# Outcome of Vaginoplasty in Male-to-Female Transgenders: A Systematic Review of Surgical Techniques: Systematic Review: Vaginoplasty in MtF Transgenders

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# Outcome of Vaginoplasty in Male-to-Female Transgenders: A Systematic Review of Surgical Techniques

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**ABSTRACT**

***Introduction.*** Gender reassignment surgery is the keystone of the treatment of transgender patients. For male-to-female transgenders, this involves the creation of a neovagina. Many surgical methods for vaginoplasty have been opted. The penile skin inversion technique is the method of choice for most gender surgeons. However, the optimal surgical technique for vaginoplasty in transgender women has not yet been identified, as outcomes of the different techniques have never been compared.

***Aim.*** With this systematic review, we aim to give a detailed overview of the published outcomes of all currently available techniques for vaginoplasty in male-to-female transgenders.

***Methods.*** A PubMed and EMBASE search for relevant publications (1995–present), which provided data on the outcome of techniques for vaginoplasty in male-to-female transgender patients.

***Main Outcome Measures.*** Main outcome measures are complications, neovaginal depth and width, sexual function, patient satisfaction, and improvement in quality of life (QoL).

***Results.*** Twenty-six studies satisfied the inclusion criteria. The majority of these studies were retrospective case series of low to intermediate quality. Outcome of the penile skin inversion technique was reported in 1,461 patients, bowel vaginoplasty in 102 patients. Neovaginal stenosis was the most frequent complication in both techniques. Sexual function and patient satisfaction were overall acceptable, but many different outcome measures were used. QoL was only reported in one study. Comparison between techniques was difficult due to the lack of standardization.

***Conclusions.*** The penile skin inversion technique is the most researched surgical procedure. Outcome of bowel vaginoplasty has been reported less frequently but does not seem to be inferior. The available literature is heterogeneous in patient groups, surgical procedure, outcome measurement tools, and follow-up. Standardized protocols and prospective study designs are mandatory for correct interpretation and comparability of data. **Horbach SER, Bouman M-B, Smit JM, Özer M, Buncamper ME, and Mullender MG. Outcome of vaginoplasty in male-to-female transgenders: A systematic review of surgical techniques. J Sex Med **;**:**–**.**

***Key Words.*** Vaginoplasty; Transsexualism; Gender Identity Disorder; Sex Reassignment Surgery; Penile Inversion Vaginoplasty; Bowel Vaginoplasty

## Introduction

The phrases "Gender Identity Disorder" and "Gender Dysphoria" apply to patients with a strong and persistent cross-gender identification, a persistent discomfort with their anatomical sex, and a sense of inappropriateness in the gender role of that sex, which causes significant distress in social, occupational, and other important areas of functioning. This commonly leads to the belief of

being born in the wrong sex and a preoccupation with losing secondary sexual characteristics of the anatomical sex [1,2].

The importance and potential benefits of genital sex reassignment surgery (SRS) were first advocated by Harry Benjamin, with the release of his book "The Transsexual Phenomenon" [3] in 1966 [2,4]. Since 1979, the Harry Benjamin International Gender Dysphoria Association (now World Professional Association for Transgender Health) has been establishing evidence-based "Standards of Care": guidelines for diagnostics and treatment of transgender patients. These clinical guidelines provide a stepwise procedure that consists of diagnostic assessment, real-life experience and psychotherapy, hormone therapy, and surgical therapy [5].

The advantages of therapy for gender dysphoric patients have been pointed out by various studies in the past decades. Recently, a large-scale study by de Vries et al. [6] found a significant improvement in psychological functioning and well-being of transgender adolescents after hormonal and surgical therapy. Most transgenders indicate an improvement in sex life and report more sexual excitement after SRS [7]. For male-to-female (MtF) transgenders, a correlation was seen between neovaginal anatomy and satisfaction with the neovagina and sexual functioning [7,8].

Nowadays, treatment of patients with gender dysphoria is becoming more and more accepted by the general public and surgical treatment for especially MtF transgenders is performed worldwide.

For MtF transgenders, the core surgical procedures are orchidectomy, penectomy, clitoroplasty, labiaplasty, and creation of the neovagina, together often referred to as "(neo)vaginoplasty." Other common surgical procedures for the establishment of a feminine aesthetic appearance are breast augmentation, facial feminization surgery, permanent hair removal, lipoplasty, and thyroid chondroplasty [9,10]. In the fields of gynecology, urology, and reconstructive plastic surgery, many surgical techniques for vaginal (re)construction have been described [2,10–13]. Not only MtF transgenders but also biological women with disorders of sexual development (such as Mayer-Rokitansky-Kustner or intersex disorders) and those who underwent vaginectomy after malignancy or trauma are possible candidates for vaginoplasty.

In transgender vaginoplasty, surgical techniques can be divided in three main categories, based on the origin of the donor tissue [2,14]:

1. Skin grafts.
2. Penile-scrotal skin flaps.
3. Pedicled small or large bowel segments.

Experimental options for creating a neovagina are the use of buccal mucosa, amnion grafts, or decellularized tissue. Most gender surgeons prefer the use of inverted penoscrotal skin flaps. However, it is still unclear what the optimal surgical technique is, as the outcomes of the available surgical techniques have never been compared.

## Key Objectives

Our main goal is to give an overview of available surgical techniques for vaginoplasty, and their outcomes in MtF transgender patients, by reviewing all published data in the past 20 years. Ideally, this would make it possible to identify the best available technique for vaginoplasty in MtF transgenders. Our second goal is to reveal gaps in current literature, which can form the basis for further research.

## Methods

For this systematic review, data collection and analysis was performed according to the guidelines of the PRISMA statement 2009 [15]. Inclusion criteria and methods of analysis were specified in advance.

### *Search Strategy*

We have performed a broad systematic search in Medline and EMBASE bibliographic databases for studies that report the outcome of vaginoplasty in MtF transgenders. This search strategy was peer reviewed by an information specialist at the VU University medical library.

A search strategy was made using a combination of (MeSH) terms such as *neovagina*, *vaginoplasty*, *transsexualism*, and synonyms (Table 1). The PubMed function "Citated references" and reference lists of all included articles were screened for additional relevant literature. A database of retrieved articles was made using Reference Manager 2012 (Thomson Reuters), and all duplicates were removed from our database.

### *Study Selection*

The first selection was made based on title and abstract without blinding to authorship or journal by one author (S.H.). Remaining articles were analyzed by two independent researchers (S.H. and

**Table 1** Search strategy EMBASE and PubMed

**PubMed/MEDLINE**
(vaginoplast*[tiab] OR neovagina*[tiab] OR vaginoplast*[ot] OR neovagina*[ot]) AND
("Transsexualism"[Mesh] OR "Sex Reassignment Procedures"[Mesh] OR "Transgendered Persons"[Mesh] OR "Health Services for Transgendered Persons-[Mesh] OR sex reassignment*[tiab] OR sex change*[tiab] OR gender reassignment*[tiab] OR transsex*[tiab] OR gender change*[tiab] OR transgender*[tiab] OR intersex*[tiab] OR gender identity disorder*[tiab] OR sex reassignment*[ot] OR sex change*[ot] OR gender reassignment*[ot] OR transsex*[ot] OR gender change*[ot] OR transgender*[ot] OR intersex*[ot] OR gender identity disorder*[ot])
**EMBASE**
"vagina reconstruction"/exp OR vaginoplast*:ab,ti OR neovagina*:ab,ti OR (vagina NEAR/3 reconstruct*):ab,ti OR (vaginal NEAR/3 reconstruct*):ab,ti OR colovagin*:ab,ti
AND
("transsexuality"/exp OR "transsexualism"/exp OR "sex reassignment"/exp OR (sex NEAR/3 reassignment*):ab,ti OR (sex NEAR/3 change*):ab,ti OR (gender NEAR/3 reassignment*):ab,ti OR transsex*:ab, ti OR (gender NEAR/3 change*):ab,ti OR transgender*:ab,ti OR ("gender identity" NEAR/3 disorder*):ab,ti)
*-Additional use of terms "vaginal reconstruct*" and "colovagin*" did not retrieve extra relevant items*
*-MeSH = Medical Subject Heading, Tiab/ab,ti = Title and abstract*
*-Date search PubMed january 22th 2014, EMBASE may 21st 2014; last search for updates july 2014*

M.B.) based on full text. Articles that met all inclusion criteria (as shown in Table 2) were included in the systematic review. No restrictions were imposed with regard to study design and surgical background of the author. If eligibility was doubtful, articles were discussed by the investigators and were in- or excluded based on consensus.

### *Data Extraction and Data Analysis*

Information from each included trial was extracted by one author (S.H.) and categorized based on (i) number of (MtF) patient group; (ii) type of surgical technique used for the creation of the neovagina; and (iii) type of outcome measure, including long- and short-term complications, sexual function, aesthetic outcome, patient satisfaction, and quality of life (QoL). The extracted data from each included article were checked and confirmed by the second author (M.B.).

Quality assessment of the studies was performed using the Quality Assessment Tool for Quantitative studies of the Effective Public Health Practice Project, which grades the papers as "weak," "moderate," or " strong" based on six different domains (selection bias, study design, confounders, blinding, data collection methods and withdrawals, and drop-outs) [16].

A statistical analyst at the VU University Medical Center was consulted to determine which method was applicable for statistical analysis of the retrieved data. Only studies that explicitly reported on a particular outcome were taken into account in the analysis of that specific outcome variable. Due to heterogeneity of the outcome measures and patient groups, meta-analysis of the pooled data was impossible [17]. Only when outcome measures were identical, a mean percentage was calculated.

## Results

With our initial literature search, a total of 216 references were retrieved, ultimately 25 studies examining the outcome of neovaginoplasty in MtF patients were included in our systematic review (Figure 1). A large number of 25 conference abstracts had to be excluded, because subsequent full-text journal publications were unavailable.

### *Skin Grafts*

In this literature search, only three eligible articles were found in which local nongenital skin flaps, full-thickness graft (FTG) or split-thickness skin grafts (STG) were used for the creation of the

**Table 2** Inclusion and exclusion criteria

| Inclusion criteria: | Exclusion criteria: |
|---|---|
| ✓ Patient group of n ≥ 5 male-to-female transgenders | x Patient groups consisting only of patients other than MtF transgenders, e.g., patients with vaginal aplasia or vaginectomy |
| ✓ All ages | x Surgical techniques for partial reconstruction of the vagina or correction of complications after vaginoplasty |
| ✓ All techniques for complete vaginoplasty | x Surgical techniques only for creation of neoclitoris or labioplasty |
| ✓ Publication year >1994 | x Unspecified surgical technique |
| ✓ Article reports at least one outcome measure; e.g., complications, patient satisfaction, sexual function or QoL | |
| ✓ Follow-up of at least 0.5 year | |

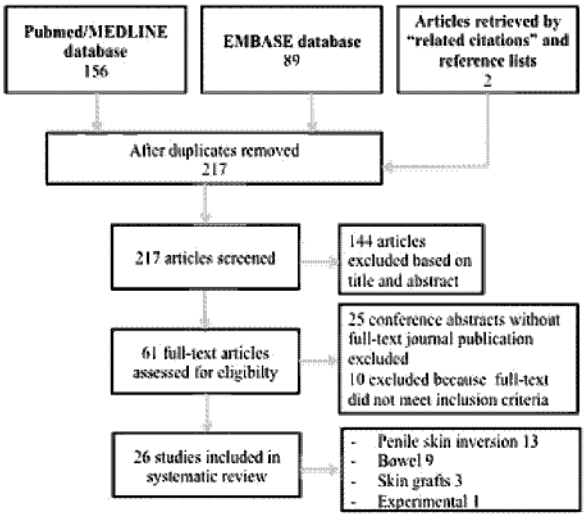


**Figure 1** Flow diagram of study selection according to PRISMA

neovagina. All were retrospective studies published in the period of 1995–1998 (Table 3) [13,18,19].

Hage and Karim [18] obtained a full-thickness skin graft from the lower abdomen of six MtF patients and used a mold to insert it in the neovaginal cavity. The mold was removed after 8 days. In a follow-up of 7 months, they saw no postoperative complications and stated that "all patients were pleased with the neovaginal results" and that "sexual intercourse was possible and satisfactory for all patients." Mean depth was 12 cm, and mean width was 3 cm.

Huang [19] used two different surgical techniques. In a group of 12, the new vagina was constructed out of a penile skin flap and an STG; in the second group of 109 patients, the neovagina consisted out of penile skin flap and an extended inguinopudendal neurovascular island pedicle flap (included the inferolateral portion of the scrotal sac and the medial skin of the inguinal crease). In the first group, vaginal stenosis was seen in 33% and urethral meatus stricture in 0%. In the second study group, these percentages were, respectively, 0% and 6%. Depth was estimated on 8–10 cm. Patient satisfaction was not mentioned.

In a group of 11 MtF transgenders, Siemssen and Matzen [13] used FTG of penile skin, STG, or a combination of both. Overall, vaginal stenosis was present in 45% of patients (n = 5) but with STG alone in 100%. Other complications were defects of transplanted skin (n = 5), hematoma (n = 4), fistula (n = 2), vaginal prolapse (n = 2), and

**Table 3** Study characteristics and outcome of vaginoplasty with nongenital skin flaps and skin grafts

| Study | Study design | Quality assessment | N (Total/MTF) | Surgical technique | Outcome complications | Outcome anatomy neovagina | Outcome sexual function | Outcome patient satisfaction | Outcome QoL | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|
| Hage and Karim [18] | Retrospective | Weak | MTF 5 | Abdominal full-thickness skin graft | No postoperative complications (FU 7 months) | Depth mean 12 cm<br>Width mean 3 cm | "Sexual intercourse was possible and satisfactory for all patients" (100%) | "all patients were pleased with the neovaginal result" (100%) | — | Mean 7 months (3–18 months) |
| Huang [19] | Retrospective | Weak | MTF 121 | 1. Penile skin graft/ flap + split-thickness skin graft 12<br>2. Inguinoperineal skin flaps 109 | Vaginal stenosis<br>1. 4/12 (33%)<br>2. 5/109 (5%)<br>Urethral meatus stricture<br>1. 0/12 (0%)<br>2. 7/109 (6%) | Depth possibly 8–10 cm | — | — | — | >6 months |
| Siemssen and Matzen [13] | Retrospective | Weak | MTF 11 | Full-thickness skin graft penis (4)<br>Combined with STG or FTG (4)<br>Split-thickness skin graft alone (3) | Vaginal stenosis 5/11 (45%)<br>STG alone: 100%<br>Vaginal defects in transplanted skin 5/11 (45%)<br>Hematoma/hemorrhage 4/11 36%<br>Fistula 2/11 (18%)<br>Vaginal prolapse 2/11 (18%)<br>Infection 1/11 (9%) | — | — | — | — | (0–86 months) |

FTG = full-thickness skin graft; FU = follow-up; MTF = male-to-female; STG = split-thickness skin graft

infection (n = 1). Neovaginal depth and width were not reported, and patient satisfaction and QoL were not mentioned.

### *Penoscrotal Skin Flaps (Penile Skin Inversion Technique)*

For many gender surgeons, the method of choice for vaginoplasty is the "penile skin inversion technique," in which inverted penile skin on an abdominal or inferior pedicle is used as an outside-in skin tube for the lining of the neovagina [2,20]. It can be split open to form a rectangular flap, and it can be combined with a urethral flap [21] or scrotal flaps of multiple designs.

A total of 12 (10 retrospective and two prospective) original studies were found in which the penile skin inversion technique was used, with or without an additional scrotal flap, in a total of 1,461 patients. One review was included [10]. Study characteristics and outcomes of these articles are shown in Table 4.

## Neovaginal Anatomy

Mean neovaginal depth ranged from 10 cm to 13.5 cm. The shallowest neovagina reported was 2.5 cm and the deepest 18 cm. The mean width of the neovagina was 3–4 cm, only described in one study [22]. Perovic et al. [21] categorized the width of 87 neovaginas in "small" (9%), "medium" (77%), or "large" (14%) groups, estimated by the diameter of the vaginal stent that was used. No information was available about the exact measurements of the vaginal stents or neovaginas in this study.

## Complications

*Genital Region.* Neovaginal stricture was reported in six studies [21,22,26,28,30,31]. Stricture of the neovaginal introitus was present in 84 of 674 studied patients (12%, range 4.2–15%). In most cases, a U-shaped introitus plasty was performed, but recurrence rates after correction were not reported in the available literature. In Jarolim [26], a second operation was necessary to "free the introitus" for easier penetration at later date in 12 of 29 patients (41%). In 43 patients of a total of 582 (7%, range 1–12%), stricture of the vagina other than the introitus was reported. Vaginal shrinkage was seen in 2–10% of treated patients [21,32].

Partial necrosis of the neovagina ranged from 2.7% to 4.2% [22,23,31] and clitoral necrosis ranged from 1% to 3% [27,28,30]. Namba et al. [29] used an M-shaped perineoscrotal flap in addition to an inverted penile skin flap for the lining of the neovaginal cavity. In this small group of six patients, there was necrosis of two scrotal flaps (33%). Neovaginal (posterior) wall rupture was seen in one patient after sexual intercourse in a group of 87 and was only described by Perovic et al. [21], who used a urethral flap for the anterior neovaginal wall. Genital pain was present in 9% [28] and 3% [31] in patient groups of, respectively, 232 and 332 MtF patients.

In four studies [10,21,22,29] with a total of 917 MtF patients, nine cases of rectovaginal fistula were reported, with a mean percentage of 1% (range 0.8–17%). The prevalence of neovaginal prolapse was 1–2% in four studies [23,27,30,31]. All surgeons in these studies had fixated the neovagina with sutures to the surrounding connective tissue during initial surgery; fixation to the sacrospinous ligament was not reported. Only two studies report secondary cosmetic corrections in 54% [22] and 31% [26] of patients.

*Urinary Tract.* Hoebeke et al. [25] are the only authors who investigated the impact of sex reassignment surgery on the lower urinary tract system in a group of 31 MtF patients. Changed voiding after SRS was reported in 32% of these patients (better 13%, same 68%, worse 19%). Six of these patients (19%) suffered from involuntary loss of urine at a mean follow-up of 3 years after surgery, two were cases of urge incontinence, two stress incontinence, one mixed incontinence, and one patient complained of dribbling. Urinary infection was seen in 10 patients (32%), with a mean episode rate of 1.7. Of the patients who were sexually active, 15% (4 out of 27) had a urinary infection after vaginal sex.

Meatal stenosis was reported in five original studies [21,22,27,28,30] with a mean percentage of 5% (33 out of 658) and a range of 1–6%. Selvaggi and Bellringer [10] claim that meatal stenosis is present in 3–4% of cases, referring to their own unpublished work. Rossi Neto et al. [31] saw meatal stenosis as the most frequent complication related to the surgery, 40% of their patients presented with an obstructive voiding disorder (with symptoms varying from involuntary urine loss to urine retention) due to meatal stenosis for which a simple Y-V plastic reconstruction was performed in a second surgery. Fifteen percent of these patients needed a second correction because of stricture recurrence. Only one case of urethral prolapse was described in literature [21].

**Table 4** Study characteristics and outcome of penile skin inversion technique

| Study | Study design | Quality assessment | N (Total/ MTF) | Surgical technique | Outcome complications | Outcome Anatomy neovagina | Outcome sexual function | Outcome patient satisfaction | Outcome QoL | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|
| Amend et al. [22] | Retrospective | Moderate | MTF 24 | Penile inversion | Intraoperative:<br>Rectal injury 1 (4.2%)<br>Bleeding 2 (8.3%)<br>Postoperative:<br>Recto-neovaginal fistula 1 (4.2%)<br>Cerebral ischemia 1 (4.2%)<br>Bleeding 2 (8.3%)<br>Meatal stenosis 1 (4.2%)<br>Transient urinary incontinence 2 (8.3%)<br>Neovaginal introitus stricture + labia asymmetry 1 (4.2%)<br>Partial necrosis 1 (4.2%)<br>Secondary post-operative cosmetic corrections 13 (54.2%) | Depth mean 11 cm (range 10–14 cm)<br>Width 3–4 cm | Regular sexual intercourse 8 (33%) (no pain reported)<br>Neoclitoral sensation<br>Excellent 18 (78%)<br>Good 5 (19%)<br>Unsatisfactory 1 (4.2%)<br>Hair growth 0 (0%) | Satisfaction with neovaginal depth 24 (100%)<br>Regret 1 (4%) | | Mean 39.7 months (19–69 months) |
| Goddard et al. [23] | Retrospective | Moderate | MTF 233<br>Early follow-up 197<br>Late follow-up 70 | Penile inversion | Perioperative:<br>Infection requiring AB treatment 15 (16.8%)<br>MRSA infection 2<br>Bleeding 7 (3.2%)<br>Necrosis 6 (2.7%)<br>Vaginal prolapse 2 (1.8%)<br>DVT 2 (0.9%)<br>Pulmonary embolism 1 (0.5%) | Early FU (mean 56 days):<br>Depth mean 13 (range 5–15)<br>Late FU (mean 3 years):<br>Depth mean 13.5 (range 2.5–18) | — | — | — | Mean 56 days (8–351 days) |
| Hess et al. [24] | Retrospective | Weak | MTF 119 | Penile inversion | — | — | Ability to achieve orgasm 75/91 (82.4%), easily 20.9%, usually easily 42.9%, rarely easily 18.7%<br>Intensity of orgasm. More intense 43/77 (55.8%), unchanged 16/77 (20.8%) | Outward appearance: satisfied 61.2%, very satisfied 26.2%.<br>Aesthetic outcome: satisfied 36.2%, very satisfied 38.3%.<br>Functional outcome: satisfied 34.4%, very satisfied 38.3% | Life easier after SRS: 68.4%, somewhat easier 14.7% | Mean 5.05 years (1–7 years) |
| Hoebeke et al. [25] | Retrospective | Moderate | MTF 31 | Penoscrotal inversion technique | Changed voiding 10/31 (32%)<br>Better 13%<br>Same 68%<br>Worse 19%<br>Urine incontinence 6/31 (19%)<br>Urinary infection 10/32 (32%) mean episodes 1.7<br>Nocturia 13/31 (41%)<br>Painful granulomas 0% | — | Sexual intercourse (vaginal) 27/31 (87%)<br>Urinary infection after vaginal sex 4/27 (15%) | — | — | Mean 3 years 8 months (1–12 years) |
| Jarolim [26] | Retrospective | Weak | MTF 29 | Penile inversion | Voiding without difficulties 100%<br>2nd operation for narrow introitus 12/29 (41%)<br>2nd operation for reduction labia majora 9/29 (31%) | — | — | — | — | — |
| Krege et al. [27] | Prospective | Moderate | MTF 66 | Penile inversion and 2nd cosmetic correction | Meatal stenosis 7 (5%)<br>Severe wound infection 6 (4%)<br>Rectal lesion 3 (2%)<br>Necrosis of the glans 3 (2%)<br>Vaginal prolapse 2 (1%)<br>Necrosis of distal urethra 1 (0.6%)<br>Lesion of external urethral sphincter 1 (0.6%)<br>Urethral fistula 1 (0.6%) | — | Sexual intercourse 58%<br>Problems with intercourse 25%<br>Dyspareunia 6%<br>Bleeding 3% | Satisfaction with external genitalia 29/31 94%<br>Disapproval of labia minora 2/31 6%<br>Satisfaction with depth 22/29 76%<br>Clitoral orgasm 87% | — | >6 months |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Lawrence [28] | Retrospective | Moderate | MTF 232 | Penile inversion | Vaginal stenosis at all times 8%<br>Vaginal stenosis during arousal 6%<br>Misdirected urinary stream 33%<br>Urethral stenosis 4%<br>Clitoral necrosis 3%<br>Genital pain 9% | — | Orgasm with masturbation<br>Almost always 36%<br>> 0.5 of time 12%<br>< 0.5 of time 15%<br>Rarely 15%<br>Never 18% | Consistent regret 0 (0%)<br>Some regret 15 (6%)<br>Happiness with sexual function 7.8 (0–10)<br>Happiness with SRS 8.7 (0–10) | Improvement QoL with SRS 7.9 (–2–10) | Mean 3 years (1–7 years) |
| Perovic et al. [21] | Retrospective | Weak | MTF 89 | Penile inversion and urethral flap | Introitus stenosis 6/87 (7%)<br>Meatus stenosis 1/87 (1%)<br>Urethral prolapse 1/87 (1%)<br>Neovaginal wall rupture 1/87 (1%)<br>Rectovaginal fistula 1/87 (1%)<br>Vaginal shrinkage 2/87 (2%) | Depth mean 11.6 (9–18)<br>Width:<br>8/87 small (9%)<br>67/87 medium (77%)<br>12/87 large (14%) | Surface moisture<br>Satisfactory 71/87 (82%)<br>Unsatisfactory 16/87 (18%)<br>Normal sexual intercourse 69/87 (79%)<br>Orgasm 73/87 (84%) | Aesthetic normal appearance 78/87 (90%) | — | Mean 4.6 years (0.25–6 years) |
| Namba et al. [29] | Retrospective | Weak | MTF 6 | Inverted penile flap and M-shaped perineoscrotal flap | Partial necrosis scrotal flap 2/6(33%)<br>Rectovaginal fistula 1/6 (17%) | — | — | "All the patients are satisfied" 100% | — | — |
| Reed [30] | Retrospective | Weak | MTF 250 | Penile skin inversion | Vaginal stenosis 3 (1%)<br>Labial hematoma 10/250 (4%)<br>Rectal perforation 7/250 (3%)<br>Surgical bleeding 6/250 (2%)<br>Unaesthetic scars/dehiscence 30/250 (12%)<br>Urethral vaginal confluence with intravaginal voiding 2/250 (1%)<br>Urethral spongiosum rest 20/250 (8%)<br>Urethral meatal stenosis 15/250 (6%)<br>Vaginal prolapse 6/250 (2%)<br>Clitoral necrosis 2/250 (1%)<br>Anterior elevation of vulvar plate 10/250 (4%) | Inadequate depth >5/250 (2%) | — | — | — | — |
| Rossi Neto et al. [31] | Retrospective | Weak | MTF 332 | Penile inversion | Stricture of vaginal introitus 58/332 15%<br>Resection of residual corpora 50/332 15%<br>Vaginal stricture 40/332 12%<br>Loss of vaginal depth 25/332 8%<br>Vaginal segment necrosis 9/332 3%<br>Vaginal prolapse 4/332 1%<br>Obstructive voiding disorder 132/332 40%<br>(Meatal) stricture recurrence 20/332 15%<br>Dribbling 26/332 8%<br>Rectal injury 11/332 3%<br>Wound healing disorders 108/332 33%<br>Genital pain 3% | — | Dyspareunia 5/332 2% | — | — | — |
| Selvaggi and Bellringer [10] | Review | Moderate | MTF 1000 | Penile inversion | Pulmonary emboli 2/1,000 (0.2%)<br>Bleeding 10%<br>Rectovaginal fistula 6/800 (0.8%)<br>Meatal stenosis 3–4% | — | — | — | — | — |
| Wagner et al. [32] | Prospective | Moderate | MTF 50 | Penile inversion | Bleeding 3/50 (6%)<br>Shrinkage of neovagina 10%<br>Rectocele 0%<br>Subcutaneous hematoma 3/50 (6%) | Depth mean 10 cm (6–14) | Regular sexual intercourse 42/50 (84%)<br>Dyspareunia 2/50 (4%)<br>Clitoral orgasm 35/50 (70%) | Satisfaction with esthetic results 45/50 (90%)<br>Dissatisfaction with labia majora 5/50 (10%)<br>Satisfaction with neovaginal depth 40/50 (80%) | — | Mean 3 years |

AB = antibiotic; DVT = deep venous thrombosis; FU = follow-up; MRSA = methicillin-resistant *Staphylococcus aureus*; MTF = male-to-female; SRS = sex reassignment surgery

*Gastrointestinal.* Rectal injury was seen by Krege et al. [27] in 2% of patients (3/66), which could be closed primarily in one case and there was need for a temporary colostomy in another case (during surgery). One patient developed a rectovaginal fistula. In the study group of Rossi Neto et al. [31], 3.3% of all patients had rectal injury (11/332); two lesions were closed primarily during surgery. Nine patients developed postsurgical fistulas, for which a transneovaginal surgical correction with a protective colostomy was necessary in seven patients. Amend et al. [22] reported only one case of rectal injury (1/24, 4.2%), which was closed primarily during surgery. In the retrospective study of Reed [30], there were seven rectal perforations in 250 treated patients (3%), but no further specification was given by the author.

