13%) (Table 3). There were no statistically significant differences in complication rates reported between those younger than 18 years vs those 18 years or older at the time of surgery. Mean (SD) chest dysphoria scores among postsurgical participants were 3.3 (3.8) and were not significantly associated with length of time between surgery and survey, complication rates, or age group (minors vs those 18 years or older). Items from the Chest Dysphoria Scale indicating functional limitations were rarely endorsed (Table 1).

Nonsurgical Cohort

Interest in chest reconstruction among respondents was high, with nearly 70% responding to the question, "How important

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is having chest surgery to you?" with the description, "one of the most important things for [them] right now"; another 17 (25%) described it as "very important." The majority (59 of 68; 87%) were using testosterone at the time of survey (Table 2). Chest dysphoria was higher for those who had been taking testosterone longer, increasing by 0.33 points for each month taking testosterone. There were no statistically significant differences in levels of chest dysphoria by age group (minors vs those 18 years and older). For items denoting functional limitations, nearly half (32 of 68; 47%) of participants avoided exercise, 11 of 68 (16%) avoided bathing, 11 of 68 (16%) slept with a chest binder at night, and 10 of 68 (13%) avoided seeking medical care because of their chest (Table 1). Half of the participants (34 of 68) found intimate partnerships more difficult because of their chest, and 40 of 68 (59%) reported feeling that their chest interfered with making future plans for their life.

Comparison of Chest Dysphoria Scale Scores by Cohort Possible chest dysphoria composite scores ranged from 0 to 51, with higher scores indicating greater distress. Chest dysphoria composite mean (SD) scores differed significantly between those who had not undergone chest reconstruction (29.6 [10.0]; n=68) and those who had (3.3 [3.8]; n=68; P<.001). There was no significant difference in mean chest dysphoria score between those who had surgery at ages younger than 18 years vs those who had surgery at 18 years or older.

Discussion

Concern exists among parents and professionals about surgical interventions for transgender youth, particularly those of minority age status. Professionals harbor concerns about liability in performing transgender-related surgeries that patients may potentially regret after the procedure. This study demonstrated very low rates of regret among postsurgical youth among minors as well as those 18 years and older at the time of surgery. Reported adverse effects in the postsurgical cohort were also relatively minimal.

Chest dysphoria can negatively affect the health of young transmasculine individuals. Within our cohort of youth who had not undergone surgery, substantial numbers of youth were avoiding seeking medical care because of their chests and were binding their chests frequently or all the time, including during sleep. Youth feeling that their chest impeded life plans is an indicator of the negative effect of having an internal masculine gender identity that is at odds with the outward appearance of a female chest contour. Comparison of postsurgical and nonsurgical youth suggests that chest reconstruction had a positive effect both transmasculine minors and young adults.

Many insurance companies require continuous 12 months of testosterone use prior to undergoing chest surgery. The nonsurgical cohort in this study had been taking testosterone for periods ranging from less than 1 month to 52 months, with chest dysphoria increasing the longer their time on hormones. This finding should not be construed as an endorsement to withhold or delay testosterone initiation to avoid chest dysphoria intensity. It is unclear if the chest dysphoria

Table 3. Complications of Chest Reconstruction Surgery

Complication	Participants, No. (%) (n = 68)
Temporary loss of nipple sensation	40 (59)
Loss of sensation of other areas of the chest	29 (41)
Long-term loss of nipple sensation	22 (32)
Keloid (excessive) scarring	10 (15)
Unequal chest appearance	9 (13)
Postoperative hematoma	7 (10)
Postoperative pain beyond normal healing time	6 (9)
Nipple/areola(s) too large	5 (7)
Complications related to anesthesia	5 (7)

increase is specific to the length of time taking testosterone or simply because of a longer waiting period between initiation of physical gender transition and surgery. The increasing chest dysphoria after testosterone treatment begins does reflect a common clinical phenomenon: a honeymoon period after testosterone initiation that quickly becomes eclipsed by the greater disparity between a more masculine presentation and a female chest contour. Clinicians should advise patients and families that chest dysphoria may increase over time after starting hormone therapy. In addition, the recommendation of many insurance companies that individuals take hormones for 12 months prior to chest surgery may create additional barriers to chest surgery and cause additional harm.

Limitations

Despite our participants being recruited from a single site, these data are likely generalizable to youth receiving care at clinic sites in similar settings: large, urban, academically affiliated clinics serving multiethnic youth. This investigation was limited by the cross-sectional research design; a prospective design collecting data on the same participants before and after surgical intervention would likely yield results more specific to the intervention of chest reconstruction.

An additional limitation of the study was the small sample size. The nonsurgical cohort was a convenience sample, recruited from those with appointments during the data collection period. There could be unknown imbalances between the nonsurgical and postsurgical cohorts that could have confounded the study findings.

Finally, the Chest Dysphoria Scale is not yet validated, and may not represent distress or correlate with validated measures of quality of life, depression, anxiety, or functioning. Our intent is to move forward with the process of validation, so that it might be useful in clinical practice.

Conclusions

In future studies, it would be informative to determine whether the outcome of either chest dysphoria or chest surgery varies with race/ethnicity, type of surgery, or gender identity (nonbinary vs masculine). Future studies should consider investigating the outcome of chest dysphoria on participation and functioning in school, work, and family activities.

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Research Original Investigation

Chest Dysphoria and Chest Reconstruction Surgery in Transmasculine Youth

Given the numerous complications associated with chest binding, the negative emotional and mental effects of chest dysphoria, and the positive outcome of chest surgery demonstrated in this study, changes in clinical practice and in insurance plans' requirements for youth with gender dysphoria who are seeking surgery seem

essential. Youth should be referred for chest surgery based on their individual needs, rather than their age or time spent taking medication. Individualized, patient-centered care plans should be considered the standard of care for all transgender adolescents, and referrals should be made accordingly.

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Mental Health of Transgender Children Who Are Supported in Their Identities

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OBJECTIVE: Transgender children who have socially transitioned, that is, who identify as the gender "opposite" their natal sex and are supported to live openly as that gender, are increasingly visible in society, yet we know nothing about their mental health. Previous work with children with gender identity disorder (GID; now termed gender dysphoria) has found remarkably high rates of anxiety and depression in these children. Here we examine, for the first time, mental health in a sample of socially transitioned transgender children.

METHODS: A community-based national sample of transgender, prepubescent children (n = 73, aged 3–12 years), along with control groups of nontransgender children in the same age range (n = 73 age- and gender-matched community controls; n = 49 sibling of transgender participants), were recruited as part of the TransYouth Project. Parents completed anxiety and depression measures.

RESULTS: Transgender children showed no elevations in depression and slightly elevated anxiety relative to population averages. They did not differ from the control groups on depression symptoms and had only marginally higher anxiety symptoms.

conclusions: Socially transitioned transgender children who are supported in their gender identity have developmentally normative levels of depression and only minimal elevations in anxiety, suggesting that psychopathology is not inevitable within this group. Especially striking is the comparison with reports of children with GID; socially transitioned transgender children have notably lower rates of internalizing psychopathology than previously reported among children with GID living as their natal sex.

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Dr Olson conceptualized and designed the study, assisted in data collection, carried out the initial analyses, and drafted the initial manuscript; Ms Durwood and Ms DeMeules collected the data, supervised data entry, and reviewed the manuscript; Dr McLaughlin conceptualized the study and substantially reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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WHAT'S KNOWN ON THIS SUBJECT: Transgender individuals have been found to have highly elevated rates of anxiety and depression, but little is known about the mental health of transgender children whose identities are affirmed and supported by their families.

WMAT THIS STUDY ADDS: More families are allowing their transgender children to live and present to others as their gender identity. This is the first study to examine mental health in these children, finding that they have low levels of anxiety and depression.

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Pl. Trial Ex. 199

National media are increasingly presenting stories of a subset of prepubescent transgender children (those who persistently, insistently, and consistently identify as the gender identity that is the "opposite" of their natal sex). More striking to many, a large number of these children have "socially transitioned": they are being raised and are presenting to others as their gender identity rather than their natal sex,1-4 a reversible nonmedical intervention that involves changing the pronouns used to describe a child, as well as his or her name and (typically) hair length and clothing. These stories have sparked an international debate about whether parents of young transgender children should support their children's desire to live presenting as their gender identity.5-9 Despite considerable and heated discussion on the topic, and despite these children's increasing appearance at gender clinics,6 there have been no reports to date on the mental health of transgender children who have socially transitioned, forcing clinicians to make recommendations to parents without any systematic, empirical investigations of mental health among socially transitioned children.

Most studies of mental health among transgender people have examined adolescents and adults. These studies consistently report dramatically elevated rates of anxiety, depression, and suicidality among transgender people.10-16 These elevated rates of psychopathology are likely the result of years of prejudice, discrimination, and stigma11,17; conflict between one's appearance and stated identity18; and general rejection by people in their social environments, including their families. 19,20 There is now growing evidence that social support is linked to better mental health outcomes among transgender adolescents and adults.21-26 These findings suggest the possibility that social transitions in children,

a form of affirmation and support by a prepubescent child's parents, could be associated with good mental health outcomes in transgender children.

Although there are no large studies of transgender prepubescent children, a number of studies have examined children who were at the time diagnosed with what was called gender identity disorder (GID), now termed gender dysphoria (GD; for more on both terms and others used throughout this article, see Table 1). The group of children diagnosed with GID likely included children who were transgender as well as others (eg, children who wished and acted but did not believe they were a member of the other gender and were distressed as a result). Importantly, most of the studies of children with GID/GD were conducted at a time when parental support and affirmation of children's gender nonconforming behaviors and identities were uncommon. In contrast, the current work focuses on what is likely a much narrower group of children, a small subset of the group that previously would have been diagnosed with GID: those who (1) identify as (not merely wish) they were the "opposite" gender as their sex at birth and (2) have socially transitioned so that they appear to others as the gender they feel, rather than that assumed by their sex at

By and large, studies of children with GID reported high rates of psychopathology, especially internalizing disorders such as anxiety and depression^{27–32}. For example, 36% of a group of 7- to 12-year-olds with GID reached the clinical range for internalizing problems.³³ Furthermore, 2 large studies of 6- to 11-year-olds with GID (including >100 children in Utrecht, the Netherlands, and 300 children in Toronto, Canada) found average internalizing scores in the clinical and preclinical range,

respectively, suggesting that many children in both samples showed high levels of internalizing psychopathology. Some have argued that these high rates of internalizing psychopathology among children with GID/GD as a sign that GID/GD is itself a form or consequence of such psychopathology.²⁷

In contrast, 2 smaller studies suggest that children whose gender identities are affirmed and supported have relatively good mental health. One study reported on 26 children aged 3 to 12 years with GID who were recruited through a clinic that advised parents to support their children's gender expression. These children showed reduced rates of psychopathology34 compared with those reported in other studies conducted at clinics that do not support such gender expression.35 However, this study has received some criticism for methodologic limitations36 and had a small sample size. Furthermore, the degree to which these findings generalize to transgender children and especially to transgender children who have been allowed to fully socially transition, is unknown. In addition, a qualitative analysis of interviews of parents of 5 transgender children who had socially transitioned found that parents recalled a reduction in mental health problems after a social transition.37 Although no formal quantitative measures were provided, these findings again suggest that socially supported transgender children might have better mental health than children with GD or transgender children who are not supported in their identities.

The current study addresses a critical gap in knowledge by examining parental reports of anxiety and depression among a relatively large cohort of transgender children, all of whom are supported by their families and have socially transitioned (ie, they present to others as the gender consistent with their identity, not

TABLE 1 Definitions of Terms

Term	Use in This Article	Other Uses, Terms, and Comments
Transgender	In this article, we use "transgender" to refer to children who have a binary identity (male or female) and for whom this identity is not aligned with their sex at birth. This means natal boys who identify as girls and natal girls who identify as boys. In our sample, these children have all socially transitioned as well.	"Transgender" is often used to mean a broader range of people—anyone whose gender identity does not align with his or her sex at birth. This categorization can include, for example, people who identify as male and female, neither male or female, or somewhere between male and female. The sample included in the current work does not include such children, hence our use of a narrower version of this term.
Social transition	This phrase is used to refer to a decision by a family to allow a child to begin to present, in all aspects of the child's life, with a gender presentation that aligns with the child's own sense of gender identity and that is the "opposite" of the gender assumed at the child's birth. Social transitions involve changes in the child's appearance (eg, hair, clothing), the pronoun used to refer to the child, and typically also a change in the child's name.	Social transitions are currently controversial in clinical psychology and psychiatry, but are increasingly being pursued by parents. More and more pediatricians, therapists, and teachers are supporting these transitions as well. Importantly, these transitions do not involve any medical, physiologic, or hormonal intervention.
Natal sex	We use this term to refer to the sex assigned by a physician at the child's birth. This phrase is meant as a synonym for "anatomical sex," "biological sex," or "sex assigned at birth."	The term "natal sex" is controversial, with many using the phrase "sex assigned at birth" instead. However, the latter term is still unfamiliar to many people with limited exposure to transgender individuals. Because this paper is aimed at reaching a broad audience of pediatric health professionals, we use the more commonly understood term "natal sex."
"Opposite" gender	We occasionally use the phrase "opposite" gender in this article when describing our sample of transgender children. Children whose gender is the "opposite" of their natal sex refers to natal boys who identify as girls and natal girls who identify as boys. Because the latter phrasing is longer and more awkward, we opted for the former.	This phrasing of "opposite" gender implies that gender is binary, when in fact it is not. There are many people who do not identify as male or female. We use this phrase because most readers will be more familiar with this terminology, and our goal is to reach a broad audience of pediatric health professionals. Gender identity is often separated from gender presentation
Gender identity	We use this term to refer to a child's sense of his or her own gender. Although in most children, gender identity "aligns" with a child's natal sex, in transgender children, it does not.	or gender expression (ie, the gender one appears to others as, or how a child expresses his or her gender identity). In this study, however, participants' gender identities align with their gender presentation/expressions because children have socially transitioned.
Gender Identity Disorder (GID)/Gender Dysphoria (GD)	Until 2014, GID was the official diagnosis given to children who had behavioral preferences and identities (or desires to be) the "other" gender. With the publication of the <i>Diagnostic</i> and Statistical Manual of Mental Disorders, Fifth Edition, this diagnostic category was renamed gender dysphoria (GD) after substantial debate about whether this is or is not a "disorder."	The term GD describes a broader segment of the population than children qualifying as "transgender" for the current study. For example, a natal male who wishes to be a female, who behaves in accordance with female cultural stereotypes, and who has considerable concern about his identity but who does not believe he is female, would be diagnosed with GD but would not count as transgender in the current study.

their natal sex and use associated gender pronouns consistent with that identity). We focused on internalizing psychopathology because previous work indicates that transgender children are particularly likely to have internalizing, as opposed to externalizing, symptoms.^{33,35} We compared these supported, transgender children's rates of anxiety and depression to their nontransgender siblings and to typically developing nontransgender children matched to transgender children on age and gender identity.