*Wound Healing Disorders.* Wound dehiscence was described by Reed [30] and Rossi Neto et al. [31] in, respectively, 12% (30 out of 250 patients) and 33% (108 out of 332 patients). Local abscesses were seen in 5% and subcutaneous hematoma in 4–6% [31,32].

*Unspecific Events.* Surgical bleeding occurred in 3.2–10% [10,22,23,30,32]. The main source of the hemorrhage was the corpus spongiosum surrounding the urethra [10]. Goddard et al. [23] reported deep venous thrombosis in 0.9% and pulmonary embolism in 0.5% of 233 MtF patients, despite stopping feminizing hormones 6 weeks prior to surgery, administering subcutaneous heparin injections, and the use of compression stockings until patient discharge.

### Sexual Function

One hundred sixty-four out of a total of 223 patients in five studies [21,22,25,27,32] were having (vaginal) sexual intercourse after surgery, which corresponds with a mean percentage of 75% (range 33–87%). Dyspareunia was present in 2–6% [27,31,32] and neovaginal bleeding in 3% [27]. Orgasm was possible in 70% [32], 84% [21], and 82.4% [24]. Lawrence [28] asked their 323 patients about the possibility to have an orgasm with masturbation. Answers were divided in different categories: almost always (36%), more than half of the time (12%), less than half of the time (15%), rarely (15%), and never (18%). Hess et al. [24] found that 55.8% of their patients had a more intense orgasm postoperatively, whereas orgasm intensity was unchanged in 20.8%. Surface moisture was satisfactory in 82% of patients and unsatisfactory in 18% [21], but it is unclear if these results were reported by the patient or treating physician. On a scale of 0–10, patients rated the happiness with their sexual function after SRS with a 7.8 [28]. Patients were dissatisfied with the functional outcome of their neovagina in 8.7% [24]. Female Sexual Function Index (FSFI) scores or other measurement scores for sexual satisfaction were not available in the included articles.

### Patient Satisfaction and QoL

Three studies [22,27,32] determined patient satisfaction with neovaginal depth, by using a patient questionnaire with "yes or no" answer options. They found that, respectively, 100% [22], 76% [27] and 80% [32] of transgenders were satisfied with the depth of the new vagina (mean percentage 83%). Wagner et al. [32] report that two out of eight dissatisfied patients, who underwent a new operation for neovaginal deepening, were still not satisfied with the results obtained.

Patient satisfaction with aesthetic appearance of the external genitalia was also questioned in a similar manner as described above and was 90–100% [22,27,32]. Degree of satisfaction with aesthetic outcome was assessed in 94 patients and was divided in very satisfied (38.3%), satisfied (36.2%), and mostly satisfied (22.3%) [24]. Outward appearance was (very) satisfying for 84.4% of patients [24]. In one study, patients who disapproved of the aesthetic appearance were dissatisfied with the labia minora [21], despite the fact that a secondary cosmetic correction was included in the standard procedure. In another study, dissatisfaction was attributed to the labia majora [33].

Few patients regretted the surgery. In a study group of 232, none of the patients noted consistent regret, but 6% of patients had some regrets regarding the surgery [28]. On a scale from 0 to 10, patients rated their happiness with the SRS with a 8.7 [28]. Patients indicated that their life was easier in 68.4%, and somewhat easier in 14.7% after the penile skin inversion technique [24].

There is only one study [28] that reports improvement in QoL in patients who underwent penile skin inversion vaginoplasty, using a Likert scale from −10 (most worsening possible) to 10 (most improvement possible). Participants' mean rating of improvement in their QoL after surgery was 7.9 (range −2 to 10). Genital pain was the only complication that was negatively correlated with the improvement in QoL ($P < 0.05$). All measures of satisfaction with genital sensation and

neovaginal dimensions also showed a significant correlation with the improvement in QoL.

### *Pedicled Intestinal Segments*

Probably the second most used vaginoplasty technique in MtF transgenders, which is primarily used when the penile skin inversion technique fails, is the use of pedicled bowel, also referred to as "intestinal vaginoplasty," "rectosigmoid neocolpopoiesis," or "ileal vaginoplasty." This technique was first reported by Baldwin in 1907 in patients with vaginal agenesis [34]. The abdomen is entered by a Pfannenstiel laparotomy, laparoscopy-assisted laparotomy, or total laparoscopy, and the vascular pedicle of the bowel segment is identified (sometimes using ultrasound, transillumination, or test clamping). After harvesting the bowel segment, intestinal continuity is restored primarily by end-to-end anastomosis. The intestinal segment is placed in the neovaginal cavity in an anti- or isoperistaltic direction, and the neovaginal-perineal anastomosis is made. Various perineal incision shapes and local interposition flaps are used to widen the introitus, in an attempt to prevent secondary stenosis [35].

The literature search yielded nine articles in which an intestinal vaginoplasty (rectosigmoid or ileum) was performed in MtF transgender patients (Table 5). One systematic review and eight retrospective studies were included, in which a total of 102 MtF patients were enrolled. In five studies, the studied patient group did not only consist of transgender patients, but also patients with congenital absence of the vagina and vaginectomy were included [33,35,37,38,40]. Results of these mixed patient groups will be mentioned separately and will not be used for calculation of mean percentages. The included systematic review [35] had the largest mixed patient group of 894 patients. A few original transgender studies [37,38,40] within this review were also included in our systematic review. In order to give a better overview of the results in our targeted transgender patient group, these original studies were also reported separately. Data were not pooled, so these results will not be taken into account twice.

### Neovaginal Anatomy

In the MtF patient group, the mean depth of the rectosigmoid neovagina was 12 cm and the diameter was 3.4–3.9 cm. The harvested bowel segment of the rectosigmoid colon measured 8–12 cm [37,38].

Measurements of the ileum-derived neovagina were only reported in mixed patient groups. In a study of 86 patients with 12 MtF transgenders, the depth was 15–18 cm and the diameter 2.5–4.0 cm. An ileal segment of 15–20 cm was used [33]. In a group of 900 patients (including approximately 50 transgenders), the sigmoid neovagina was 11.5–13 cm deep with a diameter of 3.7–4 cm and the ileum-derived neovaginas were 10.5–18 cm with a diameter of 2.5–4.5 cm [35].

### Complications

Bouman et al. [35] in a review on intestinal vaginoplasty in biological women and transgenders concluded that there was an overall complication rate of 6.4% for the sigmoid neovagina in 686 patients and 8.3% for the ileum neovagina calculated in 169 patients.

*Genital Region.* In a total of 30 (only transgender) patients, enrolled in three studies with small patient numbers [36,39,41], there were 13 cases of neovaginal stenosis (43%) after sigmoid vaginoplasty. In the largest combined gynecological and transgender patient group, stenosis of the vaginal introitus was seen in 8.6% for sigmoid vaginoplasty and 1.2% for ileum vaginoplasty [35]. Two other studies with a considerable transgender subgroup show a percentage of 6% for neovaginal introital stenosis [33,37]. Dilation was performed in most cases, but some authors prefer correction with a Z-plasty and local flaps [37].

Necrosis of the neovagina was only reported in one patient by Karim et al. [41], possibly due to leakage of the intercolic anastomosis. Only two cases of rectovaginal fistula were found in literature [36,37].

Mucosal prolapse of the sigmoid neovagina was only reported in combined patient groups with a mean percentage of 7.7% [35]; prolapse of an ileum-derived neovagina has not been reported in literature.

Discharge and malodor were only mentioned after rectosigmoid vaginoplasty, in, respectively, 0.7% and 9.5% of these patients [35].

None of the included articles report adenocarcinoma of the intestinal neovagina or diversion colitis.

*Urinary Tract.* Jarolim [26] created a functional sigmoidal neovagina in five patients and stated that all patients could urinate while seated with no difficulty. After 36 rectosigmoid vaginoplasties (of which 28 in MtF patients), Kwun Kim et al. [37]

**Table 5** Study characteristics and outcome of intestinal vaginoplasty

| Study | Study design | Quality assessment | N (Total/MTF) | Surgical technique | Outcome complications | Outcome Anatomy neovagina | Outcome sexual function | Outcome Patient satisfaction | Outcome QoL | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|
| Bouman et al. [35] | Review | Moderate | Total 894<br>MTF 50 + | Sigmoid N686<br>Ileum N169<br>Laparotomy and laparoscopy | Sigmoid overall 6.4%<br>Ileum overall 8.3%<br>Introitus stenose S8.6% I1.2%<br>Diffuse stenosis S3.5% I3%<br>Prolapse S7.7% I not reported<br>Discharge S 0.7%<br>Malodor S 9.5%<br>Diversion colitis 0%<br>Cancer 0% | Sigmoid<br>Depth 11.5–13.0 cm<br>Diam 3.7–4.0 cm<br>Ileum<br>Depth 10.5–18.0 cm<br>Diam 2.5–4.5 cm | Sexual activity 74.2%<br>Satisfactory 85.7%<br>Mean FSFI 24.8–28.9 (range 11.5–35.7)<br>Dyspareunia 24.7%<br>Vaginal bleeding 8.8% | — | — | Sigmoid mean 19.7 months (18 months–12 years).<br>Ileum mean 49.9 months (14–34.6 months) |
| Hage et al. [36] | Retrospective | Weak | MTF 12 | Rectosigmoid | Introitus stenosis 9/12 (75%)<br>Painful suture line mucosa-perineal skin 6/12 (50%)<br>Discharge/bleeding/inflammation 4/12 (33%)<br>Painful contractions neovagina 3/12 (25%)<br>Rectovaginal fistula 1/12 (8%) | — | — | — | — | Mean 12 months (2 months–7 years) |
| Jarolim [26] | Retrospective | Weak | MTF 5 | Sigmoid | Voiding without difficulties 100% | — | — | — | — | — |
| Karim et al. [14] | Retrospective | Weak | MTF 7 | Sigmoid | Stenosis 2/7 (29%)<br>Peritonitis 1/7(14%)<br>Painful scarring 0 (0%)<br>Neuroma 0 (0%)<br>Rectovaginal fistula 0 (0%)<br>Painful contractions 0 (0%)<br>Ulcerative colitis 0 (0%)<br>Adenocarcinoma 0 (0%)<br>Abdominal mucocele 0 (0%) | — | — | — | — | Mean 6.4 years (1–13 years) |
| Kwun Kim et al. [37] | Retrospective | Weak | Total 36<br>MTF 28 | Rectosigmoid | Stenosis N2 (6%)<br>Voiding disorder N2 (6%)<br>Rectovaginal fistula N1 (3%)<br>Rectovaginal protrusion N3 (8%) | Depth mean 12 cm<br>Diam mean 3.9 cm<br>(MTF) | Sexual activity 22/28 (79%)<br>Vaginal bleeding 2 (6%)<br>Excessive discharge 3 (8%)<br>Dyspareunia 1 (3%)<br>Orgasm 89% male type 42% | "Cosmetic configuration"<br>Good 24/28 (86%;<br>Fair 4/28 (14%) | — | Mean 5 years (1–10 years) |
| Djordjevic et al. [38] | Retrospective | Moderate | Total 86<br>MTF 27 | Rectosigmoid<br>Laparotomy | Mucosal prolapse 7/86 (8%)<br>Wound infection/dehiscention 0 (0%)<br>Urethral/rectal injuries 0 (0%) | Depth mean 12 cm<br>Diam mean 3.4 cm<br>(MTF) | FSFI (all patients) mean 28.9 (11.5–35.7)<br>Satisfactory sexual function 69/86 (80.23%)<br>MTF 21/27 (77.8%) | "Good esthetic appearance" 77/86 (89.5%)<br>Beck Depression Index (BDI) mean 7.55 (0–42)<br>MTF: mild 15% moderate 4% severe 4% | — | Mean 47 months (8–114 months) |
| Wedler et al. [39] | Retrospective | Weak | MTF 11 | Sigmoid<br>Laparotomy 2<br>Laparoscopy 9 | Abdominal wall infection 1/11 (9%)<br>Intestinal complications 0/11(0%)<br>Stenosis 2/11 (18%)<br>Prolapse, neuroma, fistulas, bleeding 0/11 (0%) | — | Sexual intercourse 7/11 (63%) | — | — | — |
| Wu et al. [33] | Retrospective | Moderate | Total 86<br>MTF 12 | Ileum<br>laparoscopic | Intraoperative complications 0/86 (0%)<br>Postoperative complications:<br>Intra-abdominal hemorrhage 1/86 (1%)<br>Urethral meatal stenosis 1/86 (1%)<br>Intestinal obstruction 1/86 (1%)<br>Vaginal stenosis 5/86 (6%)<br>Tumor 0/86 (0%)<br>Prolapse 0/86 (0%) | Depth 15–18 cm<br>Width 2.5–4.0 cm | Frequent orgasms >50%<br>Adequate lubrication 90%<br>Dyspareunia 0/86 (0%)<br>Vaginal bleeding 0/86 (0%) | — | — | Mean 14 months (12–18 months) |
| Wu et al. [40] | Retrospective | Moderate | Total 80<br>MTF 11 | Ileum<br>laparoscopic | As described above | As described above | As described above | — | — | Mean 18 months (16–22 months) |

Diam. = diameter; FSFI = Female Sexual Function Index; MTF = male-to-female

noted two patients with voiding disorders due to partial obstruction of the urethral meatus. The obstructive tissue could be excised successfully.

*Gastrointestinal.* In a transgender group of 30 patients, there was one case of abdominal wall infection and one case of peritonitis [36,39,41]. The first patient was successfully treated with antibiotics; the second patient required a re-laparotomy and a necrosed neovagina was resected. Wu et al. [33] observed one patient with an intestinal obstruction after 86 laparoscopic vaginoplasties with an ileal segment. No other gastrointestinal complications were reported in the included articles.

*Wound Healing Disorders.* Several authors mention that wound healing disorders, such as neuroma, painful scarring, and wound infection, did not occur in their patients [38,39,41]. In one study with 12 MtF patients, six patients complained about pain located on the suture line of the mucosa-perineal skin anastomosis [36].

*Unspecific Events.* No other serious adverse events were reported.

### Sexual Function

One year after bowel vaginoplasty, 63% [39] and 79% [37] of transgender patients were sexually active. Djordjevic et al. [38] report that 77.8% of transgenders have a satisfactory sexual function, based on FSFI scores. According to the FSFI scores, there was no sexual dysfunction in 80.23% of cases in their combined (partially nontransgender) patient group. There was no significant difference between the vaginal agenesis and transgender groups.

### Patient Satisfaction and QoL

Cosmetic configuration of the rectosigmoid neovagina was assessed in 28 MtF patients and was "good" in 88.9% and fair in 11.1% [37]. Djordjevic et al. [38] found a "good aesthetic appearance" in 89.5% of treated MtF patients. It is unclear if the assessment was made by the physician or patient and which criteria were used. In addition to this, the surgical technique for labioplasty in these patients was not reported.

Psychological outcome after surgery was evaluated in 86 patients (including 27 transgenders), using the Beck Depression Inventory (BDI), a multiple choice self-report questionnaire for measuring the severity of depression [38]. Of the 27 transgender patients, scores of eight patients (30%) were consistent with depression according to the BDI. These results were not compared with BDI scores prior to surgery.

### *Experimental*

One clinical pilot study met the inclusion criteria. Dessy et al. [42] operated on six MtF patients and covered the neovaginal walls with cultured autologous oral epithelium in a three-step procedure (oral biopsy, neovaginal cavity formation and insertion of gauze with oral epithelial cells, and clitorolabiaplasty). Complications were rectovaginal fistula (n = 1), clitoris necrosis (n = 1), surgical revision of the labia (n = 1), and short vagina, which could be deepened in a redo operation (n = 1). Neovaginal depth was 12–14 cm with a width of 3–4 cm. Biopsies of the neovagina showed a normal oral mucosal epithelium. According to the authors, all patients were sexually active after the operation and were happy with their sexual function.

## Discussion

By reviewing literature since 1995, a trend was visible in the surgeon's preference for neovaginoplasty technique. Before 2000, the use of nongenital skin grafts and flaps was a common treatment option, but although results were poorly reported and obtained from small patient groups, complications seemed to be present in a great proportion of patients. Especially split thickness skin grafts were significantly associated with neovaginal stricture. These findings, possibly in combination with clinically observed poor results, may justify the fact that this technique alone has been abandoned as a first-line therapy.

Since 2000, research groups have been reporting on the outcome of the penile skin inversion technique, and it became the most investigated and therefore most "evidence-based" technique for vaginoplasty in MtF transgenders. However, almost all evidence that has been presented so far is of low to intermediate quality. No standardized surgical technique is available, and each research group uses different outcome measures. In addition to this, methods are poorly described in most articles. This hampers the interpretation of results, and it is debatable if these results are even comparable. There is also a possibility that the patient groups of the included studies overlap, as some articles were published by the same author or institute.

When penoscrotal or urethral flaps are used in addition to the inverted penile skin flap, major complications such as necrosis and vaginal wall rupture were reported more frequently, but this was only investigated in a small number of patients.

Bowel vaginoplasty for transgenders was already a research topic in the late 1990s, but its efficacy was only based on small patient numbers and unclear outcome measures. In the past 5 years, investigators have been trying to obtain more evidence for this surgical technique, but because of heterogeneous patient groups (in which gynecological and gender patients are both included) and for which outcomes are only reported for a total of 109 MtF patients in literature, the applicability in transgender women is still uncertain.

Although the data of the included articles were not pooled, our results indicate that there were less neovaginal, wound healing, and even gastrointestinal complications in the bowel vaginoplasty group, compared with the penile skin inversion technique. Aesthetical outcome was comparable. Sexual function was reasonably good in both techniques, but these results could not be compared due to different outcome measures. Although neovaginal carcinoma and diversion colitis have been reported in literature [43–45] and have been feared ever since, they were not observed in the included studies. However, in most studies, follow-up was not longer than 3 years, and a longer follow-up would be necessary to assess the true prevalence of these long-term complications.

These results suggest that intestinal vaginoplasty is not inferior to the penile skin inversion technique, but there may be an over- or underestimation of efficacy and complications due to insufficient sample sizes. Superiority of one technique can only be evaluated in a large-scale prospective comparative trial.

Also in biological women with vaginal aplasia, the ideal modality for the construction of a neovagina remains unclear [12]. One of the common surgical techniques for the creation of a neovagina in these patients is the use of the peritoneum (Davydov procedure) [12,46].

An interesting finding is that the only available randomized controlled trial regarding vaginoplasty for vaginal aplasia compared the use of bowel with a laparoscopic peritoneal approach (Davydov procedure). The results were in favor of the laparoscopic peritoneal approach, with significant smaller intraoperative blood loss, operative time, and decreased duration of inpatient stay. The mean neovaginal length did not significantly differ between the two groups; however, abdominal discomfort and foul vaginal secretions during intercourse were increased in the bowel vaginoplasty group [12,47]. In addition to this, neovaginal prolapse has never been reported after the Davydov procedure. Peritoneum has never been used for the lining of the neovagina in MtF transgenders. It could potentially also benefit this patient group, but to date no clinical evidence is available to support this hypothesis.

The use of cultured autologous epithelial cells for neovaginal construction [42] is still controversial as it has only been performed in a small patient group. The same applies to other experimental techniques such as complete tissue engineering of the vagina, using scaffolds seeded with vaginal epithelial cells. This method has already been investigated in a preclinical [48] and clinical setting with vaginal aplasia patients [49] with promising results. However, this method cannot easily be used in transgender women, as no autologous vaginal epithelial cells can be harvested in MtF transgenders. Nevertheless, with regard to the growing knowledge in the field of bio regenerative medicine, we believe that tissue engineering may offer attractive new options for (transgender) neovaginoplasty in the future.

### Conclusion and Recommendation

It is impossible to identify the "best available" technique for vaginoplasty in MtF patients due to a lack of high-quality evidence and the heterogeneity of surgical techniques, patient groups, and outcome measures. For now, the penile skin inversion technique is the most researched method, and surgical outcome and sexual function are generally acceptable to good. The outcome of vaginoplasty with pedicled bowel segments is less frequently reported in MtF patients but does not seem to be inferior to the penile skin inversion technique. Ideally, a randomized controlled trial would differentiate between these techniques, but this study design is hard to realize in surgical fields. In addition, it is a logical first step to use the easily accessible penile skin before considering abdominal surgery. The benefit of additional urethral and penoscrotal flaps cannot be confirmed in current literature, and there is a limited role for nongenital skin flaps and grafts as a primary surgical option. The role of tissue engineering and cultured autologous cells for

vaginoplasty has to be further clarified in future research.

There is a need for prospective studies with standardized surgical procedures, larger patient groups, and a longer follow-up period. Uniformity in outcome measurement tools such as validated questionnaires and scores for sexual function and QoL is mandatory for comparability between studies and correct interpretation of obtained data. The use of these patient-reported outcome measures will enable researchers and physicians to better evaluate the outcome of gender reassignment surgery from the patient's perspective.

Unless these improvements are made in future scientific research, the ideal method for the creation of a neovagina in MtF transgender patients cannot be identified, and the choice for a certain technique will stay an expertise-based decision rather than evidence-based medicine.

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REVIEW

# The quality of evidence for medical interventions does not improve or worsen: a metaepidemiological study of Cochrane reviews

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## Abstract

**Objectives:** The objective of the study was to determine the change in quality of evidence in updates of Cochrane reviews that were initially published between January 1, 2013 and June 30, 2014. We used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system to document evidence quality.

**Study Design and Setting:** We searched the Cochrane Database of Systematic Reviews on March 20, 2020 to identify which of the reviews from the initial (2013/14) sample had been updated. Using the same methods to determine the quality of evidence in the previous analysis, we assessed the quality of evidence for the first-listed primary outcomes in the updated reviews.

**Results:** Of the 608 reviews in the original sample, 154 had been updated with and 151 contained available data for both original and updated systematic reviews (24.8%). The updated reviews included: 15 (9.9%) with high-quality evidence, 56 (37.1%) with moderate-quality evidence, 47 (31.1%) with low-quality evidence, and 33 (21.9%) with very low-quality evidence. No change in the GRADE quality of evidence was found for most (103, 68.2%) of the updated reviews. The quality of evidence rating was downgraded in 28 reviews (58.3%) and upgraded in 20 (41.7%), although only six reviews were promoted to high quality.

**Conclusion:** Updated systematic reviews continued to suggest that only a minority of outcomes for health care interventions are supported by high-quality evidence. The quality of the evidence did not consistently improve or worsen in updated reviews. 

*Keywords:* Systematic review; Evidence; Quality score; Meta-analysis; Effectiveness; GRADE

## 1. Introduction

### *1.1. Rationale*

Several metaepidemiological studies have attempted to determine the proportion of health care interventions that are evidence-based. A 2001 estimate found that about a quarter (26.7%) of health care interventions whose effectiveness was reported in 160 Cochrane reviews were considered effective, based on the interpretation of the review authors [1]. In 2007, Garrow claimed that 50% of health care treatments have good evidence to support them [2]. In the same year, El Dib et al. [3] found that

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**What is new?**

**Key findings**

- The quality of evidence (in accordance with GRADE) supporting the main finding changes in about a quarter of updated Cochrane reviews.
- Upgrading of quality of evidence (in accordance with GRADE) for the main outcome is not more common than downgrading of quality of evidence.

**What this adds to what was known?**

- Quality of evidence does not seem to improve overall with the addition of new evidence, at least within the timeframe assessed.

**What is the implication and what should change now?**

- Methods investigating when review updates are likely to change our confidence in the estimated outcome effect could inform decisions about whether to update reviews to save resources.
- The quality of evidence supporting most health care interventions remains low; higher-quality evidence is required.

just 44% of a random selection of Cochrane reviews evaluating interventions suggested that they were likely to be beneficial.

Since these studies were published, the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system has been introduced offering a less subjective way of ranking the quality of evidence [4]. An evaluation of all Cochrane reviews published between January 1, 2013 and June 30, 2014 found that 13.5% of reviews were found to have high quality of evidence for the first-listed primary outcome in accordance with GRADE [5]. High-quality evidence was more common in updated compared with new reviews and in association with pharmacological than other types of interventions. Even when any outcomes (including but not limited to the first-listed primary outcome) were considered, only 116 of 608 (19.1%) of the reviews reported at least one outcome with high quality of evidence.

Most researchers agree that it is important to update systematic reviews so that they reflect current knowledge [6,7], to maximize patient benefits and to avoid harm [8]. However, updated reviews frequently reveal no change in conclusions when compared with the original. According to French et al. [9], only about 9% of updated Cochrane reviews in 2002 presented a change in conclusion relative to their precursors from 1998. However, the claim that the updates did not overturn results from the original review was based on whether review authors stated there was a change in the conclusion of the updated review.

There is currently no consensus on the timing that would appropriately guide a review update, and the Cochrane Collaboration's policy is to update reviews when evidence accumulates, based on the availability of new data that would have a meaningful impact on the findings [10]. Previous reports have identified a median time required for an update of a systematic review of approximately 5.5 years [11]. It was therefore considered appropriate to assess whether reviews conducted back in 2013–2014 (Fleming et al., 2016) have been updated by early 2020, and if so, whether there were changes in the quality of the evidence based on GRADE [5].

### 1.2. Objectives

The primary objective was to determine whether updates from a previous sample of systematic reviews resulted in a different quality evidence, as assessed by GRADE. The secondary objective was to determine whether there is a difference in the change of quality of evidence across different interventions, outcomes, or Cochrane Review Groups, and whether Cochrane review authors deemed the intervention to be effective in clinical practice.

## 2. Methods

### 2.1. Eligibility criteria

We included any Cochrane review that was an update of a Cochrane review published in the (January 1, 2013–June 30, 2014) parent sample of reviews which included a GRADE assessment.

### 2.2. Information sources

Cochrane Database of Systematic Reviews: https://www.cochranelibrary.com/cdsr/reviews.

### 2.3. Search strategy

We searched the Cochrane Database of Systematic Reviews to identify the reviews which had updates among those in the original sample. The most recent search was on March 20, 2020.

### 2.4. Data sources and searches

One author (D.K.) retrieved the systematic reviews from the original (2013/14) sample and piloted the extraction form with one other author (J.H.). One author (D.K.) checked whether an update had been published and extracted data for the updated review. Other authors (J.H., M.L., P.F., and H.W.) were second extractors (all records

were checked by two authors). All discrepancies were resolved by discussion.

### 2.5. Data items

Extracted information included the following: titles, corresponding author name and email, Cochrane Review Group, year of publication, country, study design, intervention (and intervention category), control, and outcome. In relation to the GRADE summary of findings (SoF) tables, we recorded for the first-listed outcome the category of intervention (including surgical, pharmacological, behavioral, or medical treatments, and diet or exercise interventions). Interventions classified as "behavioral" pertained to psychological treatment, psychotherapy, cognitive training, group therapy; "diet or exercise" interventions largely related to training exercise, physiotherapy, rehabilitation, dietary modification; "medical treatments" were summarized by electronic optical/hearing aids, appliance/device use for dental treatment, ultrasound, or other radiography and medical interventions not related to surgical or pharmacological approaches. We also recorded the type of outcomes (objective, such as mortality or outcomes assessed with an instrument or prespecified measurable criteria; or subjective) and overall GRADE ranking with rationale. In cases where multiple SoF tables within the same review existed for the primary outcome, we considered only the one listed first. In cases where no high-quality evidence was recorded for the first-listed primary outcome, we documented whether any other outcome was rated as high and, if so, whether this was primary (but not first listed).

We reported whether the Cochrane review authors concluded that the experimental intervention should be used in clinical or public health practice or not. This information was obtained from the conclusions section in the review abstract and the body of the review (subsections "implications for practice" and/or "implications for research"), following the original strategy implemented in the parent study [5]. Examples of positive interpretations included: "Buprenorphine should be supported as a medication to use," and in the "Implications for research or practice" section: "There does not appear to be any need for further randomized control trials of the relative efficacy of methadone compared with buprenorphine."[12]

### 2.6. Outcomes

The primary outcome was the change in quality of the evidence for the first listed primary outcome in updated Cochrane reviews compared with reviews published in an earlier (January 1, 2013–June 30, 2014) parent sample. The secondary outcomes were the proportion of reviews in the updated sample that have high-, moderate-, low-, or very low-quality evidence. We also assessed the review authors' interpretation of results, for high-quality evidence and reports of statistically significant results.