METHODS

This work, including recruitment and methods, was approved by the Institutional Review Board at the University of Washington.

Participants

To be included in this study, transgender children had to (1) identify as the gender "opposite" their natal sex in everyday life (ie, they identified as male or female, but not the gender that aligned with their sex at birth), (2) present

in all contexts (eg, at school, in public) as that gender identity, (3) use the pronoun matching their gender rather than their natal sex, (4) be 3 to 12 years old, and (5) be prepubescent (ie, anyone eligible for hormone blockers was excluded from the present study). We recruited a national, community sample via support groups, conferences, a Web site advertised via media stories, and word of mouth. Our sample included 73 transgender children (M_{age} = 7.7 years; SD = 2.2 years; 22 natal females, 51 natal males;

TABLE 2 Sociodemographic Characteristics for Transgender and Nontransgender Children (n = 195)

	Transgender ^a (n = 73)	Controls ^b (n = 73)	Siblings ^c (n = 49)
Gender, %			
Male	30	30	61
Female	70	70	39
Natal boys ^d	70	30	61
Natal girls	30	70	39
Race/ethnicity			
White, non-Hispanic	70	71	76
Hispanic	8	5	10
Asian	6	4	2
Multiracial/other	16	19	12
Mean age, y	7.7 y	7.8 y	8.3 y
Age distribution, %			
3–5 y	30	30	22
6–8 y	40	37	37
9-12 y	30	33	41
Annual family income, %			
<\$25 000	1	1	2
\$25 001-\$50 000	7	7	4
\$50 001-\$75 000	7	14	4
\$75 001-\$125 000	41	43	39
>\$125000	44	38	51

^a Transgender children were all prepubescent and had socially transitioned.

70% white non-Hispanic) and included all consecutive cases run by our research group meeting these criteria, starting with the first for whom we had these measures.

In addition, we recruited 2 control groups. Our first control group was a set of 49 siblings (Mage = 8.3 years; SD = 2.5 years; 19 natal females, 30 natal males; 76% white non-Hispanic) of the transgender children reported earlier who were also aged 3 to 12 years. Whenever possible, the sibling closest in age was recruited. The second group of controls consisted of 73 typically developing children with no history of cross-gender behavior (Mage = 7.8 years; SD = 2.2 months; 51 natal females, 22 natal males; 71% white non-Hispanic) who were matched to each transgender child based on age and gender identity (eg, transgender girls had female controls). These unrelated controls were recruited from a university database of families in the Seattle area interested in participating in research about

child development. Importantly, all parents were informed that this was part of a longitudinal study about gender nonconforming children's development, even though their children were not gender nonconforming. Recruitment and data collection is part of the TransYouth Project, a large, longitudinal study of American and Canadian transgender children's development, and matched controls from that larger study were used in the current work.

Measures

Internalizing Psychopathology

Symptoms of anxiety and depression were reported using the National Institutes of Health Patient Reported Outcomes Measurement Information System parental proxy short forms for anxiety and depression. When possible, 2 parents completed these forms, and the averages are reported (n = 90); in all other cases, only 1 parent completed the forms (n = 115). (Importantly, results did not

change if only mothers' responses [most often the only parent present when there was one reporter] were analyzed.) These scales are nationally normed and provide t-scores such that a score of 50 represents the national mean, with a SD of 10.

Demographics

Parents completed several demographic questions, including their child's race, sex, and age, and their household income (in quintiles: 1 = <\$25 000/year, 2 = \$25 001-50 000, 3 = \$50 001-75 000, 4 = \$75 001-\$125 000, 5 = >\$125 000/ year). This information is reported by participant group in Table 2. With the exception of gender (siblings were more likely to have a male gender identity than transgender or agematched control participants; the latter 2 groups were matched on this variable), the 3 groups did not differ on demographic variables.

RESULTS

Anxiety and depression t scores are reported in Table 3 by participant sample and natal sex. Transgender children's rates of anxiety and depression were first compared with the scale's midpoint (50), an indicator of average levels of depression and anxiety symptoms.38 In terms of depression, transgender children's symptoms (M = 50.1)did not differ from the population average, P = .883. In contrast, transgender children had elevated rates of anxiety compared with the population average (M = 54.2), t(72) = 4.05, P < .001. Mean anxiety symptoms of transgender children were not in the clinical, or even preclinical, range, but were elevated.

To assess differences between transgender and control children in our sample, we ran a 3 (group: transgender, siblings, controls) × 2 (natal sex) between-subjects analysis of variance for depression and anxiety. Natal sex was used in

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^b Controls were matched to transgender children for gender identity and age within 4 months.

^c Siblings were the siblings who were closest in age to their transgender siblings.

d One natal male was diagnosed with a minor disorder of sex development, hypospadias, but consultation with endocrinologist indicated this condition is not associated with female identity.

this analysis, rather than affirmed gender, because work with children with GID/GD used this convention,35 allowing interested readers to make comparisons to past work with that sample and because previous work has suggested differences in internalizing psychopathology between natal boys compared with girls with GID.35,39 For depression, there were no main effects of group, P = .320 or sex, P = .498, nor was there an interaction between condition and sex, P = .979. For anxiety, we found a marginally significant effect of group, F(2189) =2.91, P = .057, and no effect of sex, P =.990, nor an interaction, P = .664.

DISCUSSION

Socially transitioned, prepubescent transgender children showed typical rates of depression and only slightly elevated rates of anxiety symptoms compared with population averages. These children did not differ on either measure from 2 groups of controls: their own siblings and a group of age and gender-matched controls. Critically, transgender children supported in their identities had internalizing symptoms that were well below even the preclinical range. These findings suggest that familial support in general, or specifically via the decision to allow their children to socially transition, may be associated with better mental health outcomes among transgender children. In particular, allowing children to present in everyday life as their gender identity rather than their natal sex is associated with developmentally normative levels of depression and anxiety.

Critically, socially transitioned transgender children showed substantially lower rates of internalizing symptoms than children with GID reported in previous studies³⁵ (see Table 4). Our findings align with at least 1 other report of low mental health problems among

TABLE 3 Anxiety and Depression t Scores by Sex and Sample

	Transgender (n = 73)	Controls (n = 73)	Siblings (n = 49)	Р
Depression	50.1	48.4	49.3	.320
Anxiety	54.2a	50.9	52.3	.057
Depression by gender ^b				.979≎
Natal boys	49.8 (trans-girls)	48.0	48.9	
Natal girls	50.8 (trans-boys)	48.5	49.9	
Anxiety by gender				.664°
Natal boys	53.7	51.1	52.8	
Natal girls	55.3	50.8	51.5	

^a This is the only value that is significantly above the national average (50), although it is still substantially below the clinical (>63) or even preclinical (>60) range.

TABLE 4 Comparison of Present Sample With Previous Reports of Population-Normed Internalizing Scores for children with GID²⁴

	Current Sample (n = 73)	Toronto (n = 343)	Utrecht (n = 123)
Mean age	7.7 y	7.2 y	8.1 y
Sample	Transgender ^a	GIDb	GIDb
Measure of internalizing	PROMIS [©]	CBCL	CBCL
Mean internalizing t score	52.2	60.8	64.1

Both the PROMIS and GBCL are normed such that the population mean is t = 50 and SD is 10. GBCL, Child Behavior Checklist; PROMIS. Patient Reported Outcomes Measurement Information System.

children with GID supported in their gender identities,³⁴ a sample that may have included some socially transitioned transgender children. Comparisons between previous reports of children with GID and the current sample should be made cautiously, however, because the criteria for inclusion (transgender identities vs GID) and specific measures of internalizing psychopathology (PROMIS vs CBCL) differ across studies.

One might reasonably ask whether this study provides support for all children with gender dysphoria to socially transition. A few points are key to consider. First, all children in our study (unlike many children with the GD classification), had binary identities, meaning they identified as male or female. Thus, we cannot make predictions about the expected mental health of children

who identify as male and female, as neither male nor female, or who identify as the gender associated with their natal sex but nonetheless exhibit behavior more often associated with the "other" gender after a social transition. Thus, just because a child behaves in a way consistent with a gender other than their natal sex does not mean that child is transgender nor that a social transition is advisable. Second, the children in this study were unique in many critical ways. They transitioned at a time when such transitions are quite controversial5-9 and yet did so anyway. Surely not all families with transgender children make this decision, meaning there are likely characteristics that are unique to these families. In addition, the transgender children in this study all socially transitioned much earlier than nearly all transgender adults alive today in the United States and

^b Transgender children who are natal boys and live with a female gender presentation are often called transgender girls or trans-girls; transgender children who are natal girls living with a male gender presentation are often called transgender boys or trans-boys.

c Significance value of interaction between natal sex and group.

a The current participants were transgender, socially transitioned, and prepubescent.

^b Participants in both the Toronto and Utrecht samples either met criteria for GID or showed subthreshold symptoms of GID.

⁶ To compute an internalizing score for the PROMIS, depression and anxiety scores were averaged.

Canada. Why might they have done so? Possibilities that we cannot rule out are that these children displayed earlier signs of their transgender identities, that they were more insistent about those identities, that they represent the most extreme end of the spectrum of transgender identities, or that parents today are just more educated about the existence of transgender children. It is too early to tell the ways in which these children and these families are unique. Finally, the children in this study were not randomly assigned to social transitions, precluding the ability to make causal claims about the impact of social transitions on mental health. These data are suggestive, nonetheless, that social transitions are associated with positive mental health outcomes for transgender children.

We cannot rule out several alternative explanations for our findings. First, rather than a direct impact of parental support, these generally positive mental health findings could be a more indirect result of parent support: namely, feeling supported in general (independent of a social transition) may lead to higher selfesteem,40 which in turn may lead to better mental health.41 Second, as alluded to earlier, there could be some unique third variable that explains the observed occurrence of typical mental health among socially transitioned transgender children. For example, perhaps some attribute unique to the subset of transgender children who are able to convince their parents to allow them to transition (eg, verbal skill, self-confidence) is responsible for these children having particularly good mental health, and it was this unique cognitive ability or aspect of personality that is either correlated with better mental health or leads to better mental health when a child feels he or she achieved his or her goal. Future studies examining

children before and after social transitions may be able to address this concern. Finally, parents of transgender children could have biased reporting, reflecting a desire for their children to appear healthier than they are. We have no reasons to believe this was an issue but in the future aim to include other reporters (eg, teachers) to address this concern that others are likely to raise.

In addition to studying other explanations for these data, the current work begs for more research not only on children with other transgender identities (eg, children who identify as both or neither male and female), but also for work with children who have clear binary transgender identities, like the children in the current study, but who are not supported or affirmed by their families in these identities. Finding such children and particularly convincing their parents to allow them to participate in research, will be a challenge but one that is ultimately necessary for a clear understanding of the specific impact of transitions for these children.

Despite their overall relatively good mental health, socially transitioned transgender children did experience slightly more anxiety than the population average, although still well below the preclinical range. What might explain this result? Despite receiving considerable support from their families, these children likely still experience relatively high rates of peer victimization or smaller daily microaggressions, particularly if their peers know that they are transgender42 which can in turn lead to marked elevations of anxiety symptoms and anxiety disorders.43-45 Additionally, any transgender children who are living "stealth" or "undisclosed" (ie, whose peers are unaware of their transgender status), may experience anxiety about others discovering their transgender identity; previous

work with adults has suggested that concealing a stigmatized identity can lead to psychological distress.46 Furthermore, transgender children do not have the typical bodies of children with their gender identities, which could be a source of distress. Even when transgender children are allowed to use the bathroom, locker room, or be on the team with children who share their gender, the mere existence of these distinctions likely highlights the ways in which their bodies do not align with cultural expectations for children of their gender identity group. Relatedly, some children in our sample are approaching puberty, and most are aware that puberty will cause physical changes in an unwanted direction (unless puberty blockers are administered), which could generate considerable worry and anxiety.

Importantly, although these socially transitioned prepubescent children are doing quite well in terms of their mental health at this point, parents and clinicians of such children should still be on the lookout for potential changes in the status of their children's mental health. In general, the prevalence of depression is relatively low in prepubescent children and rises dramatically during adolescence.47 It is possible that transgender children will exhibit greater anxiety and depression than their peers during the adolescent transition because of the sources of distress mentioned earlier, which will likely become worse with time (a possibility we aim to test with prospective follow-up of this sample). Thus, while adolescence is a time of increased perceptions of stress for many adolescents,48 many of these issues are exacerbated for transgender teens. Transgender adolescents, whether they do or do not delay puberty through medical intervention, often experience body dysphoria (as their bodies do not match the bodies of their

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same-gender peers), making sex and relationships even more worrisome than among their nontransgender peers.⁴⁹

CONCLUSIONS

In sum, we provide novel evidence of low rates of internalizing psychopathology in young socially transitioned transgender children who are supported in their gender identity. These data suggest at least the possibility that being transgender

is not synonymous with, nor the direct result of, psychopathology in childhood.²⁷ Instead, these results provide clear evidence that transgender children have levels of anxiety and depression no different from their nontransgender siblings and peers. As more and more parents are deciding to socially transition their children, continuing to assess mental health in an increasingly diverse group of socially transitioned children will be of utmost importance.

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ABBREVIATIONS

GD: gender dysphoria GID: gender identity disorder

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Association between gender confirmation treatments and perceived gender congruence, body image satisfaction and mental health in a cohort of transgender individuals

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Association between gender confirmation treatments and perceived gender congruence, body image satisfaction and mental health in a cohort of transgender individuals

ABSTRACT

<u>Background.</u> Transgender individuals sometimes seek gender confirmation treatments (GCTs), including hormone therapy (HT) and/or surgical change of the genitalia and other secondary sex characteristics (gender confirmation surgeries; GCS). These treatments, which alter the body so that it is more compatible with one's identity, may ameliorate distress resulting from the incongruence between one's physical appearance and gender identity.

<u>Aim.</u> The aim was to examine the degree to which individuals' body-gender congruence, body image satisfaction, depression and anxiety differed by GCT groups in cohorts of transmasculine (TM) and transferminine (TF) individuals.