### 2.7. Data synthesis and analysis

Descriptive statistics on the year of publication of the update and the time interval between the publication in the parent sample and the update were calculated. In addition, frequency of the type of intervention and related outcome were calculated for the reviews that had been updated. For studies that were updated, a change in the rating of evidence, if present, and its direction was recorded (downgrade, upgrade).

We reported proportions (n/N) and percentages of reviews reporting high-, moderate-, low-, or very low-quality evidence in the new sample of reviews. The quality of evidence in accordance with GRADE in the new subset of reviews with updates was tabulated across the respective versions in the parent sample in a matched $4 \times 4$ table. We then compared the difference in quality of evidence between the original and updated sample. We used the two-sided exact signed-rank test to assess upgrades/downgrades between the original and updated reviews. We also performed a Stuart-Maxwell marginal homogeneity test. In addition, we performed assessments considering the presence of high-quality rating for any outcome other than the first-listed primary outcome.

For outcomes reported in the SoF table to be at the extremes (very low or high), we reported the distribution of statistically significant results ($P < 0.05$ or 95% confidence interval excluding the null), along with the reviewers' interpretation of the value of the intervention in clinical practice.

All statistical analyses were conducted with STATA version 15.1 (Stata Corporation, College Station, TX, USA) and R Software, version 3.6.1, (R Foundation for Statistical Computing, Vienna, Austria).

### 2.8. Protocol amendments

In the protocol, we planned a subgroup analysis by disease area, intervention type, and Cochrane Review Group. However, data for subgroups were deemed too sparse to allow for meaningful subgroup analyses.

## 3. Results

### 3.1. Search results

Of the 608 reviews in the original sample, 154 (25.3%) had been updated, and 151 of those presented information on GRADE quality of evidence for both initial and updated reviews so were retained for further assessment (Fig. 1). The median year of the update was 2017 (interquartile range (IQR) = 2, range: 2015 to 2020), with a median of

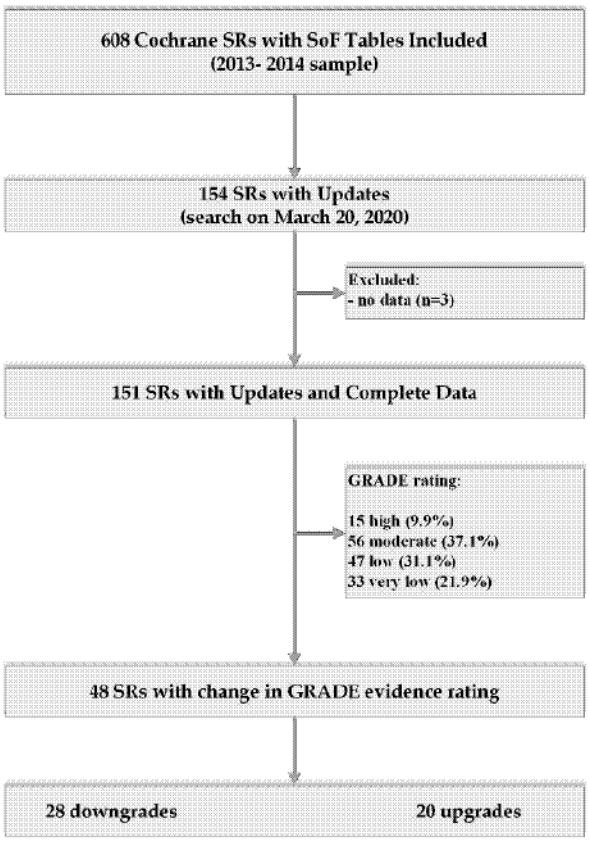


**Fig. 1.** Study selection and GRADE of evidence breakdown.

4 years (IQR = 2, range: 2 to 7 years) after the original review was published. Among the updated reviews, the original version with which it was compared (published in 2013–2014) was already an update of a previous version for 69 (45.7%) reviews.

Most reviews in the present sample of Cochrane updates pertained to pharmacological interventions ($n$ = 82; 54.4%), followed by behavioral ($n$ = 24; 15.9%) and surgical ($n$ = 23; 15.2%) interventions, the use of medical devices ($n$ = 15; 9.9%), and diet- or exercise-related interventions ($n$ = 7; 4.6%). In most of the reviews, the primary outcome considered was classified as objective (127 of 151; 84.1%).

### 3.2. Quality of evidence in the entire updated (2020) sample

Within the 151 updated reviews, 15 (9.9%) had high-quality evidence supporting the first-listed primary outcome, 56 (37.1%) had moderate-quality, 47 (31.1%) had low-quality, and 33 (21.9%) had very low-quality evidence. Compared with the original sample, there was a reduction in the proportion of reviews providing high quality evidence. However, this reduction was not statistically significant (see below). GRADE ranking comparison between the original and updated reviews is presented in Tables 1 and 2.

### 3.3. Change in quality of evidence

#### 3.3.1. Change in quality of evidence for primary outcome

Most (103 of 151, 68.2%) of the updated reviews reported no change in the GRADE quality of evidence compared with the initial sample (bold diagonal in Table 1). Of the reviews with unchanged grading, nine (8.7%) reported high-quality evidence, 40 (38.8%) had moderate, 30 (29.2%) had low, and 24 (23.3%) had very low quality of evidence. In 63 of the 103 updated reviews without a changed GRADE rating (61.2%), there were no additional data in the updates, whereas in the remaining 35 reviews, more data had been added. In five reviews without a change in quality (4.9%), the update contained fewer primary studies than the original. There was no statistical difference in the change in the quality of the evidence ratings ($P$ = 0.30) between the original and updated reviews. The $P$-value for the marginal homogeneity test was 0.55.

A change in GRADE rating was reported in 48 of the 151 updated reviews. Twenty-eight of these (58.3%) were *downgraded*, mostly (24/28) to low or very low. Of first-listed primary outcomes initially recorded as having "high" quality evidence ($n$ = 15), 11 were downgraded to low and 4 to moderate and 2 to low quality. Twenty of the 48 reviews that had a changed GRADE involved an *upgrade*. Of those, six were upgraded to "high".

Thirty of the 48 trials (62.5%) that had a changed GRADE rating included additional data. Among these, 15 resulted in upgrades, and 15 in downgrades. In 16 (33.3%), the changed GRADE rating was not based on new data. In two updated reviews (4.2%), changes were based on fewer data for the primary outcome of interest; both resulted in upgrades.

#### 3.3.2. Change evidence quality for other outcomes (those that were not first-listed primary)

Of the 151 updated reviews which did not present high quality of evidence for the first-listed primary outcome, 19 had other (nonprimary, or primary but not first listed) outcomes that were ranked as high quality. Ten of these involved primary outcomes. The overall quality of the evidence in the updates for any outcome was high in 34 out of 151 updated reviews (22.5%). Again, we did not find a significant difference between the original and updated reviews for this comparison ($P$ = 0.72). The $P$-value by the marginal homogeneity test was $P$ = 0.32.

**Table 1.** Summary of review quality from updated and original samples

| Year of review assessment | High *N* (%) | Moderate *N* (%) | Low *N* (%) | Very low *N* (%) |
|---|---|---|---|---|
| 2020 | 15 (9.9) | 56 (37.1) | 47 (31.1) | 33 (21.9) |
| 2013/14 | 82 (13.5) | 187 (30.8) | 193 (31.7) | 146 (24) |

### *3.4. Review authors' interpretations and statistical significance of results*

Among extreme evidence quality ratings (very low and high), 8 of 33 (24.2%) of those with very low-quality and 10 of 15 (66.7%) of those with high-quality evidence had statistically significant results for at least one outcome in the updated sample. Across all 151 updated reviews, only two had high-quality evidence, statistically significant results, and a favorable interpretation of the value of the intervention in clinical practice.

## 4. Discussion

### *4.1. Summary of findings*

One-quarter of the reviews in our sample had been updated over the 6- to 7-year period. Of those, a third reported a change in GRADE ratings. There was no evidence of GRADE ratings being more likely to improve than worsen in these topics, with a weak trend toward worsening.

In keeping with a previous finding that 23% of Cochrane reviews were out of date within 2 years [11], our study may also show that Cochrane reviews are not updated very frequently [13]. Specifically, we observed a median hiatus for publication of the updated review of 4 years, and most reviews were not updated at all.

In some cases, downgrading evidence quality was related to the new risk of bias assessment forming the basis for the GRADE framework. Risk of bias assessments have become stricter in the new Cochrane Handbook and might have led to automatic downgrading due to items that had previously been overlooked. This seems to be reflected in the fact that 13 of the reviews with no new data reported worsening of evidence quality.

Another explanation for different GRADE ratings for updated reviews that had no new data is inconsistency in the way the way GRADE is applied. One study found variability in the way GRADE is applied leading to different conclusions about strength of evidence [14]. Another study found low agreement among systematic reviewers using the Cochrane risk of bias tool (which influences the GRADE rating) [15]. This may partially explain why two of the updated reviews whose evidence quality was upgraded were based on fewer studies than the original (although the omitted studies also reduced imprecision or risk of bias) [16,17].

### *4.2. Limitations*

The extent to which our findings are generalizable needs to be discussed. Our sample of reviews from 2013 to 2014 may not be representative of all medical evidence. It pertains to topics where either a new review was published at that time or it was deemed that an update was then indicated. Similarly, the reviews that were updated may not be representative of the original sample. Reviews which were not updated may have been less likely to require updating. If so, the proportion of changes in GRADE ratings we found may have been exaggerated. Finally, we had a relatively small number of updated reviews; thus, we could not meaningfully explore whether improvements in the quality of evidence are more or less likely in specific fields. However, no consistent patterns were observed for the very few reviews ($n = 6$) where evidence was upgraded to high quality.

In addition, our conclusions assumed that GRADE is sensitive enough to detect changes in evidence quality. However, GRADE only has four categories, and if there were additional categories, we may have detected a change in quality in a greater number of reviews. On the other hand, a more sensitive evidence-rating tool could also be more likely to detect noise.

**Table 2.** Change in quality of evidence across 151 reviews with updates for primary outcomes (the numbers below the diagonal are those which were upgraded, whereas those above were downgraded)

| GRADE quality of evidence in original sample (2013–2014) | GRADE quality of evidence in updated reviews (sample 2020) | | | | |
|---|---|---|---|---|---|
| | High quality *N* (%) | Moderate quality *N* (%) | Low quality *N* (%) | Very low quality *N* (%) | Total *N* (%) |
| High *N* (%) | **9 (60.0)** | 4 (7.1) | 7 (14.9) | 0 (0.0) | 20 (13.2) |
| Moderate *N* (%) | 4 (26.7) | **40 (71.4)** | 8 (17.0) | 3 (9.1) | 54 (35.8) |
| Low *N* (%) | 2 (13.3) | 8 (14.3) | **30 (63.8)** | 6 (18.2) | 47 (31.1) |
| Very low *N* (%) | 0 (0.0) | 4 (7.2) | 2 (4.3) | **24 (72.7)** | 30 (19.9) |
| Total | 15 (100.0) | 56 (100.0) | 47 (100.0) | 33 (100.0) | 151 (100.0) |

## 5. Conclusion

In spite of having additional data, most reviews were not updated over the time period of our assessment with most updates not resulting in a change in evidence quality. To avoid research waste, it should be investigated whether it is possible to decide in advance whether updating a review will result in a change in results. Effects of medical interventions supported by high-quality evidence, statistically significant results, and favorable interpretations of the evidence by review authors remain very rare.

## CRediT authorship contribution statement

**Jeremy Howick:** Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Resources, Supervision, Validation, Writing - original draft, Writing - review & editing. **Despina Koletsi:** Data curation, Formal analysis, Methodology, Resources, Supervision, Validation, Writing - original draft, Writing - review & editing. **Nikolaos Pandis:** Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Resources, Supervision, Validation, Writing - original draft, Writing - review & editing. **Padhraig S. Fleming:** Conceptualization, Methodology, Validation, Writing - review & editing. **Martin Loef:** Data curation, Methodology, Validation, Writing - review & editing. **Harald Walach:** Conceptualization, Data curation, Methodology, Validation, Writing - review & editing. **Stefan Schmidt:** Conceptualization, Data curation, Methodology, Validation, Writing - review & editing. **John P.A. Ioannidis:** Conceptualization, Formal analysis, Methodology, Supervision, Validation, Writing - review & editing.

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# Testosterone Treatment and MMPI–2 Improvement in Transgender Men: A Prospective Controlled Study

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***Objective:*** Most transgender men desire to receive testosterone treatment in order to masculinize their bodies. In this study, we aimed to investigate the short-term effects of testosterone treatment on psychological functioning in transgender men. This is the 1st controlled prospective follow-up study to examine such effects. ***Method:*** We examined a sample of transgender men ($n$ = 48) and nontransgender male ($n$ = 53) and female ($n$ = 62) matched controls (mean age = 26.6 years; 74% White). We asked participants to complete the Minnesota Multiphasic Personality Inventory (2nd ed., or MMPI–2; Butcher, Graham, Tellegen, Dahlstrom, & Kaemmer, 2001) to assess psychological functioning at baseline and at the acute posttreatment follow-up (3 months after testosterone initiation). Regression models tested (a) Gender × Time interaction effects comparing divergent mean response profiles across measurements by gender identity; (b) changes in psychological functioning scores for acute postintervention measurements, adjusting for baseline measures, comparing transgender men with their matched nontransgender male and female controls and adjusting for baseline scores; and (c) changes in meeting clinical psychopathological thresholds. ***Results:*** Statistically significant changes in MMPI–2 scale scores were found at 3-month follow-up after initiating testosterone treatment relative to baseline for transgender men compared with female controls (female template): reductions in Hypochondria ($p < .05$), Depression ($p < .05$), Hysteria ($p < .05$), and Paranoia ($p < .01$); and increases in Masculinity–Femininity scores ($p < .01$). Gender × Time interaction effects were found for Hysteria ($p < .05$) and Paranoia ($p < .01$) relative to female controls (female template) and for Hypochondria ($p < .05$), Depression ($p < .01$), Hysteria ($p < .01$), Psychopathic Deviate ($p < .05$), Paranoia ($p < .01$), Psychasthenia ($p < .01$), and Schizophrenia ($p < .01$) compared with male controls (male template). In addition, the proportion of transgender men presenting with co-occurring psychopathology significantly decreased from baseline compared with 3-month follow-up relative to controls ($p < .05$). ***Conclusions:*** Findings suggest that testosterone treatment resulted in increased levels of psychological functioning on multiple domains in transgender men relative to nontransgender controls. These findings differed in comparisons of trans-

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gender men with female controls using the female template and with male controls using the male template. No iatrogenic effects of testosterone were found. These findings suggest a direct positive effect of 3 months of testosterone treatment on psychological functioning in transgender men.

*Keywords:* transgender, psychopathology, hormonal sex-reassignment therapy, female-to-male, testosterone



A transgender man is someone whose masculine gender identification is not aligned with the female sex he was assigned at birth. Compared with nontransgender individuals, transgender people experience multiple physical and mental health disparities including increased psychiatric comorbidity and higher rates of symptoms of anxiety, depression, and lifetime suicide attempts (Clements-Nolle, Marx, Guzman, Katz, & San Francisco Department of Public Health, 2001; Clements-Nolle, Marx, & Katz, 2006; Hepp, Kraemer, Schnyder, Miller, & Delsignore, 2005; Meier, Fitzgerald, Pardo, & Babcock, 2011) as well as systemic oppression; discrimination, social stigma; social, spiritual, and occupational rejection; physical and sexual violence; and harassment (Bockting, Miner, Swinburne, Hamilton, & Coleman, 2013; Budge, Adelson, & Howard, 2013; Effrig, Bieschke, & Locke, 2011; Hendricks & Testa, 2012; Meier & Labuski, 2013).

Because of these negative experiences, transgender people may hide their transgender identity from others or deny it to themselves for self-preservation. Minority stress theory (Bockting et al., 2013; Hendricks & Testa, 2012; I. H. Meyer, 2003) posits that transgender people experience stress related to "actual experiences of rejection and discrimination" as well as "perceived rejection and expectations of being stereotyped and discriminated against . . . and hiding minority status and identity for fear of harm (concealment)" (Bockting et al., 2013, p. 943). The act of concealing one's transgender status can lead to "hypervigilance and a preoccupation with hiding, which itself can become a significant source of stress" (Bockting et al., 2013, p. 943). Avoidant coping may have been learned early as many transgender people recall learning to hide their gender expression as early as childhood (Devor, 2004). Efforts to hide one's gender identity to protect oneself from harm are thought to create distress in and of themselves (Budge et al., 2013). Transgender people who are in the beginning of their gender transition may be more likely to experience more distress due to denial, hiding, and suppression of their transgender identity (Budge et al., 2012), and they may avoid social situations due to concerns about being judged by others for their appearance (Gómez-Gil et al., 2012), especially if they do not "pass" (i.e., are not perceived by others as their gender identity). Without taking the reasons behind these social patterns into account, transgender people may be assumed to be socially introverted or to have social deficits.

Many health providers have not been trained to initiate hormone treatment in transgender people (Obedin-Maliver et al., 2011) and may be reticent to do so especially when working with transgender men with lower psychological functioning. However, recent cross-sectional research suggests that testosterone treatment is associated with fewer symptoms of psychopathology in transgender men (Davis & Meier, 2014; Gómez-Gil et al., 2012; Meier et al. 2011; Newfield, Hart, Dibble, & Kohler, 2006); although no conclusive direct effects have been reported. Studies of hypogonadal males who were prescribed testosterone treatment have documented improved psychological functioning including improved mood, increased energy, and reduced depression (Dunning & Ward, 2004; Perry et al., 2002; Wang et al., 1996).

Transgender men may pursue testosterone treatment and surgical procedures to modify their primary and/or secondary sex characteristics to match their gender identity (Gómez-Gil et al. 2012), although not all transgender men opt to pursue medical treatment options. Testosterone for transgender men who desire to medically transition is a medically necessary treatment option that has been used in this capacity for more than 50 years (Coleman et al., 2011). Many transgender men who desire to pursue testosterone treatment as well as chest and/or genital surgery select testosterone only or as initial step in their transition because they are unable to access surgical treatment due the lack of insurance coverage in the United States (Bockting, Robinson, Benner, & Scheltema, 2004; Mikalson, Pardo, & Green, 2012) and the high costs of surgery (Meier & Labuski, 2013). Other transgender men may not pursue surgical treatments because they hope to preserve their reproductive capability or because the masculinizing effects of testosterone sufficiently address their body discomfort.

The physical effects of testosterone on transgender men are well documented. These include deepening of the voice; noticeable increase in hair growth on the face, pubic region, limbs, chest, back, and stomach; acne; changes in body odor; cessation of menstruation; enlargement of the clitoris; redistribution of fat; more coarse skin texture; increase in muscle mass; pelvic narrowing; and scalp hair loss if it is genetically inherited (Gooren & Giltay, 2008; Hembree et al., 2009; Moore, Wisniewski, & Dobs, 2003; Sitek, Fijalkowska, Żadzi´nska, & Antoszewski, 2012). The first changes that occur within 3 months are typically skin oiliness or acne, facial and body hair growth, body fat redistribution, cessation of menses, clitoral enlargement, and deepened voice (Gooren, 2005; Gooren, Giltay, & Bunck, 2008; Hembree et al., 2009).

Little is known, however, of the psychological effects of testosterone on transgender men. Several longitudinal studies on the effects of gender transitions focus more on physical and psychological genital surgical outcomes than on the prospective psychological effects of hormones (Cohen-Kettenis & Pfäfflin, 2003; Johansson, Sundbom, Höjerback, & Bodlund, 2010). In fact, much of the research on testosterone treatment among transgender men is cross-sectional (Davis & Meier, 2014; Dubois, 2012; Gómez-Gil et al., 2012; Meier et al., 2011; Newfield et al., 2006). The recent cross-sectional studies suggest that testosterone treatment among transgender men is associated with improved mental health and well-being, including increased quality of life (Meier et al., 2011; Newfield et al., 2006), decreased anxiety and depression (Davis & Meier, 2014; Gómez-Gil et al., 2012; Meier et al., 2011), decreased social distress (Gómez-Gil et al., 2012) and decreased

stress (Dubois, 2012; Meier et al., 2011). In addition, previous longitudinal studies of testosterone treatment among transgender men have examined its physical and cognitive effects, without examining psychosocial effects (W. J. Meyer, Walker, & Suplee, 1981; Slabbekoorn, van Goozen, Megens, Gooren, & Cohen-Kettenis, 1999; van Goozen, Slabbekoorn, Gooren, Sanders, & Cohen-Kettenis, 2002). A recent uncontrolled longitudinal study demonstrated fewer symptoms of anxiety and depression in a group of hormonally treated transgender men and women over 1 year (Colizzi, Costa, & Todarello, 2014). To our knowledge, no published controlled study has prospectively examined the effects of testosterone on the psychological functioning of transgender men compared with matched female and male controls.

The Minnesota Multiphasic Personality Inventory(2nd ed.; MMPI–2; Butcher, Dahlstrom, Graham, Tellegen, & Kaemmer, 1989; Butcher, Graham, Tellegen, Dahlstrom, & Kaemmer, 2001) is one of the oldest and most widely used psychological assessment tools (Weiner & Greene, 2006). Although it was originally designed to establish psychological diagnoses, the test provides a broader picture of a person's behaviors and symptoms of psychopathology (Weiner & Greene 2006). MMPI–2 profiles are used to assess long-term stability of personality and psychopathology (Butcher et al., 2001). Generally, MMPI–2 results remain stable over time; even in individuals who have had intensive psychotherapy, MMPI–2 profiles typically do not show significant improvement until after a few years (Spiro, Butcher, Levenson, Aldwin, & Bossé, 2000). Only intensive treatments, such as electroconvulsive therapy combined with psychotherapy, tend to alter MMPI–2 profiles in a short time period (4 months; Spiro et al., 2000). Prospective administration of the MMPI–2 should not reveal significantly different results over a 3-month assessment period in an untreated sample.

Previous cross-sectional studies have examined MMPI personality profiles of transgender people with the intent of determining if they were experiencing severe psychopathology (Gómez-Gil, Vidal-Hagemeijer, & Salamero, 2008; Leavitt, Berger, Hoeppner, & Northrop, 1980; Miach, Berah, Butcher, & Rouse, 2000; Tsushima & Wedding, 1979). Existing MMPI studies examining transgender men found elevations on the Psychopathic Deviate scale and the Masculinity–Femininity scale (Roback, McKee, Webb, Abramowitz, & Abramowitz 1976; Rosen, 1974). Roback et al. (1976) explained the elevation on the Psychopathic Deviate scale was likely related to the social difficulties that the transgender men experience due to their variation from expected sex-role conventions. The elevation on the Masculinity–Femininity scale was anticipated and indicated that transgender men reported more masculine traits than would be expected of females. A cross-sectional study comparing MMPI profiles of pre- and postsurgical transgender men found mean scale elevations on the Masculinity–Femininity and the Hypomania scale in presurgical transgender men, while postsurgical transgender men demonstrated much lower scores on the Paranoia scale, the Schizophrenia scale, and the Hypomania scale than presurgical transgender men (Fleming, Cohen, Salt, Jones, & Jenkins 1981). One recent cross-sectional study did not find significant differences in MMPI–2 clinical scales between pre- and post-hormone-treated transgender men who had been treated for at least 12 months (Gómez-Gil et al., 2008). Moreover, mean scores of both groups were found to be in the normative range.

The World Professional Association for Transgender Health's Standards of Care (Coleman et al., 2011) has urged mental and medical health practitioners to be familiar with the effects of hormone treatment. A meta-analysis of research on the quality of life and psychosocial outcomes of hormone treatment on transgender people reported that the evidence reviewed was of "very low quality" due to observational methods, lack of control groups, and cross-sectional designs (Murad et al., 2010). Recent research has called for more rigorous longitudinal research studies examining quality of life and psychosocial outcomes of hormone treatment (Gómez-Gil et al., 2012; Meier et al., 2011; Murad et al., 2010).

The current study examined the impact of testosterone treatment on psychological functioning of transgender men in a controlled longitudinal study. The aim of the present study was to investigate the psychopathology profiles of a community sample of transgender men within about 1 month of initiating testosterone treatment (baseline) and matched healthy nontransgender male and female controls and to compare these profiles with ones assessed 3 months later. Transgender men were matched to male and female controls at baseline on the variables of age and education level. Based on a review of previous cross-sectional findings, we hypothesized that transgender men's psychological profiles would show higher levels of psychopathology on the Psychopathic Deviate, Masculinity–Femininity, Paranoia, Schizophrenia, and Social Introversion scales relative to controls at baseline. Further, we hypothesized that while controls' profiles would remain stable, transgender men's profiles would demonstrate increases in psychological functioning on all scales except the Masculinity–Femininity scale after 3 months of testosterone treatment. To our knowledge, this is the first study to investigate the effects of testosterone on psychological functioning in transgender men using a controlled longitudinal design.

## Method

### Sample

Two hundred seventy-four participants were recruited to participate in a year-long longitudinal study on the psychological effects of testosterone on psychopathology, cognitive functioning, sexuality, and psychosocial well-being. A total of 233 participants consented to participate and completed the baseline assessment. The present study focused on the 163 participants who completed the MMPI–2 at the baseline assessment (Time 1) and 3-month follow-up (Time 2; retention rate = 70.0%) and who had valid MMPI–2 scores (one participant did not contribute data to analyses due to a high score on the Lie validity scale ($T$ score $>$ 80; (de Vries, Kreukels, Steensma, Doreleijers, & Cohen-Kettenis, 2011). Purposive sampling was used to recruit participants through the University of Houston subject pool, Houston community, personal contacts, transgender conferences, advertisements on transgender men-specific online groups and blogs, and transgender men's support groups in the United States. All study procedures were approved by the institutional review board at the University of Houston. The current study is part of a larger, ongoing, year-long study on the psychological effects of testosterone on psychopathology, cognitive functioning, sexuality, and psychosocial well-being. Participants were informed of the purpose of the study but were not informed of the specific hypotheses being tested. Written

informed consent was provided by all participants and, in one case, from a parent of a 16-year-old transgender participant. Participants were paid $10 in the form of a gift card for completing each assessment.

Transgender men who were recruited to be included in the study were planning to initiate testosterone treatment within 6 months of the first assessment visit. On average, participants began testosterone 21 days after completing the initial assessment. Just over one third ($n$ = 17) of participants had initiated testosterone treatment immediately prior to completing the initial assessment ($M$ = 17 days, $SD$ = 11.5 days; range 1–38 days). Testosterone treatment in the majority of transgender participants consisted of intramuscular (IM) injections ($n$ = 46; depo-testosterone cypionate or ethanate). Guidelines set forth by the Endocrine Society suggest transgender men inject 100–200 mg/14 days or 50% weekly (Hembree et al., 2009). It has been recommended that testosterone levels be monitored by laboratory testing on a regular basis (Coleman et al., 2011). Based on test results, the dose and method of administration may be changed by a medical provider (Coleman et al., 2011). Rarely, a higher dose may be indicated if a transgender man's testosterone levels remain in the low normal range after 200 mg every 2 weeks (University of California, San Francisco, Department of Family and Community Medicine, Center of Excellence for Transgender Health, 2011). Most participants' ($n$ = 32) IM dosages ranged from 50 to 400 mg every 10–14 days or 50% weekly. One participant was taking 200 mg every 3 weeks. Several participants ($n$ = 7) were started out at one dose (range: 25–100 mg weekly) and their doctors increased their dose (range: 50–200 mg weekly). Two participants' dosages were decreased from 75 to 50 mg/week and from 200 to 150 mg/14 days. Daily transdermal testosterone gel ($n$ = 1) or patches ($n$ = 1) were used by a few participants. Two participants started out using IM and then changed methods of administration within the first 3 months of treatment (IM and then patch; IM followed by cream and then IM).

Controls were required to be older than 18 years and not identify as transgender. Male and female controls must have reported a history of going through puberty and no history of hypogonadism or hormone imbalance. As a control for fluctuating hormone levels, females completed the protocol during their menstrual cycle at each assessment. One female control was excluded as she became pregnant during the study.

Transgender men who intended to begin testosterone therapy and maintain hormone treatment for a minimum of 1 year were recruited. Transgender men who had begun testosterone treatment within the previous month were included in the protocol, as masculinizing effects generally do not take place until 3 or more months after initiating testosterone treatment (Gooren, 2005; Gooren, Giltay, & Bunck, 2008; Hembree et al., 2009).