Methods. The "Study of Transition, Outcomes & Gender (STRONG)" is a cohort study of transgender individuals recruited from three XXX health plans located in Georgia, Northern California and Southern California; cohort members were recruited to complete a survey between 2015-2017. Participants were asked about: history of GCTs; body-gender congruence; body image satisfaction; depression; and anxiety. Participants were categorized as having received: 1) no GCT to date; 2) HT only; 3) HT + top surgery; 4) HT + partial bottom surgery; and 5) HT + definitive bottom surgery.

Outcomes. Outcomes of interest included body-gender congruence, body image satisfaction, depression and anxiety.

Results. Of the 2,136 individuals invited to participate, 697 subjects (33%) completed the survey, including 347 TM and 350 TF individuals. The proportion of participants with low body-gender congruence scores was significantly higher in the "no treatment" group (prevalence ratio [PR]=3.96, 95% confidence interval [CI] 2.72-5.75) compared to the "definitive bottom" surgery group. The PR for depression comparing participants who reported no treatment relative to those who had definitive surgery was 1.94 (95% CI: 1.42-2.66); the corresponding PR for anxiety was 4.33 (95% CI 1.83-10.54).

<u>Clinical Implications.</u> Withholding or delaying GCTs until depression or anxiety have been treated may not be the optimal treatment course given the benefits of reduced levels of distress after undergoing these interventions.

Strengths & Limitations. Strengths include the well-defined sampling frame, which allowed correcting for non-response, a sample with approximately equal numbers of TF and TM participants, and the ability to combine data on HT and GCS. Limitations include the cross-sectional design and the fact that participants may not be representative of the transgender population in the US.

Conclusion. Body-gender congruence and body image satisfaction were higher, and depression and anxiety were lower among individuals who had more extensive GCTs compared to those who have received less treatment or no treatment at all

KEYWORDS: Transgender, gender confirmation treatments, mental health, body image

INTRODUCTION

Transgender is a term used to describe individuals whose gender identity differs from the male or female sex designation usually occurring at birth.[1, 2] A person whose gender identity differs from a female sex designation is referred to as female-to-male or transmasculine (TM) and a person whose gender identity differs from a male sex designation is referred to as male-to-female or transfeminine (TF). The terms TM/TF include a broad spectrum of identities that differ from the gender assigned at birth and can apply to individuals who do not identify with binary categories.[3]

Some transgender individuals experience gender dysphoria (GD), defined as a feeling of distress resulting from the incongruence between physical appearance and gender identity.[4, 5] This distress, compounded by commonplace experiences of stigma, victimization and discrimination, may partly explain the disproportionately high rates of depression and anxiety among TM and TF individuals compared with the general population.[6-8] These mental health issues not only affect an individual's quality of life but are associated with other health problems and higher mortality rates.[9-12] Among transgender individuals, depression has been linked to substance abuse, high risk sexual behaviors, and most notably, suicide.[13-15]

Transgender individuals may seek medical gender confirmation treatments (GCTs), including administration of hormone therapy (HT) to achieve desired masculinization or feminization, and/or surgical change of the genitalia and other secondary sex characteristics. HT may include estrogens for TF and testosterone for TM individuals. Examples of gender confirmation surgeries (GCS) include breast augmentation and vaginoplasty for TF individuals and mastectomy and hysterectomy for TM individuals.[16] Historically, individuals seeking these interventions receive HT first and may choose to undergo surgeries later, after 12 months of continuous HT[17], although not all individuals follow this sequence.

Given that one source of GD is the incongruence between the physical body and gender identity, it follows that medical interventions that alter the body to be more compatible with one's identity could ameliorate this distress. Lindgren and Pauly, the first to explore the effectiveness of GD treatment, found that after HT and/or GCS, body dissatisfaction levels were reduced in both TF and TM study participants.[18, 19] More recent studies have provided additional support that both HT and GCS can decrease the level of overall body dissatisfaction[20, 21] and/or increase

body satisfaction.[22] Similarly, a recent systematic review suggests that HT may lead to improvements in psychological functioning, including reductions in depression and anxiety.[23]

Although these studies offer insights regarding the associations between GCTs and body dissatisfaction/body image, depression and anxiety, they have been limited by several factors. First, the sample sizes were relatively small (22 to 162 participants) and each was based at a single clinical site.[16, 18, 21, 22, 24, 25] Second, data have rarely been presented separately for both TM *and* TF individuals, thus obscuring differences that may exist between these distinct populations.[20] Third, most studies have focused on HT *or* GCS (or assessed HT and GCS together) rather than examining the extent to which individuals <u>at different stages of medical GCT</u> may differ with respect to experiences of body-gender incongruence, body image satisfaction, depression and anxiety.

With these considerations in mind, the aim of the present study was to examine the degree to which body-gender congruence, body image satisfaction, depression and anxiety differed by GCT groups among TM and TF individuals.

MATERIALS AND METHODS

Study population

The present study is based upon the cohort of participants used in the "Study of Transition, Outcomes & Gender (STRONG)." This cohort was recruited from XXX Health Plans located in Georgia (XXX), Northern California (XXX) and Southern California (XXX). The primary goal of STRONG is to assess morbidity among transgender and gender non-conforming individuals overall and among TM/TF subgroups. The three participating XXX health plans are integrated health care systems that currently provide comprehensive health services to approximately 8 million members. Enrollees are socio-demographically diverse and broadly representative of the communities in the corresponding areas.[26]

The study was conducted in partnership with XXX University, which served as the coordinating center. All activities were reviewed and approved by the Institutional Review Boards (IRB) of the four participating institutions. The three XXX organizations use similar electronic medical record (EMR) systems, and have comparably organized databases with identical variable names, formats, and specifications across sites.

The methods of cohort ascertainment were described in detail previously.[27, 28] Briefly, EMR data pertaining to all participating health plan members of all ages enrolled between January 1, 2006 and December 31, 2014 were used to identify two types of evidence supporting transgender/gender non-conforming status: 1) relevant International Classification of Diseases, Ninth Edition (ICD-9) codes; and 2) presence of specific keywords in free-text notes.

Eligibility status was independently verified by two trained reviewers with disagreements adjudicated by a committee that included the project manager and two investigators.

Survey recruitment

The survey eligibility criteria included: age 18 years or older, current enrollment in one of the participating health plans, at least one relevant ICD-9 diagnostic code, and text string-confirmed transgender status. Participants were excluded from the survey if their ICD codes and text strings were limited to mental health records, their XXX physicians did not provide consent for initiating the contact, or in their responses to the screening questions, their gender identity was the same as natal sex. All initial invitations were sent via regular mail. The letter included a website and a unique password linked to the Study ID; participants were asked to read and electronically sign the consent form online prior to survey completion. Subjects who did not respond to the initial invitation were sent up to two reminders.

Survey goal and content

As not all data elements of interest could be ascertained from the EMR data alone, the project also included a cross-sectional survey which collected self-report data via an online survey software tool or by paper for those who did not want/were not able to complete the survey on the internet.

Gender identity (TM and TF status) was determined based on a two-step question: first inquiring about participants' natal (assigned at birth) sex and then asking about their current gender identity. If the gender identity was different from the natal female sex the participant was considered TM; if the gender identity was different from the natal male sex, the participant was considered TF. Five persons who reported being born with intersex conditions were excluded from the current analysis.

GCS. Based on reported history of these GCTs, each participant was placed in one of the following five ordered categories: 1) no gender confirmation therapy to date; 2) HT only; 3) Top surgery (e.g., mastectomy or breast augmentation); 4) Partial bottom surgery (e.g., hysterectomy without vaginectomy or orchiectomy without vaginoplasty); and 5) Definitive bottom surgery (e.g., vaginectomy or vaginoplasty). These categories were ordered in this way based on the level of medical intervention involved (e.g., hormone therapy was considered the least extensive intervention, followed by top surgeries, which typically require one clinician referral; bottom surgeries were considered the most extensive medical interventions, as they are more medically complex procedures, have a higher risk of surgical

complications and typically require two clinician referrals).[29] Although nearly all participants who underwent top or bottom surgery also reported receiving hormones, a history of HT was not required in order for an individual to be classified in a subsequent category. The five-category GCT status was used as the main independent variable of interest. Participants were also asked about their history of procedures aimed at changing secondary sex characteristics such as laryngeal shave, facial feminization, and electrolysis.

Body-gender congruence was measured using the Transgender Congruence Scale (TCS), a validated 15-item instrument aimed at measuring a transgender person's level of comfort with gender identity.[30] Body image satisfaction was measured using the body attractiveness subscale of the previously validated Revised Physical Self-Perception Profile.[31] Information about the participants' depression and anxiety levels was collected using the 10-item Center for Epidemiologic Studies Depression (CESD-10) scale and the Beck Anxiety Index (BAI), respectively.[32, 33] For TCS and body image, the binary outcome of interest was defined as the total score being less than the overall study population median value. For depression and anxiety, the binary outcome was defined using the previously proposed clinically relevant cutoffs of 10 for CESD-10, and 21 for BAI.[32, 34]

Data analyses

The objectives of these analyses were to compare body-gender congruence, body image satisfaction, and levels of depression, and anxiety across categories of subjects at different stages of GCT. The distributions of dependent variables of interest were compared across GCT categories by calculating category-specific median and interquartile range (IQR) values. The differences in the distributions were examined using Kruskall-Wallis tests separately for TM and TF participants.

Multivariable logistic regression models were used to examine the association between GCT categories and each outcome of interest. The covariates in the model included age, study site, race/ethnicity, TM/TF status, and receipt of procedures for changing secondary sex characteristics (e.g., laryngeal shave or facial electrolysis for TF and "facial masculinization" for TM).

To address the effect of survey non-response on study results, each logistic regression analysis was replicated using weighted models. The weights for the models represented inverse selection probabilities. The selection probabilities were obtained from a separate logistic model, which included all STRONG cohort members who were

invited to participate in the survey. The binary dependent variable in this model was response to the survey and independent variables included age, TM/TF status, race/ethnicity, study site and receipt of HT and GCS.

The results of both weighted and unweighted multivariable analyses were expressed as adjusted prevalence ratios (PR) and corresponding 95% confidence intervals (CI) using the 'rlogist' procedure in the SAS-callable SUDAAN® statistical software package (RTI International, Research Triangle Park, NC).

RESULTS

Of the 2,136 individuals invited to participate, 697 subjects (33%) completed the survey: 347 were TM and 350 were TF individuals. TM respondents were younger than their TF counterparts (73% vs. 35% under the age of 40 years, Table 1). More than half of survey respondents (55% of TM and 57% of TF respondents) were non-Hispanic Whites. The proportion of Hispanics (19%) was similar to that reported in the overall cohort, but the proportions of Blacks and Asians were lower (3% and 7% respectively) than in the EMR-based study. Only 4% of survey respondents (n=28) had no history of GCT and approximately one-third (n=234) received HT without any surgery. Top surgery category included 41% of TM subjects, but only 8% of TF participants. By contrast, definitive bottom surgery was more common among TF (33%) compared to TM (11%) study subjects. Only 7 individuals reported receiving surgery but not HT; most of those were TM who underwent top surgery. Receipt of procedures aimed and changing secondary sex characteristics was reported in 11.5% of participants (1.2 % of TM and 21.7% of TF individuals).

Table 2 compares the distributions of the four dependent variables of interest: total TCS score, body image satisfaction score, CESD-10 depression score, and BAI anxiety score by TM/TF status and by GCT category. As the extent of GCTs increased (from no treatment to definitive bottom surgery), the TCS and body image satisfaction scores also increased (i.e., were more favorable), with no appreciable difference between TM and TF participants. The results were generally similar in the analyses that examined distributions of the CESD-10 and BAI scores.

The bivariate associations were similar to the results obtained in the multivariable logistic regression analyses.

There was no evidence of an important multiplicative interaction between gender identity and GCT, and for this reason all models include TM/TF status as a covariate.

The association of GCTs with the outcomes of interest was evident in all models, but particularly pronounced for the TCS score. The proportion of participants with low (below median) TCS scores was nearly four times higher in the "no reported treatment" category (PR=3.96, 95% CI 2.72-5.75) compared to the "definitive bottom" surgery group (Table

3). The overall patterns were similar, but the PR estimates were of lower magnitude, in the regression models that assessed body image satisfaction (Table 3). In the analyses of the CESD-10 score (Table 4) the PR for moderate/severe depression (>10 points) comparing participants who reported no treatment relative to those who had definitive surgery was 1.94 (95% CI: 1.42-2.66). The corresponding PR for clinically significant anxiety (BAI >21 points) was 4.33 (95% CI 1.83-10.54; Table 4). Procedures used to change secondary sex characteristics were not associated with TCS scores, body image satisfaction, depression or anxiety (Tables 3-4). The results of the weighted models adjusting for non-response were generally similar to those of the main analyses (Tables 3-4).

DISCUSSION

For both TM and TF participants, body-gender congruence and body image satisfaction were higher among individuals who had more extensive GCT compared to those who have received less treatment or no treatment at all. These findings are consistent with previous evidence that HT[20] and GCS[21, 22, 24] lead to improved body satisfaction among transgender individuals. This result is consistent with our understanding of GD in that one of the roots of GD is a high level of body image dissatisfaction[35] and this distress may be alleviated by receiving interventions that result in a more closely-aligned physical body with gender identity. GCTs may also increase one's confidence in passing as a member of the preferred gender. For example, TM taking testosterone experience a redistribution of fat, increased muscle mass and a deepened voice, which promotes a more masculine appearance; similarly, TF individuals taking estrogens and antiandrogens experience reduced facial hair growth, an increase in fat deposits around the hips and buttocks, breast growth and reduced muscle mass, which promotes a more feminine appearance.[36] Previous research has underscored the importance of social "passing" for positive body image and body satisfaction and feelings of "passing" have been associated with a higher quality of life and self-esteem.[37]

Evidence suggests that in addition to exacerbating symptoms of GD, body image dissatisfaction can lead to secondary health problems among transgender individuals. For example, a study conducted among German, Swiss and Austrian participants showed that TM individuals displayed higher degrees of restrained eating patterns, weight and shape concerns, body dissatisfaction, and body checking (e.g., frequent weighing, looking in the mirror, pinching the stomach, waist, thighs or arms, etc.) than male controls: TF individuals showed more restrained eating, bulimic behavior, and body checking than male controls, and higher degrees of weight and shape concerns, body image dissatisfaction, and body checking than female controls.[38] Body dissatisfaction and poor body image can also predispose individuals to chronic

depression, substance use/abuse, and several affective spectrum and somatic disorders.[39] Clearly, body dissatisfaction can lead to significant morbidities in this population and thus interventions that reduce risk for these conditions, such as GCTs, warrant serious consideration.