## Procedure

As part of a larger ongoing study, three groups of participants (transgender men and nontransgender males and females) completed a variety of written demographic and psychological measures at three time points over a 1-year period. Participants were individually administered the MMPI–2 to assess psychological functioning. The current study examined participants' MMPI–2 profiles at baseline (Time 1) and 3 months later (Time 2).

## Measures

Personality profiles were evaluated using the Minnesota Multiphasic Personality Inventory (2nd ed.; MMPI-2; Butcher et al., 2001). The MMPI–2 is the most commonly utilized assessment of psychopathology (Gómez-Gil et al., 2008). Reliability and validity of this instrument have been well established (Butcher et al., 2001). The MMPI-2 has good reliability, with both test–retest and internal consistency correlations mostly between 0.70 and 0.90 (Butcher et al., 2001). The MMPI–2 utilizes 567 true/false items in order to assess a range of personality profiles. It is estimated to take 60–90 min to complete. The second version of the MMPI is a restandardized version of the original MMPI and contains three validity scales (Lie, Infrequency, and Correction) in order to ensure that the profile is valid. It also contains 10 clinical scales: Hypochondriasis (1), Depression (2), Hysteria (3), Psychopathic-Deviate (4), Masculinity–Femininity (5), Paranoia (6), Psychasthenia (7), Schizophrenia (8), Hypomania (9), and Social Introversion (0). Raw scores are converted to $T$ scores and compared with normative data for assigned sex. The higher the mean scores, the lower the level of psychological functioning. $T$ scores above 65 (1.5 $SDs$ above the mean) are considered to be clinically significant (Butcher et al. 2001).

In previous research, the female template has been used for scoring profiles of transgender men on the MMPI–2 (Fleming et al., 1981; Gómez-Gil et al., 2008; Roback et al., 1976; Rosen, 1974). However, which sex template to score transgender men on in MMPI–2 research represents a methodological question, given that sex-normed templates do not consider sex and gender to be different constructs. The templates' standardization is based on a national sample of over 2,000 adults. Sex and gender were not queried separately in this standardization research to cross-classify respondents and identify transgender adults. We therefore scored transgender men on the female template when comparing them with female controls and on the male template when comparing them with male controls. This strategy was implemented in order to consider and be responsive to both sex-linked and gender-linked mechanisms of psychopathology (Krieger, 2003).

## Data Analysis

SAS (Version 9.3) statistical software was used for all data analyses. Statistical significance was determined at the alpha 0.05 level, and two-tailed tests of significance were conducted. Descriptive statistics were obtained for all variables (frequencies, means, standard deviations). Transgender men who had initiated testosterone treatment prior to baseline (33.3%) were compared with transgender men who had not started testosterone at treatment at baseline. There were no statistically significant differences by testosterone use in baseline mean scores in any of the MMPI–2 scales, using either the female or the male template (analyses not tabled). Analyses therefore compared all transgender men to female and male controls, respectively, focusing on (a) MMPI–2 scale scores (continuous) and (b) MMPI–2 clinical elevations (meeting a clinically elevated binary threshold for each MMPI–2 scale, $T$ score $>$ 65).

**Bivariate comparisons.** Bivariate differences in MMPI–2 scale scores and in clinical elevations by gender identity (transgender men vs. female controls on the female template and transgender men vs male controls on the male template) were estimated

separately for baseline (Time 1) and 3-month follow-up (Time 2) assessments. No direct comparisons were made between male and female nontransgender controls because the study design matched controls to the demographic distribution of the transgender men and adding comparisons between the male and female controls would require additional pairwise comparisons, which would inflate Type I error. Assuming independence at each time point, unadjusted linear (scale scores) and logistic (clinical cut points) regression models were used to compare transgender men with male and female controls.

**Analyses of change.** Because a longitudinal, repeated-measures design was used to collect identical measures on the same individuals on two measurements, assessments were positively correlated. Appropriate statistical procedures were utilized to adjust standard errors for within-person autocorrelation across time when modeling change (Fitzmaurice, Laird, & Ware, 2004; Singer & Willett, 2003). First, each of the MMPI–2 scale scores were modeled using longitudinal linear regression models as separate outcomes (two observations per individual participant; 326 total observations) to analyze the mean response profiles of participants by transgender identity over time adjusting for matching. The aim of this analysis was to characterize the patterns of change in the mean response over time and to determine if the shapes of the mean response profiles differed for transgender men compared with female and male controls, scored on the female and male template, respectively. The null hypothesis tested was that the mean response profiles of transgender men and controls were parallel (e.g., no Group × Time interactions). To test this hypothesis, a Transgender Men × Time interaction term was for each longitudinal model with MMPI–2 scale score as an outcome. Next, each of the MMPI–2 scales ($T$ scores) at Time 2 were modeled using an analysis of covariance (ANCOVA) approach to estimate whether there was a difference in means by gender identity, adjusting for baseline Time 1 MMPI–2 scores (i.e., adjusted change scores; Fitzmaurice et al. 2004). Linear models regressed each Time 2 MMPI–2 score on gender identity, adjusting for Time 1 MMPI–2 scores and appropriately accounting for matching. Transgender men were compared with male and with female controls, respectively.

Each MMPI–2 scale score was also categorized as either meeting a clinically significant threshold ($T$ score $>$ 65) or not ($T$ score $\leq$ 65; de Vries et al., 2011). Changes in clinical elevations for each MMPI–2 scale are descriptively presented but were not empirically tested due to small cell sizes. Instead, three binary outcomes were constructed using each of the dichotomized elevated scales to obtain an adequate number of cases to statistically compare changes in clinical diagnoses at Time 1 and Time 2: (a) any clinical elevation, (b) two or more clinical elevations, and (c) three or more clinical elevations. As in previous research the Masculinity–Femininity scale was excluded from this calculation (see de Vries et al., 2011). The McNemar's test, a two-sample test for binomial proportions appropriate for matched-pair data (Rosner, 2006), is equivalent to the paired $t$ test and appropriate for use with binary outcomes, so it was used to examine changes in the proportion of clinical diagnoses over time for transgender men and male and female controls, each separately.

**Attrition.** An analysis of attrition was conducted comparing baseline demographic and MMPI–2 variables for those who were lost to follow-up relative to those who were not using $t$ tests. No statistically significant differences were found by gender identity, age, race/ethnicity, or education comparing noncompleters and completers. There was a significant difference in MMPI–2 Hypomania scores at Time 1 for noncompleters ($M$ = 58.4; $SD$ = 12.9) compared with completers ($M$ = 53.8; $SD$ = 11.1), $t(225) = -2.51$, $p = .014$. Noncompleters also had elevated MMPI–2 baseline frequency scale (F) scores ($M$ = 62.0; $SD$ = 15.3) compared with completers ($M$ = 57.4; $SD$ = 14.5), $t(225) = -2.04$, $p = .044$. No other baseline differences in MMPI–2 scale scores or validity scores were found for participants lost to follow-up relative to those who completed both Time 1 and Time 2 assessments.

## Results

### Participants

Participant's ages ranged from 16 to 54 ($M$ = 26.6; $SD$ = 8.4). The breakdown of race/ethnicity was 74.2% White ($n$ = 121), 15.9% Latino/Hispanic/Chicano ($n$ = 26), 11.0% Asian/Asian American ($n$ = 18), 3.7% Black/African American ($n$ = 6), 1.8% Pacific Islander ($n$ = 3), 1.2% Middle Eastern ($n$ = 2), 0.6% Native American ($n$ = 1), and 2.5% other ($n$ = 4). For education, participants indicated the following: 13.5% high school diploma or less, 44.8% some college, 29.4% college degree, and 12.3% graduate degree.

Table 1 presents demographic data for age and education by gender identity (matching factors), including bivariate comparisons. As expected, given the matched controlled design of this study, no significant differences in age and education were noted between transgender men and male and female controls.

### Descriptive Characteristics of Psychological Functioning at Time 1 and Time 2

Table 2 descriptively presents MMPI–2 scale scores and clinical elevations, including bivariate comparisons by gender identity separately for Time 1 and Time 2 assessments.

At baseline, two of 10 MMPI–2 mean scale scores (Masculinity–Femininity and Social Introversion) were significantly higher ($p < .05$) for transgender men compared with females (Table 3); no other significant baseline differences were found for transgender men relative to female controls. At 3-month follow up, while Masculinity–Femininity mean scale scores remained significantly higher for transgender men relative to females, significant differences were no longer found on Social Introversion. Further, transgender men demonstrated statistically significantly lower mean scores on Depression and Psychasthenia than female controls.

At baseline, nine of 10 MMPI–2 mean scale scores (exception: Hypomania) were significantly higher for transgender men compared with male controls (Table 3). At 3-month follow-up, only four of 10 MMPI–2 mean scale scores (Depression, Masculinity–Femininity, Schizophrenia, and Social Introversion) remained significantly higher for transgender men relative to male controls. There were no longer statistically significant differences between transgender men and male controls on Hypochondria, Hysteria, Psychopathic Deviate, Paranoia, or Psychasthenia scale after 3 months of testosterone administration.

Table 1
*Sociodemographic Characteristics by Gender Identity*

| Characteristic | Transgender men ($n$ = 48) | | | Female ($n$ = 62) | | | Male ($n$ = 53) | | | Bivariate comparisons | | | Total ($n$ = 163) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *M* (*SD*) | % | *n* | *M* (*SD*) | % | *n* | *M* (*SD*) | % | *n* | $F(2, 159)$ | $\chi^2(2)$ | *p* | *M* (*SD*) | % | *n* |
| Age in years | | | | | | | | | | 0.39 | | .68 | 26.6 (8.4) | | |
| Mean (*SD*) | 27.0 (8.9) | | | 27.1 (8.9) | | | 25.8 (7.5) | | | | | | | | |
| Range | 16–51 | | | 18–54 | | | 18–50 | | | | | | 18–54 | | |
| Educational attainment | | | | | | | | | | | | | | | |
| High school diploma or less | | 20.8 | 10 | | 11.3 | 7 | | 9.4 | 5 | | 3.10 | .21 | | 13.5 | 22 |
| Some college/associate's degree | | 43.8 | 21 | | 46.8 | 29 | | 43.4 | 23 | | 0.16 | .92 | | 44.8 | 73 |
| College degree | | 29.2 | 14 | | 27.4 | 17 | | 32.1 | 17 | | 1.43 | .49 | | 29.4 | 48 |
| Graduate degree | | 6.2 | 3 | | 14.5 | 9 | | 15.1 | 8 | | 2.16 | .34 | | 12.3 | 20 |
| Employment status[a] | | | | | | | | | | | | | | | |
| Student | | 41.7 | 20 | | 35.5 | 22 | | 30.2 | 16 | | 1.29 | .53 | | 35.6 | 58 |
| Unemployed | | 12.5 | 6 | | 6.5 | 4 | | 5.7 | 3 | | 1.80 | .41 | | 8.0 | 13 |
| Full-time work | | 35.4 | 17 | | 32.3 | 20 | | 45.3 | 24 | | 2.45 | .29 | | 37.4 | 61 |
| Part-time work | | 27.1 | 13 | | 35.5 | 22 | | 18.9 | 10 | | 3.66 | .16 | | 27.6 | 45 |

*Note.* To examine sociodemographic differences by gender identity, we fit unadjusted regression models with gender identity (male and female each compared with transgender men) as the predictor. Linear models were fit for age and logistic models for educational attainment, employment status, and ethnicity.
[a] Employment status sums to >100% given participants could indicate all that applied.

At baseline, a significantly higher proportion of transgender men compared with male controls (male template) met clinical thresholds for eight of 10 scales (Hypochondria, Depression, Hysteria, Masculinity–Femininity, Paranoia, Psychasthenia, Schizophrenia, and Social Introversion). At follow-up, the disproportionate number of clinical elevations was reduced to two of 10 clinical elevations compared with male controls (Schizophrenia and Social Introversion). Compared with female controls (female template), a higher proportion of transgender men met clinical thresholds for Masculinity–Femininity at both baseline and follow-up. At follow-up, the proportion of transgender men meeting clinical threshold for Paranoia (2.1%) was significantly lower than among the female controls (17.7%).

## Mean Response Profile Differences for Transgender Men Versus Female and Male Controls: Transgender × Time Interaction Effects

A Transgender × Time interaction term was fit in longitudinal linear models to examine whether mean response profiles on each MMPI–2 scale score were similar or different for transgender men compared with female and male controls on their respective sex-specific templates (Table 3). Statistically significant interactions were found for two of 10 scales (Hysteria and Paranoia) compared with female controls and for seven of 10 scales (Hypochondria, Depression, Hysteria, Psychopathic Deviate, Paranoia, Psychasthenia, and Schizophrenia) compared with male controls.

Interaction effects are graphically depicted in Figure 1. Shown are Hysteria and Paranoia for transgender compared with female controls, and Depression and Psychasthenia for transgender men versus male controls (examples of Transgender Men × Time interactions compared with male controls). Transgender men showed steeper increases in functioning, and sometimes in reverse directions as controls.

## Changes in MMPI–2 Scores at Acute Postbaseline 3-Month Follow-Up, Adjusting for Baseline MMPI–2 Scores

As shown in Table 3, the ANCOVAs, regressing Time 2 scores on gender identity and adjusting for Time 1 scores, demonstrated statistically significant differences in MMPI–2 scores at 3-month follow-up relative to baseline for transgender men compared separately with female and male controls on female and male templates, respectively. Transgender men relative to female controls also showed significant reductions (main effects) in Hypochondria, Depression, Hysteria, and Paranoia, as well as significantly increased Masculinity–Femininity scores with adjustment for baseline MMPI–2 scores. No statistically significant main effect differences were found comparing transgender men and male controls after accounting for baseline MMPI–2 scores. In all models, the global $F$ test suggests that MMPI–2 scores at Time 1 significantly predicted MMPI–2 scores at Time 2.

## Changes in the Proportion of Cases Meeting MMPI–2 Clinical Elevations

MMPI–2 Masculinity–Femininity scale (Scale 5) was excluded from summary count of clinical elevations. At baseline, transgender men's MMPI–2 profiles were significantly more likely to meet any clinical elevation (72.9% vs. 41.5%), two or more clinical elevations (45.8% vs. 18.9%), and three or more elevations (33.3% vs. 5.7%) at baseline on the male template compared with male controls (Table 4). Similar differences were not found comparing transgender men and female controls on the female template at baseline.

The proportion of transgender men showing elevations for clinical scales decreased significantly from baseline to follow-up on both the female (Test Statistic A) and male (Test Statistic C) templates (Table 4). There were no statistically significant reduc-

Table 2
*Descriptive Characteristics and Bivariate Comparisons of Psychological Functioning at Baseline (Time 1) and Acute Postbaseline 3-Month Follow-Up (Time 2) by Gender Identity (N = 163)*

| | MMPI–2 scores: Mean (*SD*) | | | | MMPI–2 clinical elevations (*T* > 65, yes/no): % (*n*) | | | |
|---|---|---|---|---|---|---|---|---|
| | Female template | | Male template | | Female template | | Male template | |
| Variable | Transgender men | Female | Transgender men | Male | Transgender men | Female | Transgender men | Male |
| Scale 1: Hypochondria | | | | | | | | |
| Time 1 | 53.7 (10.1) | 54.0 (11.1) | **56.2 (10.7)** | **49.7 (8.2)**$^{**}$ | 14.6 (7) | 19.4 (12) | **16.7 (8)** | **1.9 (1)**$^{*}$ |
| Time 2 | 49.5 (9.6) | 52.8 (9.4)$^{\dagger}$ | 51.9 (9.9) | 49.3 (9.1) | 8.3 (4) | 12.9 (8) | 8.3 (4) | 3.8 (2) |
| Scale 2: Depression | | | | | | | | |
| Time 1 | 53.9 (10.1) | 56.3 (14.3) | **58.4 (10.5)** | **48.2 (9.6)**$^{***}$ | 12.5 (6) | 25.8 (16)$^{\dagger}$ | **20.8 (10)** | **3.8 (2)**$^{*}$ |
| Time 2 | **49.8 (9.9)** | **54.8 (13.1)**$^{*}$ | **53.6 (10.7)** | **48.9 (9.6)**$^{*}$ | 8.3 (4) | 19.4 (12) | 10.4 (5) | 3.3 (2) |
| Scale 3: Hysteria | | | | | | | | |
| Time 1 | 51.3 (9.8) | 51.7 (10.3) | **54.0 (10.3)** | **49.2 (9.1)**$^{*}$ | 6.3 (3) | 11.3 (7) | **16.7 (8)** | **1.9 (1)**$^{*}$ |
| Time 2 | 47.2 (9.1) | 51.1 (11.1)$^{\dagger}$ | 49.5 (9.5) | 49.3 (9.3) | 2.1 (1) | 11.3 (7) | 2.1 (1) | 5.7 (3) |
| Scale 4: Psychopathic Deviate | | | | | | | | |
| Time 1 | 60.3 (11.7) | 57.5 (11.3) | **59.0 (11.6)** | **52.6 (11.2)**$^{**}$ | 35.4 (17) | 29.0 (18) | 25.0 (12) | 11.3 (6)$^{\dagger}$ |
| Time 2 | 55.2 (9.8) | 55.5 (11.4) | 53.9 (9.6) | 50.9 (10.5) | 14.6 (7) | 17.7 (11) | 10.4 (5) | 13.2 (7) |
| Scale 5: Masculinity/Femininity | | | | | | | | |
| Time 1 | **62.9 (12.2)** | **57.8 (9.7)**$^{*}$ | **58.3 (10.5)** | **48.7 (10.3)**$^{***}$ | **52.1 (25)** | **16.1 (10)**$^{*}$ | **25.0 (12)** | **5.7 (3)**$^{*}$ |
| Time 2 | **65.1 (13.0)** | **56.8 (10.8)**$^{**}$ | **57.1 (10.8)** | **48.2 (12.7)**$^{**}$ | **58.3 (28)** | **17.7 (11)**$^{**}$ | 18.8 (9) | 11.3 (6) |
| Scale 6: Paranoia | | | | | | | | |
| Time 1 | 56.0 (11.4) | 53.9 (12.9) | **56.9 (11.7)** | **48.0 (11.1)**$^{**}$ | 25.0 (12) | 16.1 (10) | **25.0 (12)** | **5.7 (3)**$^{*}$ |
| Time 2 | 49.9 (9.0) | 53.2 (11.7) | 50.9 (9.4) | 48.0 (9.9) | **2.1 (1)** | **17.7 (11)**$^{*}$ | 2.1 (1) | 3.8 (2) |
| Scale 7: Psychasthenia | | | | | | | | |
| Time 1 | 55.2 (11.8) | 58.5 (12.4) | **57.7 (13.0)** | **50.0 (9.1)**$^{**}$ | 22.9 (11) | 25.8 (16) | **25.0 (12)** | **7.7 (4)**$^{*}$ |
| Time 2 | **51.2 (10.4)** | **56.7 (12.9)**$^{*}$ | 53.8 (11.1) | 51.0 (10.2) | 8.3 (4) | 22.6 (14)$^{\dagger}$ | 12.5 (6) | 5.7 (3) |
| Scale 8: Schizophrenia | | | | | | | | |
| Time 1 | 62.2 (12.5) | 60.5 (13.5) | **62.5 (13.5)** | **51.9 (10.1)**$^{***}$ | 43.8 (21) | 35.5 (22) | **43.8 (21)** | **9.4 (5)**$^{**}$ |
| Time 2 | 57.9 (11.8) | 57.3 (11.8) | **58.5 (13.1)** | **53.2 (8.8)**$^{*}$ | 35.4 (17) | 29.0 (18) | **35.4 (17)** | **7.6 (4)**$^{**}$ |
| Scale 9: Hypomania | | | | | | | | |
| Time 1 | 53.5 (12.2) | 54.2 (10.9) | 50.9 (12.5) | 53.8 (10.6) | 20.8 (10) | 17.7 (11) | 14.6 (7) | 17.0 (9) |
| Time 2 | 53.0 (10.9) | 52.8 (10.8) | 50.7 (10.6) | 54.5 (12.5) | 18.8 (9) | 12.9 (8) | 16.7 (8) | 22.6 (12) |
| Scale 10: Social Introversion | | | | | | | | |
| Time 1 | **54.1 (11.7)** | **49.6 (11.4)**$^{*}$ | **56.4 (12.4)** | **47.2 (11.1)**$^{**}$ | 16.7 (8) | 9.7 (6) | **27.1 (13)** | **9.4 (5)**$^{*}$ |
| Time 2 | 53.8 (10.8) | 50.1 (10.7)$^{\dagger}$ | **56.5 (11.7)** | **48.2 (11.7)**$^{**}$ | 16.7 (8) | 9.7 (6) | **27.1 (13)** | **11.3 (6)**$^{*}$ |

*Note.* Transgender men: $n = 48$, females: $n = 62$, and males: $n = 53$. Bold typeface indicates statistical significance. Bivariate, unadjusted regression models (linear models for Minnesota Multiphasic Personality Inventory [2nd ed.; MMPI–2] scores and logistic models for MMPI–2 diagnoses) were fit to compare transgender men with female controls (scored on the female template) and with male controls (scored on the male template). This was done for Time 1 and Time 2 separately (i.e., treating each time point as independent) to examine differences in MMPI–2 by transgender identity at each time point.
$^{\dagger}p < .10$. $^{*}p < .05$. $^{**}p < .01$. $^{***}p < .001$.



tions in the proportion of female (Test Statistic B) and male (Test Statistic D) controls meeting these clinical cut points from baseline to Time 2, suggesting the relative stability of MMPI–2 clinical elevations for matched controls.

## Discussion

This is the first known study in the United States to prospectively investigate the effects of testosterone on psychological functioning in transgender men using a controlled longitudinal design. This study aimed to investigate changes in psychopathology profiles of a community sample of transgender men as they are beginning hormone therapy and 3 months later compared with a community sample of matched, nontransgender male and female healthy controls.

First, relative to both male and female controls, psychological functioning of transgender men significantly improved prospectively after only 3 months of testosterone therapy. Transgender men's MMPI–2 profiles demonstrated significantly fewer clinical elevations at the 3-month follow-up assessment compared with baseline. For example, the number of transgender men who demonstrated two or more clinical elevations at baseline decreased from 43% to 25% (female template) and from 46% to 27% (male template) 3 months after initiating testosterone. This finding provides support to the idea that hormone treatment is a medically necessary intervention for transgender individuals. The Masculinity–Femininity scale was the only scale that remained significantly elevated among transgender men compared with both male and female control groups.

The Masculinity–Femininity scale was originally intended to measure 1940's stereotypical male and female vocational interests (Hathaway, 1956; Hathaway & McKinley, 1943). However, much of the early research on this scale attempted to use it to identify gay men, and although currently most clinicians do not interpret elevations on the Masculinity–Femininity scale, some may interpret

Table 3

*Longitudinal Linear Models of Mean Response Profiles Over Time and Analysis of Covariance (ANCOVA) Modeling Changes in MMPI–2 Scores From Baseline (Time 1) to Acute Postbaseline 3-Month Follow-Up (Time 2) With Adjustment for Baseline MMPI–2 Scores (N = 163)*

| | Female controls | | | | |
|---|---|---|---|---|---|
| | Change scores (female template) ΔT2 − T1 | | (A) Longitudinal models: Transgender Men × Time interaction β (95% CL) | (B) ANCOVA $F(2, 107)$ β (95% CL) | |
| Variable | Transgender men | Female | | Transgender men vs. female | MMPI–2 scores Time 1 |
| Scale 1: Hypochondria | −4.2 (9.1) | −1.1 (8.7) | −3.02 [−6.40, 0.36] | **−3.14*** [−6.00, −0.29]** | **0.55*** [0.42, 0.68]** |
| Scale 2: Depression | −4.1 (7.2) | −1.4 (8.1) | −2.68† [−5.62, 0.25] | **−3.28*** [−5.99, −0.58]** | **0.75*** [0.65, 0.86]** |
| Scale 3: Hysteria | −4.2 (7.9) | −0.6 (9.4) | **−3.52*** [−6.86, −0.18]** | **−3.66*** [−6.72, −0.61]** | **0.64*** [0.49, 0.79]** |
| Scale 4: Psychopathic Deviate | −5.1 (8.5) | −2.0 (8.8) | −3.19† [−6.51, 0.12] | −2.19 [−5.16, 0.78] | **0.65*** [0.52, 0.78]** |
| Scale 5: MF | 2.2 (11.3) | −1.0 (9.4) | 3.21 [−0.70, 7.13] | **5.05** [1.31, 8.78]** | **0.64*** [0.47, 0.81]** |
| Scale 6: Paranoia | −6.1 (8.9) | −0.7 (8.6) | **−5.41** [−8.45, −2.06]** | **−4.62** [−7.47, −1.77]** | **0.62*** [0.50, 0.73]** |
| Scale 7: Psychasthenia | −4.0 (8.6) | −1.8 (9.7) | −2.18 [−5.70, 1.34] | −3.20† [−6.46, 0.05] | **0.69*** [0.56, 0.82]** |
| Scale 8: Schizophrenia | −4.3 (8.5) | −3.2 (7.6) | −1.08 [−4.12, 1.97] | −0.59 [−3.31, 2.14] | **0.72*** [0.62, 0.82]** |
| Scale 9: Hypomania | −0.5 (8.0) | −1.4 (8.8) | 0.92 [−2.31, 4.16] | 0.70 [−2.21, 3.62] | **0.67*** [0.55, 0.80]** |
| Scale 0: Social Inversion | −0.3 (5.1) | 0.5 (5.6) | −0.78 [−2.84, 1.28] | −0.03 [−1.96, 1.95] | **0.83*** [0.74, 0.91]** |

| | Male controls | | | | |
|---|---|---|---|---|---|
| | Change scores (male template) ΔT2 − T1 | | (C) Longitudinal models: Transgender Men × Time interaction β (95% CL) | (D) ANCOVA $F(2, 98)$ β (95% CL) | |
| Variable | Transgender men | Male | | Transgender men vs. male | MMPI–2 scores Time 1 |
| Scale 1: Hypochondria | −4.3 (9.8) | −0.4 (7.0) | **−3.90* [−7.24, −0.56]** | −1.31 [−4.50, 1.88] | **0.60*** [0.44, 0.76]** |
| Scale 2: Depression | −4.8 (8.1) | 0.7 (8.1) | **−5.45** [−8.66, −2.24]** | −2.30 [−5.65, 1.04] | **0.69*** [0.54, 0.84]** |
| Scale 3: Hysteria | −4.5 (9.1) | 0.1 (7.7) | **−4.61** [−7.93, −1.30]** | −2.67 [−5.71, 0.36] | **0.60*** [0.44, 0.75]** |
| Scale 4: Psychopathic Deviate | −5.2 (8.6) | −1.7 (7.4) | **−3.51* [−6.66, −0.36]** | −1.26 [−4.11, 1.59] | **0.65*** [0.53, 0.77]** |
| Scale 5: MF | −1.1 (7.0) | −0.5 (6.7) | −0.66 [−3.36, 2.05] | −0.02 [−3.00, 2.97] | **0.93*** [0.80, 1.06]** |
| Scale 6: Paranoia | −6.0 (9.4) | 0.1 (8.2) | **−6.05** [−9.54, −2.57]** | −2.14 [−5.24, 0.96] | **0.56*** [0.43, 0.69]** |
| Scale 7: Psychasthenia | −3.9 (10.3) | 2.0 (8.8) | **−5.88** [−9.65, −2.11]** | −2.19 [−5.58, 1.19] | **0.58*** [0.44, 0.71]** |
| Scale 8: Schizophrenia | −4.0 (9.7) | 1.3 (8.1) | **−5.26** [−8.78, −1.74]** | −1.58 [−5.03, 1.86] | **0.65*** [0.52, 0.79]** |
| Scale 9: Hypomania | −0.1 (8.4) | 0.7 (7.9) | −0.83 [−4.06, 2.41] | −1.53 [−4.61, 1.56] | **0.76*** [0.63, 0.90]** |
| Scale 0: Social Inversion | −0.1 (5.9) | 1.1 (6.7) | −1.03 [−3.53, 1.46] | 0.34 [−2.26, 2.94] | **0.85*** [0.75, 0.96]** |

*Note.* Transgender men ($n$ = 48), females ($n$ = 62), and males (n = 53). Longitudinal linear models were fit to analyze the mean response profiles of respondents by transgender identity over time. The aim of this analysis was to characterize the patterns of change in the mean response over time and to determine if the shapes of the mean response profiles differ for transgender men compared with female and male controls. To test the null hypothesis that the mean response patterns of transgender men and female and male controls were parallel (i.e., no Group × Time interaction), we fit a Transgender Men × Time interaction term for each Minnesota Multiphasic Personality Inventory [2nd ed.; MMPI–2] scale score. [Null hypotheses: (A) Transgender men ΔT2 − T1 = Female ΔT2 − T1, and (B) Transgender Men ΔT2 − T1 = Male ΔT2 − T1]. ANCOVA: Linear regression models were fit with Time 2 scores as an outcome, and gender as a predictor, adjusting for Time 1 scores. Models were first fit with the referent group as female [Statistical model: (B) Time 2 MPPI–2 scale score = β 0+ β 1(MMPI–2 Time 1 score) + β 2(Transgender men) + e] and then with the referent group as male [Statistical model: (C) Time 2 MPPI–2 Scale Score = β 0+ β 1(MMPI–2 Time 1 score) + β 2(Transgender Men) + e]. Boldface indicates statistical significance. CL = confidence limits; MF = Masculinity/Femininity scale; e = error.
† $p < .10$. * $p < .05$. ** $p < .01$. *** $p < .0001$.



these high scores to be related to homosexuality in men (Martin & Finn, 2010). In the present study, elevated Masculinity–Femininity scores are thought to reflect gender dysphoria or discomfort with the female gender role as well as level of masculine interests (de Vries et al., 2011; Lothstein, 1984; Miach et al., 2000) and, consistent with previous literature using the female template (de Vries et al., 2011; Miach et al., 2000), indicate that transgender men were more likely to endorse stereotypical masculine interests than female controls. It is not surprising that transgender men still experienced discomfort with the female gender role and viewed themselves as more masculine after initiating testosterone. When scored according to the male template, although transgender men's mean Masculinity–Femininity score was within the normal range, it was found to be significantly higher than control males' at baseline and 3 months.