Our results also indicate that depression, and especially anxiety, were lower among individuals who received a more extensive GCTs compared to those who received less treatment or no treatment at all. These findings are consistent with and extend results from previous studies that have similarly reported that HT and GCS can result in lower levels of depression and anxiety.[16, 40-42] Historically, standard clinical practice has been to first treat any comorbid psychological conditions such as depression and anxiety prior to referring a transgender individual for GCTs.[43] As medical GCTs can be both physically and psychologically taxing[40] individuals with well-managed mental health issues may be best prepared to undergo this treatment. On the other hand, withholding HT or GCS until depression or anxiety have been treated may not be the optimal treatment course given the benefits of reduced levels of distress after undergoing GCT. The more recent clinical guidelines such as the World Professional Association for Transgender Health (WPATH) Standards of Care now recognize that HT may improve overall mental health status.[29] Given the alarmingly high rates of suicide attempts among transgender populations[7, 44-46] and recent evidence suggesting that suicide attempt rates decrease after GCS,[47] it is critical to consider all possible interventions with the potential to ameliorate psychological distress in this population. Healthcare providers must balance these potential benefits against possible adverse events related to HT (e.g., thromboembolism) and GCS (e.g., infections or other complications) as well as patient preferences/values and the availability/affordability of treatments.

Health insurance coverage for GCTs, particularly surgery, remains an area of controversy. For example, in 2016 the Centers for Medicare and Medicaid Services (CMS) announced the decision to not issue a National Coverage Determination on gender reassignment surgery for Medicare beneficiaries with GD because the clinical evidence was deemed inconclusive. In its decision memo, the CMS indicated that it "encourages robust clinical studies that will fill the evidence gaps and help inform which patients are most likely to achieve improved health outcomes with gender reassignment surgery, which types of surgery are most appropriate, and what types of physician criteria and care setting(s) are needed to ensure that patients achieve improved health outcomes."[48] Findings from this study indicate that GCTs may be particularly beneficial for psychosocial conditions. However, additional research is needed to ascertain the

benefits and harms of these interventions. Of particular concern are the effects on different subgroups such as those with more severe pre-existing psychiatric illness and individuals with varying levels of social support.

Several limitations of the present study should be recognized. The cross-sectional design of the survey does not allow for causal inferences with respect to the association between stage of GCT and body-gender congruence, body image satisfaction, depression, and anxiety. For example, individuals who are less depressed/anxious could be more likely to seek GCTs than those who are more depressed/anxious. However, a recent prospective study reported that, over the course of HT, participants with gender dysphoria reported significant reductions in general psychopathology and depressive symptoms, providing some evidence for the temporal association between GCTs and improvements in mental health-related outcomes.[49] The current study sample included only a small proportion of individuals who received no GCTs at all. These individuals were underrepresented because of the IRB requirement that eligible subjects had to have both a diagnostic code and a text string-confirmed transgender status, and could not receive transgender care exclusively from mental health providers. Additional prospective studies with large sample sizes and longer follow-up periods are needed to assess these constructs before and after receipt of GCTs. We also recognize that transgender individuals enrolled through integrated health care systems such as KP represent a cohort of individuals with health insurance that may not be representative of the transgender population in the US. It is expected that some of the results may differ among transgender individuals from different socioeconomic strata. Weighing against this concern is the demonstrated ability to cost-effectively identify a large cohort of transgender subjects with a high degree of internal validity. The availability of the well-defined sampling frame and extensive data on both respondents and non-respondents permitted quantitative adjustment for selection bias. Further, the present study, in contrast to prior research, included approximately equal numbers of TF and TM participants, which allowed us to examine differences and similarities of these two populations. The ability to combine data on HT and GCS allowed us to investigate the extent to which individuals at different stages of GCT may differ with respect to experiences of body-gender congruence, body image satisfaction, depression and anxiety.

CONCLUSIONS

In sum, results from the present study provide evidence for an association between participants' stage of GCT and their perceived body-gender incongruence and body image satisfaction as well as their symptoms of depression and anxiety. These findings were consistent for both TM and TF participants. Future research is needed to assess the temporal

association between GCTs and psychosocial outcomes employing robust study designs, including larger-scale longitudinal cohort studies, and utilizing standardized scales and clinician-delivered mental health outcome measures in order to facilitate inferences and draw more definitive conclusions.

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TABLES

Table 1: Characteristics of the STRONG survey participants

Participant	All subjects	Transmasculine	Transfeminine		
characteristics	n (col %)	n (col %)	n (col %)		
Total, n (row %)	697 (100.0)	347 (50.0)	350 (50.0)		
Age at time of survey					
18-29	217 (31.1)	148 (42.7)	69 (19.7)		
30-39	157 (22.5)	105 (30.3)	52 (14.9)		
40-54	168 (24.1)	69 (19.9)	99 (28.3)		
55 or older	155 (22.2)	25 (7.2)	130 (37.1)		
Presents as a woman					
Never	330 (47.3)	310 (89.3)	20 (5.7)		
Part-time	67 (9.6)	22 (6.3)	45 (12.9)		
Full-time	273 (39.2)	5 (1.4)	268 (76.6)		
Declined to respond	27 (3.9)	10 (2.9)	17 (4.9)		
Presents as a man					
Never	277 (39.7)	16 (4.6)	261 (74.6)		
Part-time	63 (9.0)	22 (6.3)	41 (11.7)		
Full-time	323 (46.3)	297 (85.6)	26 (7.4)		
Declined to respond	34 (4.9)	12 (3.5)	22 (6.3)		
Race/ethnicity					
Non-Hispanic Whites	392 (56.2)	191 (55.0)	201 (57.4)		
Non-Hispanic Blacks	20 (2.9)	13 (3.7)	7 (2.0)		
Asian/Pacific islanders	48 (6.9)	25 (7.2)	23 (6.6)		
Hispanics	133 (19.1)	68 (19.6)	65 (18.6)		
Mixed race/ethnicity	18 (2.6)	8 (2.3)	10 (2.9)		
"Other" race/ethnicity	49 (7.0)	27 (7.8)	22 (6.3)		
Declined to respond	37 (5.3)	15 (4.3)	22 (6.3)		
Education					
High school graduate or less	74 (10.6)	45 (13.0)	29 (8.3)		
At least some college	242 (34.7)	100 (28.8)	142 (40.6)		
College graduate	197 (28.3)	104 (30.0)	93 (26.6)		

150 (21.5)	81 (23.3)	69 (19.7)
34 (4.9)	17 (4.9)	17 (4.9)
127 (18.2)	69 (19.9)	58 (16.6)
138 (19.8)	65 (18.7)	73 (20.9)
120 (17.2)	65 (18.7)	55 (15.7)
93 (13.3)	47 (13.5)	46 (13.1)
128 (18.4)	51 (14.7)	77 (22.0)
91 (13.1)	50 (14.4)	41 (11.7)
28 (4.0)	11 (3.2)	17 (4.9)
234 (33.6)	76 (21.9)	158 (45.1)
171 (24.5)	142 (40.9)	29 (8.3)
80 (11.5)	64 (18.4)	16 (4.6)
153 (22.0)	39 (11.2)	114 (32.6)
31 (4.4)	15 (4.3)	16 (4.6)
80 (11.5)	4 (1.2)	76 (21.7)
617 (88.5)	343 (98.8)	274 (78.3)
	34 (4.9) 127 (18.2) 138 (19.8) 120 (17.2) 93 (13.3) 128 (18.4) 91 (13.1) 28 (4.0) 234 (33.6) 171 (24.5) 80 (11.5) 153 (22.0) 31 (4.4) 80 (11.5)	34 (4.9) 17 (4.9) 127 (18.2) 69 (19.9) 138 (19.8) 65 (18.7) 120 (17.2) 65 (18.7) 93 (13.3) 47 (13.5) 128 (18.4) 51 (14.7) 91 (13.1) 50 (14.4) 28 (4.0) 11 (3.2) 234 (33.6) 76 (21.9) 171 (24.5) 142 (40.9) 80 (11.5) 64 (18.4) 153 (22.0) 39 (11.2) 31 (4.4) 15 (4.3)

^a Only 7 individuals reported receiving surgery but not HT. Most of those were TM who underwent top surgery.