Although the Social Introversion scale was not clinically elevated for over 80% of the sample, transgender men were still found to function psychologically worse than male controls on this domain at both time points and worse than female controls at baseline only. As transgender men's average $T$ score on this scale was closer to females' than males' at baseline (difference scores: 4.5 and 9.2, respectively), their scores did not have to decrease as much to become similar to female controls' scores. The Social Introversion scale measures self-consciousness, social avoidance, and self/other alienation. Transgender men's scores on these constructs are thought to be impacted by the

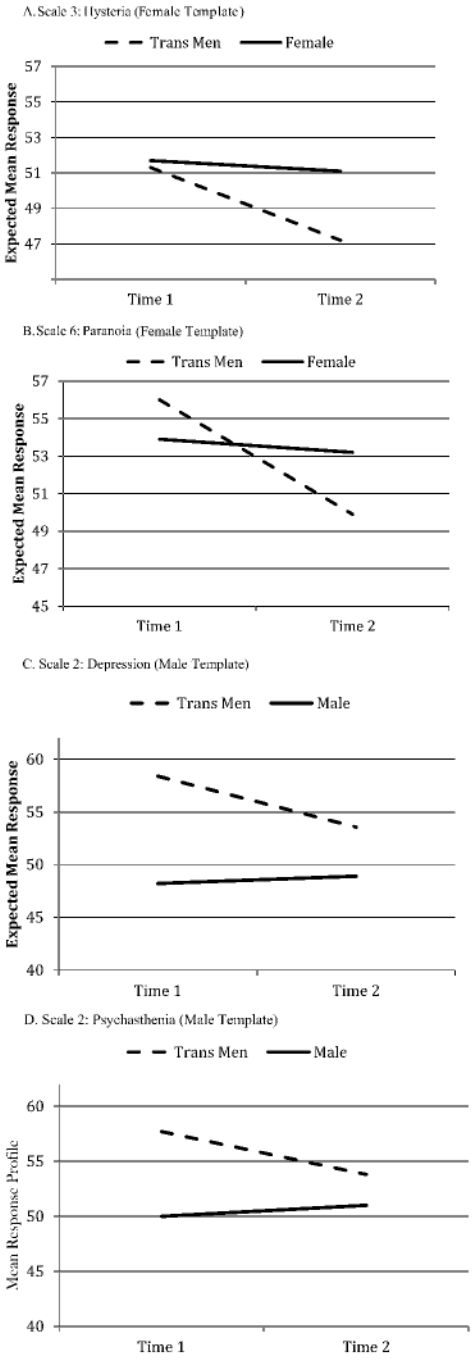


*Figure 1.* Graphical depiction of selected Transgender Man × Time interaction effects shown in Table 3. Panel A. Scale 3: Hysteria (female template). Panel B. Scale 6: Paranoia (female template). Panel C. Scale 2: Depression (male template). Panel D. Scale 2: Psychasthenia (male template). Trans = transgender.

social stigma of transgender identities. Prior to coming out, transgender men are typically expected by society to function in the female gender role. However, many pretransition and early transition transgender men feel uncomfortable in their body for many years prior to transitioning and often avoid social situations where they are not likely to be seen as males (Hendricks & Testa, 2012). Budge, Adelson, and Howard (2013) reported that while social support is important for the mental health and well-being of transgender people, there are "major deficits" in social support for this population. The minority stress theory (Bockting et al., 2013; Hendricks & Testa, 2012) posits that transgender men face high levels of social trauma and discrimination (Bradford, Reisner, Honnold, & Xavier, 2013; Clements-Nolle et al., 2006) and may be more likely to be hypervigilant or engage in isolation in order to protect themselves. Therefore, transgender men may be more likely to feel disconnected from others and lack a sense of belonging. As many transgender men's bodies are just beginning to masculinize at 3 months of testosterone treatment, they may not be perceived as men by others, and this may contribute to self-consciousness (Devor, 2004). It is thought that this scale may be sensitive to social stigma, trauma, and rejection and may not be measuring an introverted personality structure in transgender men. While transgender men's scores in this domain did not change compared with male controls, their scores were no longer significantly different from female controls at 3 months; however, a trend remained. This finding suggests that transgender men begin to become more comfortable in social situations, gain self-confidence, and become less sensitive to what others think of them after 3 months of testosterone treatment. These positive changes are likely influenced by environmental factors including a supportive transgender community, acceptance by family members and friends, and acceptance in social environments including school, work, and place of worship. Future research could elucidate these findings. Elevations on the Social Introversion scale may dissipate after further time on testosterone therapy. It remains a question if, as transgender men are more consistently witnessed socially as males (colloquially, "passing"), they report increased comfort in social situations (Gómez-Gil et al., 2012; Meier et al., 2011).

Second, transgender men functioned psychologically worse at baseline on multiple domains relative to female and male controls and demonstrated relatively higher rates of co-occurring problems. However, on average, transgender men's levels of psychological functioning were within the normative range. This finding is consistent with several previous studies of transgender people (Colizzi et al., 2014; Davis & Meier, 2014; Gómez-Gil et al., 2008; Hoshiai et al., 2010; Meier et al., 2011; Miach et al., 2000). Considering the societal oppression and high levels of discrimination this population faces, several findings showing that, on average, transgender men's psychological functioning is in the normative range, highlight the incredible resilience of this population and calls into question the pathologizing idea that a transgender identity is a mental illness. These findings further call into question policies that restrict the lives of transgender people on the basis of conflating transgender identity with mental illness or poorer psychological functioning.

One additional interesting pattern emerged from the data. Prior to beginning testosterone, transgender men did demonstrate lower psychological functioning when compared with an identity-matched gender group (i.e., healthy males). However, after initiating testosterone therapy MMPI–2 profiles of trans-

Table 4
*Statistical Comparisons of MMPI–2 Clinical Elevations at Baseline (Time 1) and Acute Postbaseline 3-Month Follow-Up (Time 2) (N = 163)*

| | Female template | | | | | | Male template | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Transgender Men | | | Female | | | Transgender men | | | Male | | |
| Variable | % | *n* | (A) Test statistic | % | *n* | (B) Test statistic | % | *n* | (C) Test statistic | % | *n* | (D) Test statistic |
| Any clinical elevation | | | | | | | | | | | | |
| Time 1 | 77.1 | 37 | **7.12**$^{**}$ | 54.8$^{\dagger}$ | 34 | 0.40 | 72.9 | 35 | 3.77$^{\dagger}$ | 41.5$^{**}$ | 22 | 0.07 |
| Time 2 | 54.2 | 26 | | 51.6 | 32 | | 58.3 | 28 | | 43.4 | 23 | |
| Two or more clinical elevations | | | | | | | | | | | | |
| Time 1 | 43.8 | 21 | **9.00**$^{**}$ | 35.5 | 22 | 0.89 | 45.8 | 22 | **7.36**$^{**}$ | 18.9$^{**}$ | 10 | 1.29 |
| Time 2 | 25.0 | 12 | | 37.1 | 23 | | 27.1 | 13 | | 13.2$^{*}$ | 7 | |
| Three or more clinical elevations | | | | | | | | | | | | |
| Time 1 | 27.1 | 13 | **5.44**$^{*}$ | 30.6 | 19 | 3.57$^{\dagger}$ | 33.3 | 16 | **6.23**$^{*}$ | 5.7$^{**}$ | 3 | 1.80 |
| Time 2 | 12.5 | 6 | | 22.6 | 14 | | 14.6 | 7 | | 11.3 | 6 | |

*Note.* Trangender men: $n = 48$; females: $n = 62$; males: $n = 53$. Pairwise comparisons were conducted using logistic regression models with each clinical elevation indicator as a binary outcome, and comparing transgender men with male and female controls, respectively. Minnesota Multiphasic Personality Inventory [2nd ed.; MMPI–2] Masculinity/Femininity scale (Scale 5) was excluded from summary count of clinical elevations. Boldface indicates statistical significance. Test statistic = McNemar's test statistic (1 degree of freedom) for matched pairs.
$^{\dagger} p < .10$. $^{*} p < .05$. $^{**} p < .01$.

gender men shifted in a healthier direction compared with both control groups, yet more so when using the identity-matched template (i.e., male template). Thus, in 3 months, transgender men's scores became more similar to controls who shared their gender identity. In fact, by 3 months on testosterone, transgender men's MMPI–2 profiles were no longer significantly different than male controls on the Psychastenia (anxiety) scale, and they were found to be functioning better than female controls in that domain and on Depression.

The baseline MMPI–2 profiles (based on the female MMPI–2 scoring template) of transgender men are consistent with previous cross-sectional research. For example, research has consistently reported that transgender men's average MMPI scale scores fall within the normative range prior to the initiation of testosterone (de Vries et al., 2011; Gómez-Gil et al., 2008; Rosen, 1974; Tsushima & Wedding, 1979). Prior research has also reported that before initiating testosterone therapy, transgender men demonstrate higher rates of co-occurring psychological problems (Hepp et al., 2005).

Because MMPI–2 interpretations have significant implications for the lives of transgender people (e.g., maintaining custody of their children, gaining employment, accessing medical treatments, and so forth), several considerations should be taken when interpreting transgender men's MMPI–2 scale scores, especially prior to transition or in the early weeks of initiating testosterone. First, the gender template chosen to score profiles as well as the stage of transitioning impacts the profiles of transgender men in that they are likely to appear psychologically worse at earlier stages of transitioning, especially if the male template is used. As the MMPI–2 was not normed for use with the transgender population, scores should be interpreted with caution. Because of the many significant changes in MMPI–2 profiles in a short period of time after hormone initiation, it is thought that MMPI–2 profiles should not be relied upon to evaluate readiness for hormone treatment in this population.

Scales of the MMPI–2 may be impacted by cultural variables unique to the transgender population. The Hypochondria and Hysteria scales may be influenced by feelings of gender dysphoria. The Psychopathic Deviate scale is believed to be elevated in transgender men due to interpersonal difficulties related to the lack of acceptance of transgender people in society (de Vries et al., 2011). Elevations on the Paranoia scale before initiating hormone treatment may be due to feeling misunderstood, mistreated, suspicious and guarded, lonely, resentful toward family members, and afraid of physical attack (Duckworth & Anderson, 1995). More recent research, however, supports the argument that the elevations on the Paranoia scale may in fact be an artifact of the high rates of discrimination and family rejection among transgender people (Bockting et al., 2013; Hendricks & Testa, 2012; Lombardi, Wilchins, Priesing, & Malouf, 2002) and thus may be realistic appraisals and not a true measure of paranoia. Finally, increased scores on the Schizophrenia scale may be reflective of transgender men's lived experiences including strained family relationships, social alienation, and questioning of one's self-worth and identity (Butcher et al., 2001).

This study also adds to the current body of research in that previous controlled studies of transgender individuals typically only compared transgender men with females; given that the transgender men typically report gender identities as males, this study offers a novel side-by-side comparison with both nontransgender females and nontransgender males. This allows a more nuanced summary of MMPI–2 profiles among transgender men. For example, at baseline, transgender men differed from both males and females on Social Introversion and Masculinity–Femininity, but they also differed from males on seven additional domains: Hypochondria, Depression, Hysteria, Psychopathic Deviate, Paranoia, Psychastenia, and Schizophrenia.

The most important finding in the current study was that 3 months of testosterone treatment improved psychological functioning in transgender men in multiple domains. This is important because MMPI–2 profiles are thought to remain stable over time even with intensive psychotherapy (Gordon, 2001; Spiro et al., 2000). Compared with control males in this study, scores for seven of the 10 scales—Hypochondria, Depression, Hysteria, Psycho-

pathic Deviate, Paranoia, Psychastenia, and Schizophrenia—significantly decreased in transgender men in 3 months, which is indicative of substantial improvements (Spiro et al., 2000); similar decreases were found for Hysteria, Paranoia, and Social Introversion when transgender men were compared with female controls. Moreover, the prospective decreases in depression and anxiety observed in the current study are consistent with prior cross-sectional studies of transgender men (Davis & Meier, 2014; Gómez-Gil et al., 2012; Meier et al., 2011). These testosterone-related improvements in psychological functioning have implications for the overall quality of life and physical health of transgender men.

There are several clinical implications of the MMPI–2 changes observed over 3 months of testosterone therapy with transgender men. First, because reductions in depression symptoms may correlate with reduced suicide risk in transgender men, withholding testosterone treatment on the basis of depression or suicidality may be iatrogenic (Levy, Crown, & Reid, 2003; Meier et al., 2011). Some clinicians believe that even if a person is certain that he or she is transgender, has some social support, is informed of the risks and benefits of cross-sex hormone treatment, is likely to adhere to treatment, and is able to make an informed decision, depression and suicidality must be decreased prior to initiating hormone treatment. Their practice may include withholding professional letters to support initiating hormone treatment and targeting interventions at depression and suicidality as a first step. However, this evidence suggests that hormone treatment directly decreases symptoms of depression. Therefore, it is suggested that clinicians consider providing a letter of support for hormone initiation at the same time as providing treatment options for depression and suicidality instead of denying access to hormone treatment on the basis of depression or suicidality alone. Second, improvements in the Hypochondria and Hysteria scales may indicate increases in health related to accessing medical care, increased comfort in social situations, and feelings of happiness (Duckworth & Anderson, 1995). Third, decreases in Psychopathic Deviate, Paranoia, Psychastenia, Schizophrenia, and Social Introversion may result from increased feelings of acceptance, decreased attempts to conceal transgender identity, increased passing in the self-identified gender (Bockting et al., 2013; Gómez-Gil et al., 2012); which may also consequently correlate with lower risk of discrimination and battery and less hypervigilance. It is also possible that the initiation of testosterone improves psychological functioning in and of itself, regardless of "passing." Fourth, although the Hypochondria scale does not typically change over time (Greene & Clopton, 1999), transgender men's improvements may be related to developing a more optimistic outlook on life and decreased gender dysphoria, which may occur when the secondary sex characteristics associated with testosterone use emerge. Fifth, increases on the Masculinity–Femininity scale based on the female template indicate that transgender men have further consolidated their male identity after beginning testosterone treatment.

There are several reasons that testosterone treatment might improve psychological functioning in transgender men. First, our results provide support to the idea that the act of initiating a gender transition may be the key factor in reducing psychopathology (Gómez-Gil et al., 2012). Second, beginning testosterone treatment is a form of validation of their gender identity by a professional and marks an important step for many transgender men in their gender transition. It is possible that this leads to improved psychological well-being (de Vries et al., 2011). Third, access to gender-affirming care for the first time sets transgender men on a path to living the gender with which they identify, and concealment or avoidance of their transgender identity is no longer occurring (Bockting et al., 2013). As Yalom (2005) stated,

> When we deny or stifle parts of ourselves, we pay a heavy price: we feel a deep, amorphous sense of restriction; we are constantly on guard; we are often troubled and puzzled by internal but seemingly alien impulses that demand expression. When we are able to reclaim these disavowed parts, we experience a wholeness and a sense of liberation. (pp. 92–93).

Results from this study point to the positive impact of testosterone treatment in transgender men on psychological functioning. Short-term psychotherapy is not typically associated with increased psychological functioning on the MMPI–2, much less several significant improvements, as were observed in this study following 3 months of testosterone treatment. Thus, although standard practice has been to treat psychological conditions in transgender men, including depression and anxiety, prior to considering any medical treatment for a gender transition (Hale, 2007), psychotherapy alone is not thought to be sufficient for clinical treatment of transgender men's psychological wellbeing.

Results from this study also have several implications for the interpretation of the MMPI–2 among transgender men. First, the MMPI–2 is currently used for assessing readiness for gender reassignment, personnel selection, and parental custody. Results indicate that transgender men's profiles improve once they begin testosterone treatment; thus, it is recommended that clinicians interpret MMPI–2 results with caution among pretestosterone transgender men and reassess the MMPI–2 after at least 3 months of testosterone therapy. Interpreting pretransition MMPI–2 results without taking transition status into account may inadvertently discriminate against transgender persons. Second, results from this study highlight that future research studies should consider using both male and female control groups and gendered scoring templates to test hypotheses concerning transgender men. Baseline profiles of transgender men initially showed significantly higher scores on nine scales when compared with males (all but Hypomania) than when compared with females (two scales: Masculinity–Femininity and Social Introversion); however, at the follow-up assessment, transgender men scored higher than males on four scales (Depression, Masculinity–Femininity, Schizophrenia, and Social Introversion) and did not score higher than females on any scale except the Masculinity–Femininity scale. In fact, by follow-up, females actually scored higher than transgender men on Depression and Psychastenia. Although transgender men's improvement in psychological functioning is clear relative to both male and female control groups, comparisons using gender identity-matched controls (i.e., males) demonstrate a much stronger effect.

This study is distinct from the few previous longitudinal studies with transgender samples for several reasons. First, these data are the first in the Western hemisphere to use both male and female control groups in a nonclinical, prospective research design. It is possible that transgender participants would have responded differently in clinical samples, when their testosterone treatment is contingent on their MMPI–2 profiles (Gómez-Gil et al., 2012). The

sample size in the current study is at least double compared with samples in previous longitudinal research with transgender men. This study also includes a wide age range of transgender men beginning testosterone.

This study has clinical implications that impact disciplines concerned with transgender health and well-being, including medicine, public health, and behavioral health. Some medical professionals hesitate or even avoid prescribing medications, especially controlled substances like testosterone, due to lack of training and research. Therefore, the results of this study may provide more information to providers who wish to (or need to) assess transition readiness or to otherwise meet the transition needs of their transgender patients.

## Limitations

This study's generalizability is limited by the demographics of the nonprobability transgender sample, which in this study is primarily White and highly educated, not capturing the diversity inherent in the overall population of transgender men. In accordance with the Institute of Medicine (2011) recommendations on LGBTQ research, future research should include nonprobability samples that represent the diversity of transgender experiences and thus help create a more informed dialogue about the needs of the population overall. Next, transgender participants in this sample had access to medical care in the United States and had access to testosterone as part of their gender transition. The prevalence of psychopathology is yet unclear among transgender men who do not have access to or desire to initiate testosterone treatment. A limitation of our design is that one third of the sample had initiated testosterone therapy prior to baseline (e.g., potential bias); however, within-groups comparisons found no statically significant differences in baseline MMPI–2 psychopathology between transgender men on hormones ($M = 17$ days) and those who were not at baseline assessment. An additional limitation is that we did not measure therapy utilization over the course of the study; therefore, psychotherapy represents a potential confounder. It may be that hormone use and therapy have additive effects, and future research would benefit from examining the efficacy and effectiveness of combined bio-behavioral treatments (hormones and therapy). Additionally, levels of discrimination, acceptance, and hiding one's transgender identity were not measured. These variables may mediate the impact of hormonal transitioning on the psychological functioning of transgender men.

## Future Directions

In the future, researchers who look at current psychological functioning of transgender samples should take transition status into account when interpreting current and past research reports, as the growing body of literature indicates that those who have started hormone treatment often report better psychological functioning (Gómez-Gil et al., 2012; Meier et al., 2011). Prior research that aggregates different transgender identified groups together (e.g., transgender men with transgender women or those who began medical treatment with those who have not) may have generated inaccurate conclusions on mental health status among transgender samples. Future researchers should examine if the same positive effects of feminizing hormone treatment are found in transgender women and if genderqueer individuals also demonstrate improvements in mental health related to cross sex hormone treatment. Longer term follow up studies are needed to determine if this positive effect is maintained over time. Consistent with the report of the Institute of Medicine (2011), we recommend that future studies include nonprobability samples representing the diversity of transgender experiences in order to create a more informed dialogue about the needs of the overall transgender population.

## Conclusion

The current study is the first to demonstrate the direct positive impact of initiating testosterone treatment on the psychological functioning of transgender men. Overall, the results suggest that the majority of transgender men report subclinical levels of psychological distress before initiating testosterone treatment. Also, although they initially demonstrated poorer psychological functioning than nontransgender males, transgender men, by their third month on testosterone, were functioning as well as male and female controls and demonstrated positive gains in multiple clinical domains. The MMPI–2 profiles of transgender men who completed 3 months of testosterone treatment demonstrated significantly more psychological improvements than what is typically reported in the same time frame with psychotherapy alone. Overall findings here suggest significant, rapid, and positive effects of initiating testosterone treatment on the psychological functioning in transgender men.

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JCEM ONLINE

Brief Report

# Bone Mass in Young Adulthood Following Gonadotropin-Releasing Hormone Analog Treatment and Cross-Sex Hormone Treatment in Adolescents With Gender Dysphoria

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**Context:** Sex steroids are important for bone mass accrual. Adolescents with gender dysphoria (GD) treated with gonadotropin-releasing hormone analog (GnRHa) therapy are temporarily sex-steroid deprived until the addition of cross-sex hormones (CSH). The effect of this treatment on bone mineral density (BMD) in later life is not known.

**Objective:** This study aimed to assess BMD development during GnRHa therapy and at age 22 years in young adults with GD who started sex reassignment (SR) during adolescence.

**Design and Setting:** This was a longitudinal observational study at a tertiary referral center.

**Patients:** Young adults diagnosed with gender identity disorder of adolescence (DSM IV-TR) who started SR in puberty and had undergone gonadectomy between June 1998 and August 2012 were included. In 34 subjects BMD development until the age of 22 years was analyzed.

**Intervention:** GnRHa monotherapy (median duration in natal boys with GD [transwomen] and natal girls with GD [transmen] 1.3 and 1.5 y, respectively) followed by CSH (median duration in transwomen and transmen, 5.8 and 5.4 y, respectively) with discontinuation of GnRHa after gonadectomy.

**Major Outcome Measures:** How BMD develops during SR until the age of 22 years.

**Results and Conclusion:** Between the start of GnRHa and age 22 years the lumbar areal BMD *z* score (for natal sex) in transwomen decreased significantly from −0.8 to −1.4 and in transmen there was a trend for decrease from 0.2 to −0.3. This suggests that the BMD was below their pretreatment potential and either attainment of peak bone mass has been delayed or peak bone mass itself is attenuated. (***J Clin Endocrinol Metab*** **100: E270–E275, 2015)**



Adolescents with gender dysphoria (GD) can be treated with gonadotropin releasing hormone analog (GnRHa). Pubertal suspension enables them to reflect on their GD without the distress caused by the development of unwanted secondary sexual characteristics of their natal sex. In our center, children with GD can be treated with GnRHa from the age of 12 years (1). If the desire for sex reassignment (SR) persists, at the age of 16 years cross-sex hormones (CSH) are added. The psychological benefits of this treatment protocol have been clearly demonstrated (2). Previously, concerns regarding the long-term effects of GnRHa therapy on bone mass development have been expressed. Children with central precocious puberty treated with GnRHa have normal bone mass at final

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Abbreviations: aBMD, areal bone mineral density; BMAD, bone mineral apparent density; BMD, bone mineral density; CSH, cross sex hormones; FN, femoral region; GD, gender dysphoria; GnRHa, gonadotropin releasing hormone analog; LS, lumbar spine; PBM, peak bone mass; SR, sex reassignment.

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height attainment at age 16–17 years (3–5). In contrast, adolescents with GD remain hypogonadal until at least the age of 16 years, when CSH are added. Long-term effects on bone mineral density (BMD) of GnRHa and CSH have not been reported. We assessed peak bone mass (PBM) in young adults with GD that had been treated with GnRHa and CSH during their pubertal years.

## Patients and Methods

### Treatment protocol

(See also Supplemental Data.) Patients were treated as previously described (1). Briefly, triptorelin (Decapeptyl-CR, Ferring) 3.75 mg every 4 weeks sc was started in patients diagnosed with gender identity disorder (DMS IV-TR) in the age range from 11.4–18.3 years. In the age range from 15.6–19 years transwomen were prescribed incremental dosing of 17-$\beta$estradiol orally and transmen were given im mixed T esters (Sustanon 250 mg/ml, MSD) every 2–4 weeks in incremental dosages. At a minimum age of 18 years, after gonadectomy, GnRHa treatment was terminated and CSH therapy continued. During the entire treatment patients were advised on calcium intake and weight-bearing physical exercise.

### Study subjects

Study subjects were included when they were at least 21 years of age, gonadectomy had taken place in the period from June 1998 to August 2012, and data on BMD at start of GnRHa treatment, at start of CSH therapy, and at the age of 22 years were available. The 34 eligible subjects and their parents or legal representatives gave written consent for followup at start of treatment.

### Bone densitometry

Areal bone mineral density (aBMD, g/cm$^2$) of the lumbar spine (LS) and femoral region (nondominant side) (FN) was measured at the aforementioned time points by dual energy x-ray absorptiometry (Hologic QDR 4500, Hologic). During the study period, the Hologic apparatus was updated in July 2004 and

**Table 1.** Patient Characteristics During Sex-Reassignment Treatment

| Characteristic | Start GnRHa | Start CSH | 22 y | *P*-Value[a] | *P*-Value[b] |
|---|---|---|---|---|---|
| Transwomen (n = 15) | | | | | |
| Age, y | 14.9 ± 1.9 | 16.6 ± 1.4 | 22.1 ± 0.9 | — | — |
| Height, cm | 174.6 ± 8.9 | 179.9 [17.1] | 181.0 ± 9.3 | .01 | .001 |
| Height SDS[c] | 0.14 ± 1.3 | −0.97 ± 1.3 | −0.42 ± 1.3 | .001 | ns |
| Weight, kg | 64.8 ± 10.4 | 67.0 ± 10.2 | 74.6 ± 14.5 | .004 | .01 |
| BMI, kg/m$^2$ | 20.3 ± 2.3 | 21.2 ± 2.8 | 22.7 ± 4.4 | .01 | ns |
| BMI-SDS[c] | 0.17 ± 0.90 | 0.07 ± 1.11 | 0.62 ± 2.1 | ns | ns |
| Bone age[c], y | 15.5 ± 1.9 | 15.9 ± 1.8 | — | ns | |
| LH, mU/L | 1.7 [1.6] | 0.5 [1.0] | — | .02 | — |
| FSH, mU/L | 2.7 [2.2] | <0.5 [0.7] | — | .03 | — |
| T, nmol/L | 6.7 [18.0] | <0.1 [1.6] | — | .04 | — |
| Estradiol, pmol/L | 46 ± 24.6 | 25.0 [18.5] | — | .03 | — |
| Androstenedion, nmol/L | 4.9 ± 1.9 | 3.9 ± 1.2 | — | ns | — |
| DHEAS, $\mu$mol/L | 5.6 ± 3.1 | 5.3 ± 2.5 | | ns | |
| Tanner P | 5 [2] | 4 [2] | — | — | — |
| Tanner G | 5 [1] | 5 [1] | — | — | — |
| Testicular volume, ml | 20 [14] | 12 [11] | — | .01 | — |
| Transmen (n = 19) | | | | | |
| Age, y | 15.0 ± 2.0 | 16.4 [2.3] | 21.9 ± 0.5 | — | — |
| Height, cm | 165.2 ± 9.1 | 168.4 ± 8.3 | 170.6 ± 7.9 | .03 | <.0001 |
| Height-SDS[c] | −0.06 ± 1.2 | −0.1 ± 1.3 | −0.1 ± 1.2 | ns | ns |
| Weight, kg | 57.6 ± 12.1 | 64.1 ± 11.5 | 68.2 ± 9.8 | .01 | ns |
| BMI, kg/m$^2$ | 20.9 ± 3.2 | 22.9 ± 3.7 | 23.4 ± 2.6 | .02 | ns |
| BMI-SDS[c] | 0.3 ± 1.0 | 0.5 ± 1.2 | 0.96 ± 1.2 | ns | ns |
| Bone age[c], y | 15.0 [4.4] | 16.3 [3.25] | — | .002 | — |
| LH, mU/L | 3.5 [3.0] | 0.3 [0.8] | — | .002 | — |
| FSH, mU/L | 4.3 [2.1] | 1.9 [1.3] | — | .02 | — |
| T, nmol/L | <1.0 [1.4] | <1.0 [0] | — | — | — |
| Estradiol, pmol/L | 96.5 [250.5] | <20.0 [0.] | — | .001 | — |
| Androstenedion, nmol/L | 5.9 [4.8] | 4.8 [2.4] | — | ns | — |
| DHEAS, $\mu$mol/L | 3.8 [2.5] | 4.4 [3.0] | — | .008 | — |
| Tanner B | 4 [1] | 5 [2] | — | ns | — |
| Tanner P | 5 [1] | 5 [0] | — | ns | — |

Abbreviations: ns, not significant; BMI, Body Mass Index; DHEAS, dehydroepiandrosterone sulfate; SDS, standard deviation score.

Data are presented as median [interquartile range] or as mean ± SD.

[a] Start GnRHa vs start CSH.

[b] Start CSH vs at the age of 22 years.

[c] In reference to natal sex.

replaced in February 2011. Phantom calibration allowed for comparison of absolute BMD values. aBMD *z*-scores according to natal sex, age, and ethnicity were based on the National Health and Nutrition Examination Survey reference (6), which did not change during the study period. LS *z* scores were available from the start of the study but FN *z* scores became available in 2003, 5 years after the start of the study. Volumetric BMD (bone mineral apparent density [BMAD]) of the LS and FN were calculated as previously described and *z* scores were determined using a UK reference population (7). Reference values of BMAD in young adulthood are not available. In females lumbar PBM expressed as BMAD is attained at age 18–20 years and in males between 18 and 23 years (8). Therefore, to calculate the *z* score of the LS BMAD at age 22 years, the reference of LS BMAD of 17 years was used. Anthropometry, bone age, and hormonal levels are described in Supplemental Data.

### Statistical analyses

For the statistical analysis SPSS Version 22 (IBM) was used. Normally distributed data were expressed as mean ± SD and compared with the paired sample *T* test with post-hoc Bonferroni correction. Data that were not normally distributed were expressed as median and interquartile range and the Wilcoxon Signed Rank test was used for comparison. For correlation analyses, the Pearson's correlation coefficient ($\rho$) was calculated for normally distributed data. When data were not normally distributed the Spearman's rank correlation coefficient was calculated. $P < .05$ was considered statistically significant.

## Results

### Study population

Clinical characteristics are summarized in Table 1. Median duration of GnRHa monotherapy in transwomen and transmen was 1.3 years (range, 0.5–3.8) and 1.5 years (range, 0.25–5.2), respectively. The median duration of CSH therapy was 5.8 years (range, 3.0–8.0) and 5.4 years (range, 2.8–7.8), respectively. The median duration of combined GnRHa and CSH therapies was 3.1 years (range, 2.1–4.5) and 2.2 years (range, 1.4–3.1), respectively.

**Table 2.** Bone Mineral Density During Sex Reassignment Treatment of Adolescents with Gender Dysphoria

| | Start GnRHa | (n) | Start CSH | (n) | Age 22 y | (n) | $P^a$ (n) | $P^b$ (n) | $P^c$ (n) |
|---|---|---|---|---|---|---|---|---|---|
| Transwomen | | | | | | | | | |
| LS | | | | | | | | | |
| BMAD, g/cm$^3$ | 0.22 ± 0.03 | 11 | 0.22 ± 0.02 | 13 | 0.23 ± 0.03 | 13 | ns (11) | .003 (13) | ns (11) |
| BMAD *z* score | −0.44 ± 1.10 | 12 | −0.90 ± 0.80 | 14 | −0.78 ± 1.03 | 14 | ns (12) | ns (14) | ns (12) |
| Range | — | | — | | −2.76–1.18 | 14 | — | — | — |
| aBMD, g/cm$^2$ | 0.84 ± 0.13 | 12 | 0.84 ± 0.11 | 15 | 0.93 ± 0.10 | 15 | ns (12) | <.001 (15) | .006 (12) |
| aBMD *z* score | −0.77 ± 0.89 | 12 | −1.01 ± 0.98 | 13 | −1.36 ± 0.83 | 13 | ns (11) | ns (13) | .003 (12) |
| Range | — | | — | | −3.1–0.30 | 13 | — | — | — |
| T-score | — | | — | | −1.5 ± 1.10 | 15 | — | — | — |
| Range | — | — | | | −3.1–0.40 | 15 | — | — | — |
| FN | | | | | | | | | |
| BMAD, g/cm$^3$ | 0.28 ± 0.04 | 12 | 0.26 ± 0.04 | 14 | 0.28 ± 0.05 | 14 | ns (12) | ns (14) | ns (14) |
| BMAD *z* score | −0.93 ± 1.22 | 11 | −1.57 ± 1.74 | 10 | — | — | ns (10) | — | — |
| aBMD, g/cm$^2$ | 0.88 ± 0.12 | 14 | 0.87 ± 0.08 | 15 | 0.94 ± 0.11 | 15 | ns (14) | .009 (15) | ns (14) |
| aBMD *z* score | −0.66 ± 0.77 | 7 | −0.95 ± 0.63 | 11 | −0.69 ± 0.74 | 11 | ns (6) | ns (11) | ns (7) |
| Range | — | | — | | −2.0–0.5 | 11 | — | — | — |
| T-score | — | | — | | −0.75 ± 0.78 | 15 | — | — | — |
| Range | — | | — | | −2.0–0.10 | 15 | — | — | — |
| Transmen | | | | | | | | | |
| LS | | | | | | | | | |
| BMAD, g/cm$^3$ | 0.25 ± 0.03 | 18 | 0.24 ± 0.02 | 19 | 0.25 ± 0.28 | 19 | ns (18) | .001 (19) | ns (18) |
| BMAD *z* score | 0.28 ± 0.90 | 18 | −0.50 ± 0.81 | 19 | −0.033 ± 0.95 | 19 | .004 (18) | .002 (19) | ns (18) |
| Range | — | | — | | −1.8–2.03 | 19 | — | — | — |
| aBMD, g/cm$^2$ | 0.95 ± 0.12 | 18 | 0.91 ± 0.10 | 19 | 0.99 ± 0.13 | 19 | .006 (18) | <.001 (19) | ns (18) |
| aBMD *z* score | 0.17 ± 1.18 | 18 | −0.72 ± 0.99 | 19 | −0.33 ± 1.12 | 19 | <.001 (18) | ns (19) | .02 (19) |
| Range | — | | — | | −2.3–2.5 | 19 | — | — | — |
| T-score | — | | — | | −0.43 ± 1.2 | 19 | — | — | — |
| Range | — | | — | | −2.5–0.8 | 19 | — | — | — |
| FN | | | | | | | | | |
| BMAD, g/cm$^3$ | 0.32 ± 0.04 | 18 | 0.31 ± 0.04 | 19 | 0.33 ± 0.05 | 19 | ns (18) | .010 (19) | ns (18) |
| BMAD *z* score | 0.01 ± 0.70 | 18 | −0.28 ± 0.74 | 18 | — | — | ns (18) | — | — |
| aBMD, g/cm$^2$ | 0.92 ± 0.10 | 18 | 0.88 ± 0.09 | 19 | 0.95 ± 0.10 | 19 | .005 (18) | <.001 (19) | ns (18) |
| aBMD *z* score | 0.36 ± 0.88 | 13 | −0.35 ± 0.79 | 16 | −0.35 ± 0.74 | 16 | .001 (13) | .006 (16) | ns (13) |
| Range | — | | — | | −1.80–0.80 | | | | |
| T-score | — | | — | | 0.005 ± 0.87 | 19 | — | — | — |
| Range | — | | — | | −1.90–1.10 | 19 | | | |

Abbreviaton: ns, not significant.

Data are expressed as mean ± SD and compared with paired *t* test, significance $P < .017$.

*z*- and T-scores were calculated to natal sex.

[a] Start GnRHa vs Start CSH.

[b] Start CSH vs age 22 years.

[c] Start GnRHa vs age 22 years.

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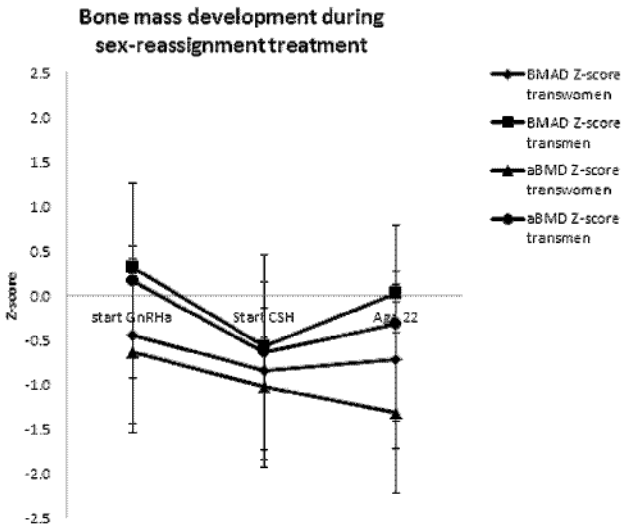


**Figure 1.** Longitudinal *z*-score (mean ± SD) development of the LS from start medical treatment until the age of 22 years in transmen and transwomen.

### BMD development

Bone mass development is summarized in Table 2 and in Figure 1.

In transwomen absolute aBMD and BMAD did not change during GnRHa monotherapy and the respective *z* scores decreased but not significantly. During CSH absolute LS aBMD increased but the *z* score at age 22 years was lower than at start of treatment.

In transmen both absolute LS and FN aBMD and the respective *z* scores decreased during GnRHa monotherapy and subsequently increased between start of CSH therapy and age 22 years. At age 22 years, LS aBMD *z* scores were lower compared with start GnRHa but this was not significant.

The duration of GnRHa monotherapy in both transwomen and transmen was not correlated with BMD, BMAD, and the respective *z* scores at the age of 22 years.

At age 22 years, six transwomen (40%) had an LS aBMD *z* score $<-2$. In addition, five transwomen (33%) had a T-score $<-1$ and $>-2.5$ and three subjects (20%) a T-score $< 2.5$. In transmen these numbers were 1 (5%), 5 (26%), and 0, respectively.

BMD development during GnRHa monotherapy in these subjects, and in 44 additional subjects in which dual energy x-ray absorptiometry measurements in young adulthood were not available, is described in Supplemental Data.

## Discussion

The main finding of this study is that young adult transwomen treated with GnRHa during adolescence have decreased LS aBMD *z* scores compared with the pretreatment level. In transmen, this loss of *z* score is also observed as a trend. In addition, in both groups absolute bone mass of the LS and FN decreases during GnRHa monotherapy, followed by an increase after the start of CSH.

According to the World Health Organization classification, both groups had individuals that would classify as osteopenic according to their T-score (6). However, T-scores are mainly relevant for middle-age patients and in this study it is more appropriate to use *z* scores that normalize for age, ethnicity, and sex. We used natal sex as a reference for aBMD *z* scores because the size and quality of cortex of the bone is determined during puberty and adolescence (9, 10), in line with recent studies on bone mass in transgender adults (11, 12). In adults, comparison of absolute values for BMD over time may be preferred, but in our subjects, the comparison of absolute values is less meaningful because BMD normally advances over time and therefore comparison of *z* scores is more appropriate. When using *z* scores of natal sex it should be taken into consideration that androgens and estrogens affect bone differently (13) and it was shown that bone properties in transgender population differ from their age- and natal sex—matched controls (11, 12, 14).

In transwomen, LS aBMD *z* score was below the population mean at the start of treatment. This finding is consistent with previous reports in transwomen populations (15, 16). It is conceivable that young transwomen may not feel comfortable engaging in sports activities typical for their natal sex. LS aBMD *z* score did not increase during CSH treatment, which may be explained by the relative initial low dose of estrogens. Indeed, a need for higher dosages has been reported (17, 18).

In the transmen, absolute LS aBMD and *z* score were normal at the start of treatment but decreased during GnRHa monotherapy. This may reflect the advanced pubertal state and increased dependence on sex steroids for bone mass maintenance at the start of treatment. In contrast with transwomen, in transmen the LS aBMD *z* scores improved under CSH, which may be due to the CSH scheme that allowed rapid dose increments. However pretreatment *z* scores were not reached at age 22 years. This is consistent with previous studies in adult transgender population, which reported loss of bone mass after 2–3 years on T maintenance therapy (19).

The relevance of these findings with respect to fracture risk is not clear. At present, as for transgender populations who had sex reassignment as adults (16), in adolescents with GD it is unknown whether medical intervention leads to an increased risk of fractures later in life. Furthermore, several limitations must be considered.

First, the findings of the present study should be interpreted cautiously because the primary outcome was bone mass at age 22 years and there were only 34 subjects available with complete data at 22 years. Second, it could not be determined whether the loss of bone mass at age 22 years can be attributed to the duration of GnRHa, initial low CSH dosage scheme, or the pharmacodynamic characteristics of CSH. Most patients were late pubertal at start and therefore part of their bone mass development had already occurred and GnRHa monotherapy therapy was relatively short before start of CSH therapy. The latter may explain why a correlation between duration of GnRHa monotherapy and bone mass at age 22 years was not found. The contribution of GnRHa treatment is at best tentative. Third, the data on *z* scores were limited. At the time of start of the study FN aBMD *z* scores were not available and only a small number of subjects could be compared from pretreatment to age 22 years. BMAD *z* scores are not available for adults (7) but since it was demonstrated that LS BMAD PBM is attained at the end of the second decade the reference at 17 years was used as a proxy. Given that females reach PBM earlier, around 18 years (8), this was more appropriate for the transmen. In males PBM is reached later (8) and therefore the LS BMAD *z* score may be overestimated. Fourth, our study lacked information on other factors influencing bone mass accrual, such as dietary calcium intake, vitamin D level, and weight-bearing exercise (20). Although patients were strongly advised on dairy intake and physical exercise, these factors were not recorded. Future studies should include serial measurement of vitamin D level and assessment of dairy intake and strenuous activities using standardized questionnaires (12).

Despite these limitations, our findings are relevant given that most the patients currently treated in our clinic is late pubertal at start of GnRHa treatment, as is observed in other transgender populations (21, 22). If CSH is postponed beyond the age of 16 years it should be taken into account that these subjects may be particularly prone for loss of bone mass. In addition, concerns for possible long-term deficits in bone health may be amplified in subjects who present at a more "ideal" pubertal stage, ie, Tanner stage 2–3.

In conclusion, this is the first study on the effects of early medical intervention of adolescents with GD regarding bone mass and demonstrates a loss of LS BMD *z* score at age 22 years. This decrease may reflect either a delay in PBM attainment or loss of PBM potential and may be attributed to the GnRHa-induced hypogonadal state, the relative low hormone dosage during the initial period of CSH therapy, or the pharmacodynamics characteristics of CSH. Continuous monitoring of the bone mass development in this population is warranted, preferably by a specialist endocrinologist with experience in transgender healthcare and knowledge of the adolescent treatment protocol.

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AOGS PATIENT PERSPECTIVE

# Fertility options in transgender and gender diverse adolescents

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Transgender coverage in the media is becoming more commonplace and children and adolescents from resource-rich countries are accessing transgender healthcare at an exponentially increasing rate. What factors should care providers, adolescents and parents/guardians or caretakers take into consideration with respect to fertility?

The World Professional Association for Transgender Health (WPATH) is the only global interdisciplinary association that is solely devoted to transgender health. WPATH's mission is to promote evidence-based care, education, research, advocacy, public policy and respect in transgender health. WPATH has produced seven versions of the *Standards of Care* (SOC) with the most recent version (SOC 7) released in 2012 (1).

SOC 7 includes a chapter on adolescent medical transition, as well as a chapter on transgender fertility. The latter marked a milestone in moving transgender healthcare forward, as discussing fertility options did not feature as prominently in earlier versions. In 2001, reproductive endocrinologist Petra De Sutter stated in her seminal paper that trans people should not have to forego reproductive options in exchange for medical transition (2). This is still the case in many countries, but the tide is shifting as individuals who identify as transgender and/or gender-diverse are gaining ground in the human rights area.

Three areas of intervention can affect fertility in the person who is undergoing medical transition. The first is hormone blockers; the second, hormone therapy; and the third, gonadectomy, where gametes can be retrieved and stored before the procedure. The criteria for hormone therapy for adults include the following: the patient should have persistent, well-documented gender dysphoria; be of the age of consent in a given country; be in reasonable control of any medical and mental health conditions; and have the capacity to consent to treatment. Adolescents may be eligible to begin feminizing/masculinizing hormone therapy, preferably with parental consent. In many countries, 16-year-olds are legal adults for medical decision-making and do not require parental consent. Ideally, treatment decisions should be made among the adolescent, the family and the treatment team (3).

Many younger adolescents may benefit from pubertal suppression (3). Pubertal suppression reversibly buys time for these individuals before a decision regarding more irreversible interventions can be made. It also prevents the development of unwanted secondary sex characteristics of the sex assigned at birth – often preventing the need for invasive procedures later on.

The options for retrieving sperm or eggs in children this young often depends on how mature the individual is at the time pubertal suppression is initiated. Although reversible, should an adolescent pursue cross-gender hormones after pubertal suppression, it is unlikely that eggs or sperm can be retrieved, and therefore conversations about fertility are being held with families of adolescents who are younger and younger.

Feminizing hormones in people assigned male at birth block testosterone production, and the results are variable as to whether sperm production will resume, based on the amount of time that the person has been taking hormones. Sperm cryopreservation is therefore recommended before the initiation of hormone therapy. With individuals for whom self-stimulation is difficult, testicular sperm extraction is a possible alternative method for sperm retrieval; although potentially costly and not covered by insurance.

Masculinizing hormones in people assigned female at birth block estrogen production, which causes a cessation in ovulation, but does not necessarily affect the quality of

 

the eggs, which is determined more by the age of the individual. Some trans masculine people are choosing to discontinue testosterone therapy for a period of time to carry a pregnancy and deliver and then resume therapy. It is not always guaranteed that the person is able to become pregnant after discontinuing testosterone.

Adolescents and adults alike should be counseled on fertility preservation, with more robust discussion taking place with adolescents on a number of occasions. Do younger adolescents have the capacity to discuss fertility options before initiating pubertal suppression? Similarly, are slightly more mature adolescents able to consent for masculinizing/feminizing hormone therapy that may disrupt their reproductive potential? It is an interesting question, as adolescents in this stage of development are often prioritizing their need to present in a way that is authentic to themselves and which allows others to perceive them as the gender they affirm, vs. preserving their reproductive potential. Are adolescents able, at this stage, to predict whether they wish to have their own biological children in the future? This must be balanced with the danger of withholding treatment, which is not a neutral option for adolescents, as it "might prolong gender dysphoria and contribute to an appearance that could provoke abuse and stigmatization" (3). A number of organizations, in addition to WPATH, strongly state that conversion therapy, an a priori attempt to change an individual's gender identity and/or sexual orientation, is no longer considered ethical.

Not only can fertility be affected by introducing hormones, changes can also be irreversible through gonadectomy. Genital surgery is usually delayed until the person is over the age of majority in a given country. However, the age of majority does not necessarily correlate with healthcare decisions that adolescents are able to make without the consent of their parent or guardian. Very few case reports exist on the outcome of individuals under the age of 18 years having surgery, and this is an important area for future research. The age criteria for lower surgery will most likely decline in the subsequent version of the Standards of Care, and a question that emerges is: what factors will be used to determine that an adolescent has the capacity to consent for gonadectomy? Should the adolescent have the capacity to consent for gonadectomy and has good parental/guardian/caretaker support, their quality of life in many cases will improve.

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Patient Perspective

# Gender dysphoria Fact Sheet

**Gender dysphoria** is a condition where a person experiences distress because there is an incongruence between their assigned sex and their gender identity (1). Biological sex is assigned at birth depending on the appearance of the genitals while gender identity is the gender that a person identifies with or feels themselves to be. Some people with gender dysphoria experience a strong desire to align their gender expression with their gender identity, which is different than the sex assigned to them at birth.

Gender dysphoria is a recognized medical condition, for which treatment is sometimes appropriate. Most psychologists and medical professionals do not consider it a mental disorder although it is still classified as one, nor is it a sexual disorder (2). The World Health Organization's scheduled update of their diagnostic tool in 2018 (ICD-11) plans to reclassify it as "Gender incongruence of adolescence and adulthood" (3).

The exact percentage of people who experience gender dysphoria is not known as the condition is highly stigmatized in many societies, but in many countries the number of people being diagnosed with the condition is increasing, due to growing public awareness. Estimated rates range from about 0.3–0.5% (25 million) of the global population (5). The first signs of gender dysphoria can appear at a very young age and may continue through childhood and into adulthood.

## Treatment for gender dysphoria

Treatment for gender dysphoria aims to help reduce or remove the distressing feelings of a mismatch between assigned sex and gender identity and help people live as their preferred gender identity (3). The World Professional Association for Transgender Health (WPATH) Standards of Care are used by many clinicians as treatment guidelines (6). Treatment may include mental health services (for example assessment, counseling, psychotherapy), primary care, gynecologic and urologic care, reproductive options, voice and communication therapy, and hormonal and surgical treatments. Treatment options vary between countries.

## Treatment for adolescents

Youth treatment should be arranged with a multi-disciplinary team that would include mental health professionals and pediatric endocrinologists.

### *Hormone therapy*

When a youth with gender dysphoria and a strong desire to change their gender presentation to align with their gender identity reaches Tanner Stage 2 of puberty, one (fully reversible) treatment option is taking gonadotrophin-releasing hormone (GnRH) analogues that suppress the naturally produced hormones driving pubertal changes. By suppressing puberty, GnRH analogues can help delay potentially distressing physical changes until the person is ready for further treatment options.

## Adult treatment

Teenagers who reach the age of medical consent are entitled to consent to their own treatment and follow standard adult protocols. Besides offering ongoing assessments, treatments and advice, specialist care should include mental health support, cross-sex hormone treatment, speech and language therapy and support groups. The amount of treatment needed depends on the

### Disorders of sex development

(DSDs, also referred to as diversity of sex development or intersex) are a group of rare conditions in which the reproductive organs and genitals don't develop as expected. People with DSD will have a mix of male and female sexual characteristics (4) and in some cases they may be infertile. This may be genetic (such as in Klinefelter syndrome or XXY) and/or because of how the body responds to sex hormones. It can be inherited but often is not. Some DSDs are suspected soon after birth and others are often diagnosed in puberty. As the child grows, they may need hormone therapy and psychological support. In some cases of DSD, gender dysphoria may also be present and the person may want to change their appearance.

individual and some patients will choose more extensive treatment including surgery.

### *Hormone therapy*

Adult hormone therapy entails taking the hormones of the preferred gender. Hormone therapy usually needs to be taken indefinitely, even if genital reconstructive surgery is undertaken.

- A trans man (female to male) will take testosterone. Changes may include increase in body and facial hair, increase in muscle mass, enlargement of the clitoris, end of menstruation, increased sex drive, deepening of the voice.
- A trans woman (male to female) will take estrogen and a testosterone blocker such as spironolactone. Changes may include reduction in the size of the penis and testicles, decrease in muscle mass, increase in fat on the hips, breast development, and thinning of body hair. Estrogen does not affect the voice of a trans woman who may choose to have voice therapy and, rarely, modifying surgery.

### *Risks and fertility*

Hormonal treatment can be stopped although some changes are irreversible, such as a deeper voice in trans men and breast growth in trans women. There is some uncertainty about the possible risks of long-term masculinizing and feminizing hormone treatment. Some of the potential side affects include: blood clots, gallstones, weight gain, acne, hair loss from the scalp and sleep apnoea. Hormone therapy has variable effects on trans women and trans men. For trans women, there is no guarantee that sperm production will resume after cessation of hormone therapy, and it is very unlikely after 18 months on hormone therapy. Trans men may become pregnant after stopping testosterone. However, ovulation may not be completely suppressed while on testosterone so preventative options are necessary. Discussion of implications with fertility before starting treatment is paramount, including the storing of eggs or sperm (gamete storage), if this is a viable option.

### *Surgery*

For trans men, surgery may involve removal of breasts, removal of the uterus, removal of the fallopian tubes and ovaries, construction of a penis, construction of a scrotum and testicular implants and a penile implant. The aim is to create a functioning penis that allows passing urine standing up and to retain sexual sensation.

For trans women, surgery may involve removal of the testes, removal of the penis, construction of a vagina, construction of the labia, construction of a clitoris with sensation, breast implants and facial feminization surgery. The aim of this type of surgery is, to create a vulva and vagina but in some cases a vagina is not desired.

***Fact sheet compiled by Maya Acharya and Susana Benedet.***

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Article

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# Australian children and adolescents with gender dysphoria: Clinical presentations and challenges experienced by a multidisciplinary team and gender service

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**Abstract**

This prospective study examines the clinical characteristics of children ($n = 79$; 8.42–15.92 years old; 33 biological males and 46 biological females) presenting to a newly established, multidisciplinary Gender Service in New South Wales, Australia, and the challenges faced by the clinicians providing clinical services to these patients and their families. The clinical characteristics of the children were comparable to those described by other paediatric clinics providing gender services: a slight preponderance of biological females to males (1.4: 1); high levels of distress (including dysphoria about gender), suicidal ideation (41.8%), self-harm (16.3%), and suicide attempts (10.1%); and high rates of comorbid mental health disorders: anxiety (63.3%), depression (62.0%), behavioural disorders (35.4%), and autism (13.9%). The developmental stories told by the children and their families highlighted high rates of adverse childhood experiences, with family conflict (65.8%), parental mental illness (63.3%), loss of important figures via separation (59.5%), and bullying (54.4%) being most common. A history of maltreatment was also common (39.2%). Key challenges faced by the clinicians included the following: the effects of increasingly dominant, polarized discourses on daily clinical practice; issues pertaining to patient and clinician safety (including pressures to abandon the holistic [biopsychosocial] model); the difficulties of untangling gender dysphoria from comorbid factors such as anxiety, depression, and sexual abuse; and the factual uncertainties present in the currently available literature on longitudinal outcomes. Our results suggest the need to bring into play a biopsychosocial, trauma-informed model of mental health care for children presenting with gender dysphoria. Ongoing therapeutic work needs to address unresolved trauma and loss, the maintenance of subjective well-being, and the development of the self.

**Keywords**

gender dysphoria, gender identity, gender diversity, transgender, adverse childhood experiences, family narratives, systems theory, holistic (biopsychosocial) practice, children and adolescents

## 1. Introduction

Over the last decade, across Europe and the United States, the rates of children (including adolescents) presenting with psychological distress have continued to increase (Twenge et al., 2019; World Health Organization, 2019). The reasons for this increase are the subject of current research and broader social debate. As part of this global trend, the incidence of children presenting with distress pertaining to sex assigned at birth—termed *gender dysphoria* (American Psychiatric Association, 2013)—has also been reported to be increasing (Zucker, 2019). The current study examines the clinical characteristics of children presenting to a newly established, multidisciplinary Gender Service at a tertiary care hospital in New South Wales, Australia, and the challenges faced by the clinicians providing clinical services to these patients and their families.