Outcome measure by gender		Transmasculine			Transfeminine	
confirmation category	Median	IQR ^e	p-value ^f	Median	IQR ^e	p-value ^f
Transgender congruence score ^a						
No treatment	30	22-36	< 0.0001	30	25-46	< 0.0001
HT only	43	32-51		44	33-50	
Top surgery	50	44-56		44	39-52	
Partial bottom surgery	49	42-55		51	37-57	
Definitive bottom surgery	55	49-59		53	48-57	
Body image satisfaction score ^b						
No treatment	9	9-16	< 0.0001	11	6-18	0.0065
HT only	12	7-18		15	10-20	
Top surgery	17	12-22		12	9-19	
Partial bottom surgery	15	9-18		14	10-22	
Definitive bottom surgery	16	13-21		18	13-22	
CESD-10 depression score ^c						
No treatment	16	13-23	0.0016	14	10-21	0.0002
HT only	12	8-18		10	5-16	
Top surgery	8	4-13		11	6-16	
Partial bottom surgery	9	4-15		8	3-16	
Definitive bottom surgery	6	3-14		6	3-11	
BAI anxiety scored						
No treatment	25	16-26	0.0006	12	7-25	0.0015
HT only	12	7-26		9	2-17	
Top surgery	7	4-17		7	3-13	
Partial bottom surgery	9	2-17		9	3-13	
Definitive bottom surgery	5	2-13		5	1-10	

Definitive bottom surgery

**Composite of 12 questions, possible range: 12-60; higher scores indicate greater level of comfort with gender identity.

**Composite of 5 questions, possible range: 5-25; higher scores indicate a higher level of body image satisfaction.

**Composite of 10 questions, possible range: 0-30; higher scores indicate higher levels of depression.

**Composite of 21 questions, possible range: 0-63; higher scores indicate higher levels of anxiety.

Interquartile range

Kruskal-Wallis test

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Table 3: Associations of gender confirmation, gender identity, and procedures aimed at changing secondary sex characteristics with low transgender congruence and body image scores

Variables		N (%) within	Unweighted analyses			Weighted analyses			
of interest	N	treatment category	PR^a	95% CI ^b		\mathbf{PR}^{a}	95% CI ^b		
Transgender congruence score below median ^c									
Gender confirmation category									
Definitive bottom surgery	149	33 (22%)	1.00	(refe	erence)	1.00	(refe	(reference)	
Partial bottom surgery	77	34 (44%)	2.11	1.38	3.23	2.15	1.37	3.37	
Top surgery	161	71 (44%)	2.06	1.39	3.05	2.10	1.39	3.17	
HT only	210	138 (66%)	3.03	2.14	4.30	3.22	2.25	4.61	
No treatment	27	23 (85%)	3.96	2.72	5.75	3.66	2.28	5.88	
Gender identity									
Transfeminine	306	150 (49%)	1.00	(refe	erence)	1.00	(reference)		
Transmasculine	318	149 (47%)	0.95	0.77	1.15	1.03	0.83	1.28	
Changes in secondary sex characteristics									
Yes	75	30 (40%)	1.00	(reference)		1.00	(reference)		
No	549	269 (49%)	0.88	0.68	1.12	0.87	0.68	1.13	
Body image score below median ^d									
Gender confirmation category									
Definitive bottom surgery	150	49 (33%)	1.00	(reference)		1.00	(reference)		
Partial bottom surgery	79	39 (49%)	1.42	1.01	2.01	1.58	1.10	2.26	
Top surgery	167	67 (40%)	1.19	0.85	1.65	1.25	0.88	1.78	
HT only	220	116 (53%)	1.59	1.20	2.10	1.72	1.27	2.32	
No treatment	28	17 (61%)	1.81	1.22	2.68	1.75	1.08	2.83	
Gender identity									
Transfeminine	319	139 (44%)	1.00	(reference)			(reference)		
Transmasculine	325	149 (46%)	1.09	0.88	1.36	1.11	0.88	1.39	
Procedures to change secondary sex characteristics									
Yes	77	24 (31%)	1.00	(reference)			(reference)		
No	567	264 (47%)	1.24	0.87	1.76	1.29	0.87	1.90	

^a PR, prevalence ratio adjusted for age, race, study site, and all variables listed in the table.

b CI, confidence interval

⁶ Model based on 624 observations

d Model based on 644 observations

Table 4: Associations of gender confirmation, gender identity, and procedures aimed at changing secondary sex characteristics with high

Variables of interest		N (%) within treatment category	Unweighted analyses			Weighted analyses		
			PR ^a 95% CI ^b		PR^{a}	95% CI ^b		
CESD-10 score above 10 ^c								
Gender confirmation category								
Definitive bottom surgery	141	50 (35%)	1.00	(reference)		1.00	(reference)	
Partial bottom surgery	75	34 (45%)	1.19	0.84	1.67	1.18	0.84	1.6
Top surgery	158	66 (42%)	1.00	0.73	1.38	0.96	0.69	1.3
HT only	198	113 (57%)	1.40	1.07	1.83	1.38	1.05	1.8
No treatment	26	20 (77%)	1.94	1.42	2.66	2.01	1.51	2.6
Gender identity								
Transfeminine	293	139 (47%)	1.00	(reference)			(reference)	
Transmasculine	305	144 (47%)	0.92	0.74	1.15	0.91	0.73	1.1
Changes in secondary sex characteristics								
Yes	71	30 (42%)	1.00	(reference)			(reference)	
No	527	253 (48%)	0.91	0.69	1.18	0.93	0.72	1.2
Anxiety score above 21 ^d								
Gender confirmation category								
Definitive bottom surgery	139	8 (5.8%)	1.00	(reference)		1.00	(reference)	
Partial bottom surgery	73	13 (18%)	1.93	0.82	4.53	1.41	0.57	3.4
Top surgery	159	34 (22%)	1.90	0.86	4.18	1.51	0.68	3.3
HT only	195	47 (24%)	2.59	1.21	5.54	2.15	1.02	4.5
No treatment	26	11 (42%)	4.33	1.83	10.54	2.74	1.10	6.8
Gender identity								
Transfeminine	296	42 (14%)	1.00	(reference)		1.00	(reference)	
Transmasculine	296	71 (24%)	1.26	0.81	1.94	1.38	0.87	2.2
Procedures to change secondary sex characteristics		. ,						
Yes	72	6 (8.3%)	1.00	(reference)		1.00	(reference)	
No	520	107 (21%)	1.00	0.48	2.11	1.05	0.49	2.2

^a PR, prevalence ratio adjusted for age, race, study site, and all variables listed in the table.

^b CI, confidence interval

^c Model based on 598 observations ^d Model based on 592 observations