Our gender clinic was established in December 2013 in the wake of increased referrals to our hospital Endocrinology Department for children experiencing gender dysphoria. Along with their distressed families, these children (sometimes with court orders in hand) came to Endocrinology typically seeking treatment with puberty-suppressing medications.

In establishing a clinical service, we consulted published guidelines and data from other services. At the time, the two available sets of guidelines were roughly equivalent (Hembree et al., 2009; World Professional Association for Transgender Health, 2011). The guidelines suggested a model of treatment that involved the following: (1) provision of

information, psychological support, and parental or family counseling in younger children; (2) puberty suppression with gonadotropin-releasing hormone (GnRH) agonists in children for whom the gender dysphoria persisted and who were distressed by the development of secondary sex characteristics with the onset of puberty; (3) *medical* gender-affirming treatment (with cross-sex hormones) for children 16 years and over; and (4) a subsequent option for *surgical* gender-affirming treatment. Despite the existence of guidelines, the evidence base for all aspects of treatment was and remains sparse.

Many clinics and researchers had observed that a significant proportion of youth with gender dysphoria presented with psychological or psychosocial vulnerability factors and psychological comorbidities (Di Ceglie et al., 2002). More recently, the Australian Trans Pathways study (2020) in youth (14–25 years) has likewise reported high levels of distress, expressed in high rates of self-harm (79.7%), suicidal thoughts (82.4%), and attempted suicide (48.1%), and in substantial psychological comorbidities (depression [74.6%], anxiety [72.2%], post traumatic stress disorder [25.1%], personality disorders [20.1%], and psychosis [16.2%]) (Strauss et al., 2020). In parallel, Warrior et al. (2020) found elevated rates of autism diagnosis or traits related to autism in transgender adults and gender-diverse individuals. Studies also reported that youth with gender dysphoria experienced high levels of social and relational problems—difficulties with parent/carers, relationship difficulties with peers, and bullying/harassment/victimization (De Vries et al., 2016; Di Ceglie et al., 2002)—and that those with supportive families and supportive peer relationships had better psychosocial outcomes (Simons et al., 2013).

In addition, we—the clinicians working in the Gender Service—became aware of a broad array of sociopolitical discourses, perspectives, beliefs, points of view, stories, and counter-stories (Delgado, 1989; Scher and Kozlowska, 2018) that affected our work and challenged us in a variety of ways. In particular, two dominant discourses came into play in our interactions with patients and families, support groups, and other medical professionals, both within and outside our hospital network, and in the context of public discourse and controversy.

One point of view—under the rubric of the *gender affirmative model* (Hidalgo et al., 2013; Keo-Meier and Ehrensaft, 2018)—supported the acceptance and affirmation of the child's felt sense of gender. It also suggested that "decision-making should be driven by the child or adolescent whenever possible" (p133) (Telfer et al., 2018).[1] Children, families, self-help groups, and clinicians adhering to this point of view support social and medical interventions that—if the child so desired—correct the identity/body mismatch. Social interventions include a transition in which the child, family, and school use the child's preferred name and encourage the child to dress in whatever way supports the child's subjective experience of gender. Medical interventions equate with those in published guidelines (see above). And, though the gender affirmative model explicitly acknowledged that "gender identity and expression [should be] enabled to unfold over time, as a child matures, acknowledging and allowing for fluidity and change" (Hidalgo et al., 2013: 287–288), the available options under this model were strongly influenced and progressively constrained by the imminent approach of puberty.

Another point of view—antithetical to that described above—came to be presented by older patients who regretted their treatment under the gender affirmative model (BBC, 2019; BBC News 2020; Bell, 2020a; D'Angelo, 2017; 2020b) and by clinicians who were

concerned about the medicalization of gender questioning or distress, the irreversible nature of some gender-affirming interventions, and the lack of a solid evidence base (D'Angelo, 2020a; Entwistle, 2019). This perspective emphasized that children's conceptions of themselves are still developing through the teenage years and that they can be harmed when clinicians unquestioningly accept the individual child's assertion of gender identity or when clinicians fail to challenge the child's beliefs pertaining to that identity or fail to understand the developmental trajectory that had brought the child to what is often a place of distress and suffering. It highlighted that gender dysphoria and the child's suffering did not arise de novo but needs to be understood and contextualized in relation to the child and family story. As noted by one patient speaking from this perspective, individuals with gender dysphoria "need . . . access to psychological support from impartial practitioners who do not subscribe to gender identity ideology and are able to help people explore their thoughts and feelings about their sex, sexuality and the underlying causes of their gender dysphoria" (Personal Communication, Keira Bell, September 2020).

In the above context of diverse sociopolitical discourses, the clinicians in our Gender Service tried to provide children presenting with gender dysphoria—and their families—a comprehensive biopsychosocial assessment that endeavored to explore and understand each individual child's story, along with that of the family, in an effort to identify and address the broad range of factors that were contributing to the child's distress and loss of well-being. The assessment was run in a stepwise manner. Clinicians from adolescent medicine provided referral triage, a baseline biopsychosocial assessment, a medical assessment (including puberty staging), and medical information and education to the child and family. Clinicians from Psychological Medicine conducted a comprehensive individual and family assessment, put together the child's developmental story (the context in which the issues, dysphoria, and distress have arisen), and documented (or not) the diagnosis of gender dysphoria and mental health comorbidities. The Psychological Medicine team also provided the child and family with an individualized mental health treatment plan. Clinicians from Endocrinology, who saw a subset of children, again provided advice about the broad range of options and pathways, and in some cases they oversaw the initiation of puberty blockers. Because of the imminent approach of puberty, puberty blockers—because they are reversible—afforded the child and family time for additional reflection. The team hoped that against the background of such explorations, the child and family would be in a better position to consider, reflectively and with full awareness of the consequences, the decisions that they would make—and the pathway that they would eventually choose—to respond to the child's gender dysphoria. Children and families who decided to engage in ongoing psychotherapy and family work—which was recommended for the majority of children and families—were encouraged to identify appropriate local resources, most likely in cooperation with their primary care providers. Older children and families who wanted to pursue cross-sex hormones were transitioned to adolescent/adult services as they neared the age of 16.

In the current study, we report the clinical characteristics of the children presenting for assessment of gender dysphoria to our Gender Service. We also report on the manner in which a broad array of sociopolitical discourses, perspectives, beliefs, points of view, stories, and counter-stories played themselves out in the assessment and treatment processes—between the child, family, and multidisciplinary team, within the

multidisciplinary team itself, and in the broader hospital network (overseeing two paediatric hospitals).

## 2. Method

The Gender Service is a multidisciplinary service located in a tertiary care children's hospital in New South Wales. From December 2013 to November 2018—a 5-year period—children and their families presenting to the service were given the opportunity to participate in a research project documenting clinical presentations, clinical pathways, and outcomes.

Measures included the following: age-of-onset of the child's dysphoria; the child's distress pertaining to gender; social connectedness with peers; family clinical functioning (including the family's response to the child's gender dysphoria); adverse childhood experiences (ACEs) reported as part of the developmental story; and the Global Assessment of Functioning (GAF), where patients with physical or psychological impairment fall into the lower brackets (score <81) (see Kozlowska et al., 2021, for more detail regarding measures). The *Diagnostic and Statistical Manual of Mental Disorders* (DSM)–5 was used to document clinical diagnoses (including gender dysphoria) (American Psychiatric Association, 2013).

Prior to the clinical assessment, children and families filled out two self-report questionnaires: the Depression, Anxiety, and Stress Scales (DASS) (Lovibond and Lovibond, 2004; Patrick et al., 2010) and the SCORE family assessment questionnaire (SCORE-15) (Carr and Stratton, 2017; Fay et al., 2013).

Qualitative assessments of key themes were undertaken. The child and family's expectations from the clinic—what they wanted from the Gender Clinic on presentation—were documented. In addition, the main challenges faced by the clinicians in the multidisciplinary team—as discussed in monthly multidisciplinary meetings and documented through notes taken by team members—were brought together and synthesized into key themes (Braun and Clarke, 2006).

The study was approved by the Hospital Ethics Committee. Participants and their legal guardians provided written informed consent in accordance with national health and medical research council guidelines.

## 3. Data analysis

Descriptive statistics were used to assess the clinical characteristics and comorbidities for key variables of interest. T-tests and chi-square tests were used for comparative analyses between groups for continuous and categorical variables, respectively. Qualitative data were analyzed thematically.

For further between-group analyses, the age-of-onset variable—four categories—was transformed into a binary variable: early developmental pathway (toddlerhood) vs. school-age developmental pathway (primary school, as puberty approaches, and post-pubertal). Likewise, the gender distress variable—four categories—was transformed into a binary variable: low distress (no distress and some distress) vs. high distress (very distressed and extreme distress). Only one child had reported no distress.

For the analyses, all scores on the DASS-21 were multiplied by 2 to calculate subscores and total scores for children, mothers, and fathers (Lovibond and Lovibond, 2004). For a normative reference point, DASS values from a group of healthy controls ($n = 155$) were provided (Hilton et al., in preparation).

Information from family narratives—as it emerged through family assessment interviews—was transformed into continuous or categorical variables (where appropriate) or otherwise subjected to thematic analysis, to bring out the texture of the child and family's lived experience (Braun and Clarke, 2006).

Information regarding the challenges for us, as clinicians, in the first 5 years of the Gender Service was also subjected to thematic analysis (Braun and Clarke, 2006; Dallos and Vetere, 2005).

## 4. Results

### *4.1. Demographic characteristics of the children and their families*

The final sample comprised 79 children aged 8.42–15.92 years (mean = 12.84; SD = 1.90; median = 13.33) presenting with feelings of dysphoria pertaining to the gender that had been assigned to them at birth (see Figure 1 and Table 1). Thirty-three (41.8%) children were biological males, and 46 (58.2%) were biological females (confirmed on chromosomal testing). The children and their families came from all parts of the state of New South Wales—the Sydney metropolis area ($n = 48$; 60.8%), other small cities (Newcastle and Wollongong) ($n = 13$; 16.5%), and country regions ($n = 18$; 22.8%). They were predominantly from a Caucasian-European background (see Table 1). Just over a third lived in a nuclear family with both biological parents: the remainder lived in a range of family constellations (see Table 1).

### *4.2. Family expectations from the gender clinic*

The majority of children ($n = 61$; 77.2%) said that they were attending the clinic because they were seeking a referral to Endocrinology for medical intervention—most commonly, the prescription of puberty-blocking medications. The majority of parents had the same goal(s) as their children ($n = 56$; 70.9%), but more parents ($n = 70$; 88.6%) than children ($n = 33$; 41.8%) were interested in a more holistic approach that included psychological support and intervention for the child and family. The second most common expectation was the provision of a formal diagnosis of gender dysphoria (52; 65.8% of children [and families]).

In nine cases (11.4%), the children or attending parent reported that the child's other parent was—or would be if they were aware—strongly opposed to the idea of gender dysphoria, the child attending the Gender Clinic, and any interventions that affirmed the child's subjective experience of gender. In these nine cases, the attending family intimated that the other parent's opposition could potentially be enacted as violence toward the child or in the form of legal action pertaining to the child's treatment.

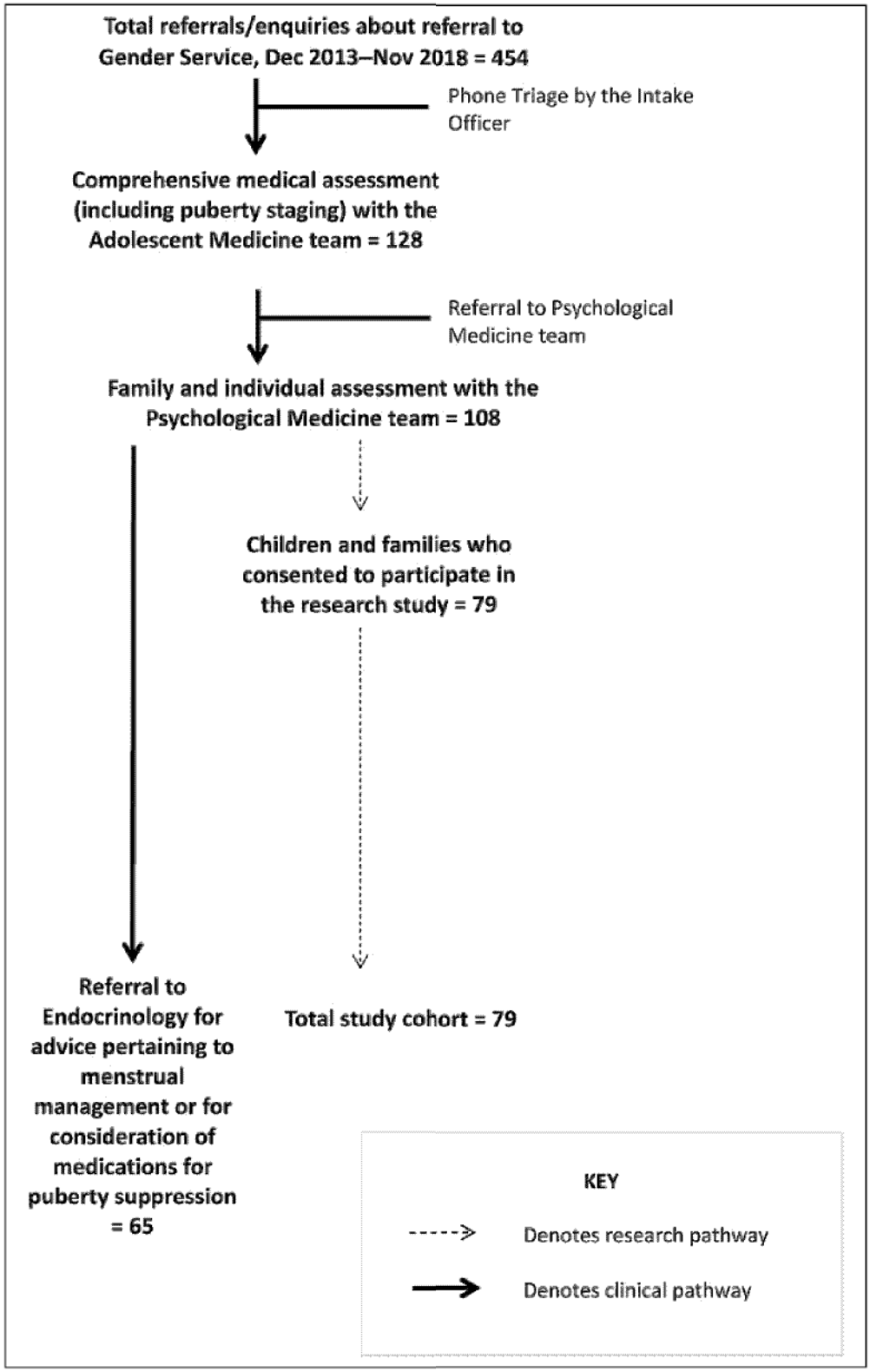


**Figure 1.** Referral and assessment pathway in the Gender Service.

**Table 1.** Demographic characteristics of the children and their families.

| Demographic characteristic | Participant no. ($n$ = 79) | Percentage |
|---|---|---|
| Biological sex | | |
| Male (XY) | 33 | 41.8 |
| Female (XX) | 46 | 58.2 |
| Race | | |
| European Caucasian | 68 | 86.1 |
| Aboriginal | 4 | 5.1 |
| Asian | 2 | 2.5 |
| Eastern | 1 | 1.3 |
| Maori | 1 | 1.3 |
| South American | 1 | 1.3 |
| Mixed (European + other) | 2 | 2.5 |
| Family constellation | | |
| Bio mother and bio father | 30 | 38.0 |
| Bio mother (re-partnered) | 14 | 17.7 |
| Bio father (re-partnered) | 10 | 12.7 |
| Bio mother alone | 21 | 26.6 |
| Bio father alone | 1 | 1.3 |
| Foster care | 3 | 3.8 |
| Family socioeconomic status | | |
| Professional | 27 | 34.2 |
| White collar | 23 | 29.1 |
| Blue collar | 22 | 27.9 |
| Unemployed | 7 | 8.9 |

### *4.3. Clinical characteristics of the children*

Forty-one (51.9%) children had reported experiencing dysphoria about gender from toddlerhood or preschool age; 22 (27.8%) from the early primary school years; 12 (15.2%) as puberty approached or was in process in late primary school or early high school years; and 4 (5.1%) when they were postpubertal. Statements of disclosure, for example, "Is it true they can do an operation to make me a girl?" (age 5) or "I want to be a boy" (age 13)—most commonly to the child's mother ($n$ = 43 [54.4%]) or both parents ($n$ = 9 [11.4%])—were reported at 2.5–14.8 years (mean = 10.5; median = 12.00) (see Table 2). The role of the internet in the child's inner story and disclosure process varied. While the majority of children reported that the internet/documentary films had not played a role in their growing awareness of gender dysphoria (45/79; 57.0%), a subset (28/79; 35.4%) reported that seeing information on the internet or via a documentary had contributed to their feeling, "This is me" (see Table 2). The remainder (6; 7.6%) reported using the internet to gain more information—often together with a parent—after they had disclosed their feelings of dysphoria.

Levels of distress pertaining to puberty commencement and secondary sex characteristics were high (see Table 2). Prepubertal children expressed their distress in

**Table 2.** Clinical characteristics of children presenting for assessment of gender dysphoria.

| Clinical characteristic | Participant no. ($n$ = 79) | Percentage |
|---|---|---|
| Gender identity at presentation | | |
| Male to female | 26 | 32.9 |
| Female to male | 42 | 53.2 |
| Neutral | 1 | 1.3 |
| Gender fluid | 3 | 3.8 |
| Confused | 7 | 8.9 |
| Time of onset of gender dysphoria | | |
| Toddlerhood | 41 | 51.9 |
| School-age (5–10 years) | 22 | 27.8 |
| Prepubertal (as puberty approaches) | 12 | 15.2 |
| Postpubertal | 4 | 5.1 |
| Age of first disclosure | | |
| Preschool years (2.5–5 years) | 13 | 16.5 |
| School-age years (7–12.5 years) | 30 | 38.0 |
| Adolescent years (13–14.8 years) | 28 | 35.4 |
| No verbal disclosure | 8 | 10.1 |
| Whom the child disclosed to | | |
| Mother | 43 | 54.4 |
| Father | 3 | 3.8 |
| Both parents | 9 | 11.4 |
| Friend (face to face) | 7 | 8.9 |
| Therapist | 5 | 6.3 |
| Online (to friends or class) | 4 | 5.1 |
| No verbal disclosure | 8 | 10.1 |
| Role of the internet/film | | |
| No role | 45 | 57.0 |
| Found gender dysphoria online or via film documentary "this is me" pre-disclosure | 28 | 35.4 |
| Used the internet to get more information—often with a parent—after disclosure | 6 | 7.6 |
| Puberty stage on presentation | | |
| Tanner stage 1 (prepubertal) | 18 | 22.8 |
| Tanner stage 2 (pubertal) | 23 | 29.1 |
| Tanner stage 3 (pubertal) | 11 | 13.9 |
| Tanner stage 4 (pubertal) | 14 | 17.7 |
| Tanner stage 5 (postpubertal) | 13 | 16.5 |
| Child gender distress | | |
| No distress | 1 | 1.3 |
| Some distress | 21 | 26.9 |
| Very distressed | 35 | 44.3 |
| Extreme distress | 22 | 27.8 |

(continued)

**Table 2. (continued)**

| Clinical characteristic | Participant no. ($n$ = 79) | Percentage |
|---|---|---|
| GD diagnosis at assessment | | |
| No GD diagnosis given at assessment | 4 | 5.1 |
| DSM-5 GD | 61 | 77.2 |
| DSM other specified GD (insufficient information) | 10 | 12.7 |
| DSM unspecified GD (clear reason why GD criteria were not met) | 4 | 5.1 |
| Comorbid mental health conditions and symptoms | | |
| No comorbid mental health condition/symptoms | 9 | 11.4 |
| Anxiety | 50 | 63.3 |
| Depression | 49 | 62.0 |
| History of self-harm | 39 | 49.4 |
| Suicidal ideation (past or current) | 33 | 41.8 |
| Any behavioural disorder (includes ADHD) | 28 | 35.4 |
| Behavioural (other than ADHD) | 18 | 22.8 |
| ADHD | 13 | 16.5 |
| Current self-harm | 13 | 16.3 |
| Autism (diagnosis by paediatrician or formal testing) | 11 | 13.9 |
| Learning difficulty | 11 | 13.9 |
| Suicide attempt | 8 | 10.1 |
| Eating disorder | 2 | 2.5 |
| Psychosis | 1 | 1.3 |
| Intelligence quotient (per formal testing or estimated from school report) | | |
| Superior (≥120) | 14 | 17.7 |
| Average (80–119) | 57 | 72.2 |
| Borderline (70–79) | 7 | 8.9 |
| Delayed (>70) | 1 | 1.3 |

GD: gender dysphoria; DSM: Diagnostic and Statistical Manual of Mental Disorder; ADHD: Attention Deficit Hyperactivity Disorder.

statements such as "I don't want to have my puberty," "I didn't want any of it [puberty] to happen," or "Boys don't have boobies." Some children's statements were tinged with more extreme expressions of distress: "I felt broken [when puberty commenced]"; "I don't care if there are side effects or risk of death . . . I've wanted to be a girl my whole life." A minority expressed fear of future regret or uncertainty regarding medical intervention: "I am worried I will make a mistake and not be able to change it"; "I don't want to go against Mother Nature to change my body." The pattern of the gender dysphoria (male-to-female, female-to-male, gender neutral, gender fluid, and confused), pubertal staging at presentation, and percentage of children meeting criteria for a gender dysphoria diagnosis (DSM-5) are reported in Table 2.

Comorbid mental health diagnoses and other indicators of psychological distress were common (70/79; 88.6%) (see Table 2). Functioning on the GAF was impaired (range, 25–95; mean = 54.68; median = 55): 4/79 (5.1%) fell into the two upper brackets (≥81) denoting healthy function.

### 4.4. Comparisons between toddlerhood onset and later-onset gender dysphoria

There were no differences between children with later onset of gender dysphoria (38/79; 48.1%) and those with an early onset in toddlerhood and the preschool years (41/79; 51.9%) with regard to DSM-5 diagnoses, ACEs, child total DASS score, family functioning (clinician rated), and SCORE-15 total score (child rated). The differences pertaining to history of self-harm ($\chi^2 = 3.64$; $p = 0.056$) and suicidal ideation ($\chi^2 = 3.55$; $p = 0.060$) were trend level only and raised the possibility that children with a later onset of gender dysphoria might be more likely to have a history of self-harm or to experience suicidal ideation.

### 4.5. Comparisons between children with high and low gender distress

Children with high levels of gender distress (57/79; 72.2%) were more likely to have a diagnosis of depression ($\chi^2 = 11.81$; $p < 0.001$) and a history of self-harm ($\chi^2 = 11.86$; $p < 0.001$), and to have experienced suicidal ideation ($\chi^2 = 6.98$; $p = 0.008$), than those with lower gender distress (22/79; 27.8%). There were no differences between groups with regard to DSM-5 diagnoses, ACEs, child total DASS scores, family functioning (clinician rated), and SCORE-15 total scores (child rated).

### 4.6. ACEs and family functioning

The majority of families (77/79; 97.5%) reported one or more ACEs (0–13; mean = 5.0; median = 4) during the family assessment interview. The most common ACEs pertained to relational stressors, including family conflict, loss by separation (e.g., from a parent or grandparent), bullying, maternal mental illness, and paternal mental illness (see Table 3). In almost two-fifths of families (31/79, 39.2%), the ACEs included one or more maltreatment events—emotional abuse, physical abuse, sexual abuse, or exposure to domestic violence (1–5 maltreatment events; mean = 2.1; median = 2). Child protection services had been involved with approximately half of these families reporting some type of maltreatment event (14/31; 45.2%)—that is, in almost a fifth (14/78; 17.9%) of the sample as a whole. Not surprisingly, clinicians rated almost three-quarters of the families (58/79; 73.4%) as presenting in a state of stress due to family conflict or perturbations to family function in the context of other ACEs (see Table 3).

Families were challenged by the children's experience of gender dysphoria. Just under half the children (36/79; 45.6%) described their families as supportive. In these families, everyone with whom the child was close knew about the child's dysphoria, and the child felt supported by the family as a whole. In the other families (43/79; 54.4%), one or more family members—including siblings, grandparents, or extended family—were rejecting/ambivalent or had not been told about the child's dysphoria in order to

**Table 3.** Family functioning, ACEs, and peer relationships as reported by the child and family during the clinical interview process.

| Characteristic of interest | Participant no. ($n$ = 79) | Percentage |
|---|---|---|
| Family functioning (clinician rated based on information from the clinical interview) | | |
| Harmonious | 21 | 26.6 |
| Some conflict | 27 | 34.2 |
| High conflict | 22 | 27.8 |
| Other major stress | 9 | 11.4 |
| ACEs | | |
| No adverse childhood experiences reported | 2 | 2.5 |
| Family conflict | 52 | 65.8 |
| Loss by separation | 47 | 59.5 |
| Bullying | 43 | 54.4 |
| Maternal mental health | 39 | 49.4 |
| Paternal mental health | 30 | 38.0 |
| Financial stress | 21 | 26.6 |
| Domestic violence | 18 | 22.8 |
| Frequent moves of house | 17 | 21.5 |
| Maternal physical health issue | 15 | 19.0 |
| Loss death | 15 | 19.0 |
| Sexual abuse | 15 | 19.0 |
| Physical abuse | 12 | 15.2 |
| Emotional abuse | 11 | 13.9 |
| Neglect | 9 | 11.4 |
| Custody issues | 8 | 10.1 |
| Out-of-home placement (foster care)/change of placements (whom the child lived with) | 8 | 10.1 |
| Illness (the child's own physical health) | 8 | 10.1 |
| Paternal physical health issue | 7 | 8.9 |
| Migration | 3 | 3.8 |
| Peer relationships | | |
| More than one close friend | 50 | 63.3 |
| One close friend | 5 | 6.3 |
| No close peer relationship ever | 16 | 20.3 |
| No close peer relationship now, but has in past | 5 | 6.3 |
| Negative peer relationship | 3 | 3.8 |

ACE: adverse childhood experience.

avoid conflict or rejection. Overall, one-quarter of children (21/79; 26.6%) had a parent who, because of personal or religious beliefs, was struggling to accept the child's gender dysphoria (for patterns of parental response, see Table 4). Four children (5.1%) had experienced threats of violence from a family member in regard to their gender identity.

### 4.7. Peer relationships

Despite the high rate of reported bullying (43/79; 54.4%), at the time of assessment, 50 children (63.3%) had more than one close friend, and 5 (6.3%) had one close friend (see Table 3).

**Table 4.** Parent responses to the child's gender dysphoria (reported at the family assessment interview).

| Parent response | Mothers (including foster mothers) ($n$ = 79) | Fathers ($n$ = 79) |
|---|---|---|
| Accepting | 66 (83.5%) | 41 (51.8%) |
| Rejecting | 3 (3.8%) | 5 (6.3%) |
| Ambivalent | 7 (8.9%) | 14 (17.7%) |
| No information | — | 18 (22.8%) |
| Others | 3 (3.8%)[a] | 1 (1.3%)[b] |

[a]One mother was deceased; one was absent from the child's life due to past abuse and neglect; and one was erroneously perceived as unsupportive by the child due to the child's psychosis.
[b]One father was erroneously perceived as unsupportive by the child due to the child's psychosis.

**Table 5.** DASS scores for children with gender dysphoria, their mothers and fathers, and healthy cis-controls

| | Depression subscale | Anxiety subscale | Stress subscale | Total DASS score[a] |
|---|---|---|---|---|
| | Range | Range | Range | Range |
| | Mean | Mean | Mean | Mean |
| | Clinical cutoff range[a] | Clinical cutoff range | Clinical cutoff range | Clinical cutoff range |
| Child healthy cis-controls ($n$ = 155) | 0–24<br>12.9<br>10/155 (6.5%) | 0–24<br>2.77<br>19/155 (12.3%) | 0–14<br>5.68<br>13/155 (8.4%) | 0–72<br>11.26 |
| Child DASS ($n$ = 54) | 0–42<br>20.26<br>41/54 (75.9%) | 0–40<br>18.15<br>46/54 (85.2%) | 0–42<br>21.72<br>44/54 (81.5%) | 2–112<br>56.79 |
| Mother DASS ($n$ = 40)[b] | 0–40<br>10.29<br>21/48 (43.81%) | 0–30<br>6.7<br>17/48 (35.4%) | 0–34<br>15.33<br>26/48 (54.6%) | 0–86<br>32.33 |
| Father DASS ($n$ = 25)[b] | 0–24<br>6.24<br>7/25 (28.0%) | 0–14<br>3.04<br>3/25 (12.0%) | 0–24<br>9.68<br>4/25 (16.0%) | 0–52<br>18.96 |

DASS: Depression, Anxiety, and Stress Scale.
[a]Adult clinical cutoffs are as follows: Depression subscale (≥10); Anxiety subscale (≥8); and Stress subscale (≥15).
[b]In children, the total DASS score is a validated measure of perceived distress (Patrick et al., 2010).

### *4.8. Self-report about depression, anxiety, and stress on the DASS*

Data were missing on the DASS for 25/79 (31.6%) children, 39/79 (49.4%) mothers, and 12/37 (32.4%) fathers. Only 37 fathers had attended the family assessment.

DASS scores confirmed the high levels of depression, anxiety, and stress felt by the children and their mothers (see Table 5). Children presenting with gender dysphoria had significantly higher (t[61.79] = 11.946; $p < 0.001$) total DASS scores (range, 2–112 [mean = 56.79]) than 155 (age, 8.33–15.97 years; mean = 12.9) healthy cis-controls (range, 0–73 [mean = 11.26]). The two groups were comparable on age (t[207] = 0.237; $p = 0.813$) and biological sex ($\chi^2 = 0.09$; $p = 0.760$).

### *4.9. Self-report about family function on the SCORE-15*

Data were missing on the SCORE-15 for 20/79 (25.3%) children, 14/79 (17.7%) mothers, and 47/79 (59.5%) fathers.

Self-report data about family function were discrepant with the narratives of the presenting children and their families during the family assessment interview. On self-report, only a small number of children, mothers, and fathers identified family adjustment and family function in the clinically severe range (see Figure 2 and Table 5).

## 5. Key challenges facing the multidisciplinary team

The key themes relating to the clinical challenges confronted by the Gender Service clinicians from 2013 onward—a regular subject of discussion in multidisciplinary meetings—are reported below.

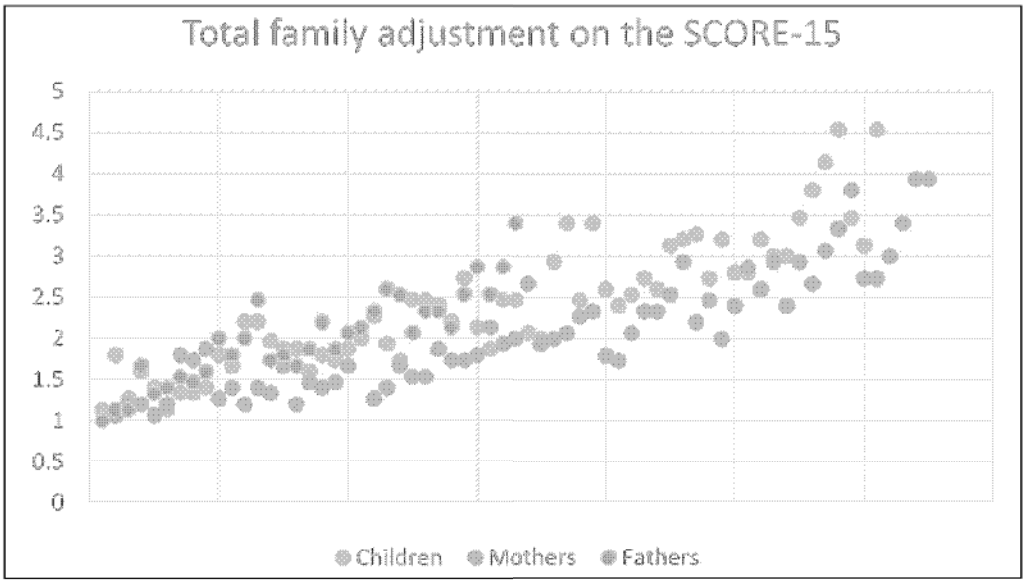


**Figure 2.** SCORE-15. Scatter plot of overall family functioning for children, mothers, and fathers. The overall score represents an average of the 15 five-point Likert scale items. Low scores of 1 or 2 on that scale indicate few family adjustment problems, and high scores of 4 or 5 indicate clinically significant problems.

### 5.1. Enactment of sociopolitical discourses in the health system

The first theme was the enactment—within the health system on multiple system levels—of different sociopolitical discourses. On the team level, while all clinicians were affirming of the children as individual persons who were experiencing substantial distress, some clinicians were more sympathetic to the gender affirmative model, whereas others tried to maintain a more neutral position of holding in mind the potential diversity of patients' needs and the associated paths into the future. On the hospital network level—with two paediatric hospitals within the network—the clinicians in one hospital consistently strived to provide effective clinical services, whereas clinicians at the other hospital declined to see the patients at all, citing lack of resources/funding, philosophical and ethical issues, and lack of an evidence base. And on the health ministry level, yet to be announced are guidelines, a service plan, and designated funding for gender dysphoric patients. On the broader societal level, the news media regularly published emotionally charged, one-sided stories that polarized public discussions concerning children with gender dysphoria (Australia Associated Press, 2018; Knox, 2019; Our Duty, 2020).

### 5.2. Conflation of gender affirmation and medical intervention

The second theme concerned the way in which the gender affirmative model—the dominant sociopolitical discourse—shaped the expectations of the children (and families) presenting to the service (see Section 4.2). It appeared to us that a large subgroup of children equated *affirmation* with *medical intervention* and appeared to believe that their distress would be completely alleviated if they pursued the pathway of medical treatment. Very often, we the clinicians felt that our efforts to work from a biopsychosocial perspective, along with our therapeutic efforts to discuss different aspects of the medical situation, fell on deaf ears. Lost were our efforts to highlight the many different pathways in which gender variation could be expressed, to explain potential adverse effects of medical treatment, to explore issues pertaining to future fertility and child rearing, and to highlight the importance of ongoing psychotherapy. With regard to the last item, we had a strong commitment to exploring issues of self and to helping the children both to understand the context in which their own distress (and potential mental health comorbidities) had arisen and to reflect, more generally, on their concerns, expectations, and future prospects. This same overall dynamic also put many parents—who were trying to support their children in a more holistic way but who were aware of potential long-term harms—in a difficult and untenable situation. The drivers of this dynamic appeared to include not simply the gender affirmative model itself but information from peers, previously encountered health workers, and the internet; many children arrived at the clinic with strongly entrenched beliefs and with no interest in further exploring their medical, psychological, social, or familial situation. It also became apparent to us that many children did not have the cognitive, psychological, or emotional capacity to understand the decisions they were making (see also Section 7).

### 5.3. Patient safety

The third theme that emerged was that of long-term patient safety. A number of factors contributed to this particular challenge. First, the voices of various older patients who perceived themselves as being harmed by the treatments that they had sought and received under the gender affirmative model began to be heard in conferences and news reports (BBC, 2019; Bell, 2020b; D'Angelo, 2020b); these narratives highlighted that children, families, and clinicians had no reliable way of ascertaining whether a child's decision to engage in irreversible medical interventions for gender dysphoria would prove to be "right" or "wrong" in the long term for that particular individual. Second, the evidence base for using puberty blockers and cross-sex hormones—and for their potential long-term side effects—continued to be sparse and contradictory (Bränström and Pachankis, 2020a, 2020b; De Vries et al., 2011, 2014). Third, it became apparent to us that children in early and mid-adolescence found it difficult to consider issues concerning parenthood and fertility, along with the impact of medical interventions on their future capacity to bear children, because the issues were not yet pertinent to them at their present developmental stage.

Patient safety in the short term was also of concern, especially in relation to the following: the children's high rates of suicidal ideation and reported maltreatment (see Table 2), including a potential for violence from a parent because of the child's gender dysphoria or because the child was seeking treatment for gender dysphoria; the mental health's system reluctance to provide services to the children; the children and families' reluctance to engage with the mental health system; and the potential additional stresses on the child and family system that can arise when parents disagree about the correct treatment pathway—which can also potentially give rise to future, deeply divisive legal actions (Whitbourn, 2020).

### 5.4. Clinical challenges

The fourth set of themes related to clinical challenges that we encountered in our daily clinical work and that we discussed on many occasions in our multidisciplinary meetings.

*5.4.1. At the threshold: clinical engagement.* Despite the clinicians' perspective that families presenting to the Gender Service were typically in substantial distress and struggled in many domains of family function—as evidenced by their stories of conflict, relationship breakdown, parental mental illness, and maltreatment (see Table 3)—the families themselves did not perceive themselves in this way (see Figure 2 and Table 6). The families did not seem to understand the possible connections between the family story—sometimes across generations—and the child's clinical presentation with distress, anxiety, depression, and gender dysphoria. Not surprisingly, families tended to medicalize the child's distress, attributing it solely to gender dysphoria as an isolated phenomenon, with the consequence that the family identified the medical pathway as providing the only potential way forward. The motivation to engage in individual or family work to explore the broad range of difficulties and psychological, family, or loss/trauma issues contributing to the clinical picture was generally low.

**Table 6.** SCORE-15: clinical cutoffs on family strengths, difficulties, communication, and adjustment.

| | Family strengths score | Family difficulties score | Family communication score | Total family adjustment score |
|---|---|---|---|---|
| | Range | Range | Range | Range |
| | Mean | Mean | Mean | Mean |
| | Clinical cutoff[a] (percentage of sample above clinical cutoff) | Clinical cutoff (percentage of sample above clinical cutoff) | Clinical cutoff (percentage of sample above clinical cutoff) | Clinical cutoff (percentage of sample above clinical cutoff) |
| Child | 1.00–4.80 | 1.00–5.00 | 1.00–4.40 | 1.13–4.53 |
| SCORE-15 | 2.38 | 2.44 | 2.42 | 2.41 |
| ($n$ = 59) | 4.91 (0.00%) | 4.25 (6.78%) | 4.55 (0.00%) | 4.29 (3.39%) |
| Mother | 1.00–4.20 | 1.00–4.40 | 1.00–4.40 | 1.00–3.93 |
| SCORE-15 | 1.96 | 2.12 | 2.05 | 2.07 |
| ($n$ = 65) | 2.89 (9.23%) | 3.17 (16.92%) | 3.40 (3.08%) | 2.92 (15.38%) |
| Father | 1.00–3.20 | 1.00–3.80 | 1.00–2.80 | 1.00–2.87 |
| SCORE-15 | 1.98 | 1.95 | 2.07 | 1.91 |
| ($n$ = 32) | 2.89 (9.38%) | 3.17 (6.25%) | 3.40 (0.00%) | 2.92 (0.00%) |

[a]Clinical cutoffs—≥90th percentile—are drawn from normative data for parents and high school teenagers (Fay et al., 2013, #7578).

*5.4.2. The complex relationship between gender dysphoria and sexual abuse.* One of the first clinical challenges that emerged via a number of cases was the complex relationship between gender dysphoria and sexual abuse. The two amalgam cases outlined below highlight the core questions that we asked ourselves: were the children's negative feelings toward their bodies related to gender dysphoria or were they a manifestation of past trauma in the context of past sexual abuse? And how were these factors to be disentangled?

> Avery was an adolescent male (XY chromosomes) in the early stages of puberty who experienced substantial feelings of disgust and distress when looking at, touching, or washing the genitals. Avery was clear that he did not want to mature into a man, but he was not clear about his subjective sense of gender. Avery had been sexually abused as a young prepubertal boy, and the abuse had involved inappropriate touching of the genitals.

> Jordan was an adolescent female (XX chromosomes) who identified as a boy. Jordan was adamant that he wanted male sex hormones and to surgically remove his breasts. Jordan was not interested in lower surgery. Jordan had experienced puberty early, and as a school-aged child, Jordan had been sexually abused by a neighbor over a long period of time. The touching of Jordan's breasts had been a key element of the abuse.

*5.4.3. The complex relationship between gender dysphoria and depression.* The clinical presentations of numerous patients flagged that the causal relationship between depression and gender dysphoria was potentially complicated.

> Brooklyn suffered from bouts of depression. When Brooklyn was depressed, Brooklyn experienced severe gender dysphoria—which included unrelenting intrusive thoughts at night—and wanting to be of the opposite sex. When Brooklyn was euthymic, the gender dysphoria dissipated, and Brooklyn experienced their gender as being the same as the gender that they had been assigned at birth.

Learning from these clinical cases, we prioritized the need to identify and treat depression in children presenting with gender dysphoria. We emphasized to children and families that attending to the treatment of comorbid depression—and other mental health disorders—would improve the child's well-being and facilitate the decision-making process.

What these cases of depression—represented by our amalgam vignette—made clear to us is that the individual's experience may change across time and that longitudinal outcome research—which includes, but is not limited to, the complex role of depression and its potential impact on feelings of gender dysphoria—is much needed.

*5.4.4. The complex relationship between gender dysphoria and autism.* We experienced there to be a complex interplay between the presence of autistic traits, gender dysphoria, and the associated difficulties that emerge for parents and clinicians. In paediatric clinical practice, children with autistic traits frequently display repetitive behaviours and restricted interests, and the children perseverate on objects, topics, or themes—which can change over time. In this context, we found that a key concern for many parents (and clinicians) is whether the child's gender dysphoria will be stable over time or whether with time, the child's intense focus on, and experience of, gender dysphoria will shift to something else. In parallel, parents (and clinicians) find themselves in a state of anxiety not knowing whether the child is so focused on gender dysphoria that the child is unable to attend to and process the wide-ranging information and difficult issues that need to be considered. In such situations—where the child with autistic traits does not engage in conversations exploring the numerous options, potential side effects, fertility issues, and such matters—how is capacity for assent (in children, <16years) and consent (in adolescents, ≥16 years) to be ascertained? Here we note again that though gender identity and expression should, in the abstract, be allowed to unfold over time, the time available for this unfolding is often short because of the imminent approach of puberty.

*5.4.5. Gender dysphoria and psychosis.* The literature on psychosis and gender dysphoria is sparse. Though uncommon, nothing precludes patients with psychosis from becoming gender dysphoric. We have also clinically encountered a number of cases, however, in which the gender dysphoria emerges not along the dimension of gender/sexuality but as an expression or product of the psychosis itself—as illustrated by the following amalgam case.

Ezra had been diagnosed with autism as a toddler. Ezra's milestones had been delayed. As a preschooler Ezra was fascinated by ceiling fans, dripping water, and opening and closing doors, and was uninterested in conventional toys. At school, Ezra had ongoing difficulty making friends. Eventually, Ezra learnt to engage in boy-type games with the boys and girl-type games with the girls. But Ezra never felt close to any of the boys or girls. By the end of primary school, Ezra felt distressed about not fitting in but did not talk to anyone about it. In early high school Ezra watched a documentary about gender dysphoria and identified strongly with the idea of not belonging in one's own body. Ezra tried out the opposite gender role but did not feel comfortable with that either. At assessment Ezra was very distressed, said they did not feel comfortable with the human body, and said that the species they came from did not belong on earth with humans.

*5.4.6. Gender dysphoria and the agendas of parents.* Although the majority of children with gender dysphoria present with the support (at least to some degree) of one or both parents, the situation is not always that straightforward. Disagreement between the parents is common, and in such cases, the dissenting parent (usually the father) may even assert that the gender issue and treatment request were being driven by the other parent (usually the mother). A further potential complication is that the child can be triangulated into marital conflict between the parents, acted out via the issue of gender dysphoria. Understanding such cases within family systems and child protection frameworks, and possibly even calling in protection services, may sometimes be necessary. In yet another scenario, it becomes clear that whatever particular problems or conflicts the child may be experiencing, the motivation for engaging with the Gender Service and seeking medical intervention comes from the parent(s), not the child. In such cases, the multidisciplinary team needs to ensure that the child's voice is heard and heard clearly.

## 5.5. Research challenges

The fifth challenge pertained to the issue of research. In this context, we had set up research as part of the clinic's routine activity, enabling us to contribute to the evidence base regarding children who present with gender dysphoria. In the process of writing up data from our clinic, we became aware that the process of knowledge development—ours and that of other researchers—was at risk of being thwarted by ideology (Singal, 2020). In 2019, in response to this issue, the Society for Evidence-Based Gender Medicine was founded "to promote safe, compassionate, ethical and evidence-informed healthcare for children, adolescents, and young adults with gender dysphoria" (Society for Evidence-Based Gender, 2020) (https://www.segm.org).

## 5.6. Clinician safety

The sixth issue that emerged was clinician safety.

*5.6.1. The experience of the endocrinology (medical) members of the multidisciplinary team.* Despite the existence of published guidelines (see Section 1) and the understanding that the effects of puberty-suppressing medication—the GnRH agonists—

were temporary and reversible, no data were (or are) available on whether delaying the exposure of the brain to a sex steroid affects psychosexual, cognitive, emotional, or other neuropsychological maturation. Moreover, GnRH agonists for puberty suppression were neither governmentally approved nor publicly reimbursed; their use and paid supply within the Gender Service was therefore "off-label" and outside of an established legal or government-endorsed medical framework. These factors undermined clinicians' felt sense of safety.

Unlike puberty-suppressing medications, many of the effects of cross-sex hormones are long-term and not reversible. In 2017—the fourth year of the study—a change in Australian laws allowed prescription of cross-sex hormones to children ≥16 years who were assessed by clinicians to be competent to provide informed consent—or if not deemed competent, to have the parent or legal guardian provide informed consent (Telfer et al., 2018). Under this new law, responsibility for the decision to prescribe cross-sex hormones was put onto the clinician rather than, as before, onto the court. With the change in law, some families began to put increased pressure on clinicians from our Gender Service (and clinicians in New South Wales, more generally) to provide cross-sex hormones before the children turned 16 and sometimes as young as 12 (data from our clinic). Clinicians found themselves needing to rebuff demands from some families for cross-sex hormone treatment before the age of 16 years.

The issue of consent—for puberty blockers, cross-sex hormones, and the medical treatment pathway more broadly—has recently been brought up by detransitioner Keira Bell in the court system in the United Kingdom (Bowcott, 2020).

*5.6.2. The experience of the psychological medicine members of the multidisciplinary team.* In the wake of the above-described change in Australian law, some families presented to the clinic with the expectation that a child nearing the age of 16 could attend the Gender Service, see the mental health team for a one-off consultation, collect a diagnosis of gender dysphoria, and move to another service to obtain Stage 2 treatment (cross-sex hormones), with no engagement in a therapeutic process. From the clinician perspective, we recognized the emergence of this "conveyor belt," or "tick the box," mentality—the medical model for treating gender dysphoria stripped bare of holistic (biopsychosocial) care—as being driven by the misguided belief that affirmation of gender dysphoria equates to a medical intervention pathway. Enacted in this way, we felt that this particular sociopolitical discourse put significant pressure on us as clinicians within the Gender Service to abandon ethical, reflective practice in mental health. As is highlighted by the material in Text Box 1—excerpts from two letters by UK clinicians—our experience of these pressures is not unique. Importantly, the clinicians' concerns mirror research findings pertaining to high rates of loss and trauma (Giovanardi et al., 2018; Kozlowska et al., 2021) and of social disadvantage (Sandfort, 2020) in individuals with gender dysphoria.

**Text Box 1. Psychosocial concerns of clinicians: Two letters from the United Kingdom.**

The following is an excerpt from a 2019 letter that Kirsty Entwistle, a clinical psychologist who previously worked at the Gender Identity Development Service (GIDS) in Leeds, wrote to Polly Carmichael, Director of the GIDS at the Tavistock Clinic.

> There are children who have had very traumatic early experiences and early losses who are being put on the medical pathway without having explored or addressed their early adverse experiences. At GIDS no one directly tells you that you're not allowed to suggest that perhaps these early experiences might be connected to a child's wish to transition but if you make the mistake of suggesting this in a team meeting you run the risk of being called transphobic.
>
> I also felt that [we were seeing] an overrepresentation of the young people who were living in poverty. I had a young person whose family were living within such extreme financial constraints that he considered it a treat to buy a can of pop. I also had another young person who was living in a very complex and unstable arrangement who arrived to sessions in a poor state of hygiene and said that there wasn't money for hygiene products. How is it ethical to undertake a gender identity assessment with the view to a medical pathway when there are children and young people do not have their most basic needs met? (Entwistle, July 19 2019)

The following is an excerpt from a 2019 resignation letter that Catherine Williamson sent to the Senior Operational Manager covering Sheffield GIDS, Sheffield Health and Social Care, NHS Foundation Trust.

> Over the last eighteen months, I have repeatedly discussed my clinical concerns about the inadequacy of the assessment pathways at the clinic. I have also regularly highlighted the increasing vulnerability and complexity of people referred to the clinic. That is, that although a minority of people have gender identity concerns, for a majority, medical transition is the solution to difficulties separate from gender. This is supported by audits I have undertaken. These patients may meet the diagnostic criteria for gender dysphoria and transsexualism, but their primary difficulties are not about gender. These include autism, past trauma, significant childhood and adolescent bullying, personality disorder, mental illness, body dysmorphia and eating disorders. The clinic is wedded to a medically-focused pathway which does not adequately explore this context. The service fails to fully consider the psychological and social factors which might influence a person's decision to transition. Wider political pressures and the demands of a lengthy waiting list have led to a focus on streamlining the service which has eclipsed clinical robustness. Similar concerns have been raised by clinicians working in gender services in other NHS Trusts.

## 6. Study limitations

This study has a number of limitations, including the cross-sectional nature of the study, relatively small sample size, probable underreporting of autism—the diagnosis was reported only if it had been formally made by a paediatrician or by clinicians from a specialist autism service—and relatively low number of postpubertal children and children with late-onset gender dysphoria (because our hospital takes referrals only up to 16 years of age). Future research will need to examine whether children with late-onset gender dysphoria are continuous with those who present at earlier ages or whether they reflect a different clinical group. Future studies will also need to ascertain whether the challenges that we have described while providing clinical services to children with gender dysphoria and their families are reflective of other clinicians and other gender clinics around the world.

## 7. Discussion and conclusion

The current prospective study examined the clinical characteristics of children (including adolescents) presenting to a newly established, multidisciplinary Gender Service in New South Wales, Australia, along with the challenges that clinicians faced in providing clinical services to these patients and their families. We found that the clinical characteristics of the children presenting to our service were comparable to those described by other paediatric clinics: a slight preponderance of biological females to males and high levels of distress and comorbid mental health disorders. While previous studies of children have highlighted high rates of abuse, bullying, discrimination, victimization, and family rejection or lack of family support in a general way—often under an umbrella heading of "abuse and victimization experiences" (p326) (Chew et al., 2020)—the results from our study, including the developmental stories told by the children and their families, highlight that many of these experiences have occurred within the family setting itself. That is, our results highlight that many of the ACEs reported by the children and families—family conflict, bullying, parental mental illness, financial stress, maltreatment, and a breakdown of the family system—occur within the family system itself and that the ACEs reflect a long-standing history of relational stress and a chronic disruption of what are normally comfortable and nurturing attachments.

Our findings indicate that engagement with families, a trauma-informed model of mental health care, and ongoing discourse pertaining to the effects of unresolved trauma and loss need to be part of all gender dysphoria clinics and the services with which they collaborate. Because of their impact on subjective well-being and the development of the self, specific loss and trauma events present crucial opportunities for both long-term psychotherapy and more immediate, targeted treatments. The move to a more comprehensive, holistic model of care—one that takes into account the individual's developmental history and the experiences that make up that history—has also been echoed in the work of other clinician-researchers (D'Angelo, 2020a; Entwistle, 2019; Giovanardi et al., 2018; Kozlowska et al., 2021; Williamson, 2019).

Our study found that the children and families who came to the clinic had clear, preformed expectations: most often, children and families wanted a diagnosis of gender

dysphoria to be provided or confirmed, together with referral to endocrinology services to pursue medical treatment of gender dysphoria. Parents (vs. children) also largely came with the same expectations, though they were more likely to be interested in incorporating holistic (biopsychosocial) elements, including treatment of mental health comorbidities, family support/therapy, and long-term psychotherapy for the child. It was our impression that these expectations had been shaped by the dominant sociopolitical discourse—the gender affirmative model. It will be interesting to track the expectations of children and families in the years to come as sociopolitical discourses become more varied and diverse and as the voices are heard of both those who have done well and those who not done well via the medical pathway.

Our study also found that despite the high rates of family conflict, relationship breakdowns, parental mental illness, and maltreatment (see Table 3)—and our own clinical perspective that both individual and family work were indicated for the majority of families—few families rated themselves as being in a clinically severe range on self-report (SCORE-15). Coupled with the dominant sociopolitical discourse—the gender affirmative model that prioritizes the medical treatment pathway—it is not surprising that the large majority of children and families were not motivated to engage in or to remain engaged in ongoing therapy. These data bring three important phenomena into focus. First, when children and families were given the space and structure to tell the child's developmental story—nested in the story of the family—they were able to identify and provide a detailed narrative of the key issues that had contributed to the child's presentation and distress. Without this space and structure, the issues remain undeclared and unaddressed. Second, some families—but also some clinicians—function within a non-holistic (non-biopsychosocial) framework where the child's developmental experiences are disconnected from their clinical presentation. This non-holistic framework is likely to promote a healthcare delivery model that dehumanizes the child (by not examining the child's and family's lived experience) and that promotes medical solutions (correcting the identity/body mismatch) for a problem that is much more complex. Third, as noted earlier, our experience suggests that, insofar as the gender affirmative model is taken as equivalent to medical intervention, clinicians (including ourselves) who work in gender services are coming under increasing pressure to put aside their own holistic (biopsychosocial) model of care, and to compromise their own ethical standards, by engaging in a tick-the-box treatment process. Such an approach does not adequately address a broad range of psychological, family, and social issues and puts patients at risk of adverse future outcomes and clinicians at risk of future legal action.

We conclude our discussion with a brief note about the issue of polarization. One of the biggest challenges for clinicians working with children who present for assessment of gender dysphoria is the effect of polarized sociopolitical discourses on their daily clinical practice. Polarization happens when people become divided—in this case with reference to their views about gender dysphoria in children—into sharply opposing groups. Complex phenomena are then often simplified along a single dimension that disregards other dimensions, that dismisses the lived experience of others, and that closes off questioning, hypothesizing, and consideration of, and engagement with, opposing viewpoints. We have seen these processes at work throughout our clinical practice, as described in the present article. Polarized views are unhelpful to clinicians who are at the

front line trying to provide holistic clinical care to a distressed group of children and such views are just as unhelpful to the children and families themselves. To provide adequate care, clinicians need to understand and confront the complexity of the clinical presentations. They need, in particular, to use a broad, holistic, systemic (i.e., biopsychosocial) framework that takes into account the full range of interacting factors—social, economic, relational, family, psychological, and biological—that have defined the life circumstances of the child and the family seeking care for gender dysphoria.

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## Note

1. In Australian law, decision-making pertaining to puberty suppression and cross-sex hormones that is driven by the child or adolescent is sanctioned if the child or adolescent is Gillick competent and if both of the child's parents and clinicians are in agreement.

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# Body Dissatisfaction and Mental Health Outcomes of Youth on Gender-Affirming Hormone Therapy

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abstract

**OBJECTIVES:** Our first aim was to examine baseline differences in body dissatisfaction, depression, and anxiety symptoms by gender, age, and Tanner (ie, pubertal) stage. Our second aim was to test for changes in youth symptoms over the first year of receiving gender-affirming hormone therapy. Our third aim was to examine potential differences in change over time by demographic and treatment characteristics. Youth experiences of suicidal ideation, suicide attempt, and nonsuicidal self-injury (NSSI) are also reported.

**METHODS:** Participants ($n$ = 148; ages 9–18 years; mean age 14.9 years) were receiving gender-affirming hormone therapy at a multidisciplinary program in Dallas, Texas ($n$ = 25 puberty suppression only; $n$ = 123 feminizing or masculinizing hormone therapy). Participants completed surveys assessing body dissatisfaction (Body Image Scale), depression (Quick Inventory of Depressive Symptoms), and anxiety (Screen for Child Anxiety Related Emotional Disorders) at initial presentation to the clinic and at follow-up. Clinicians completed the Quick Inventory of Depressive Symptoms and collected information on youth experiences of suicidal ideation, suicide attempt, and NSSI.

**RESULTS:** Affirmed males reported greater depression and anxiety at baseline, but these differences were small ($P < .01$). Youth reported large improvements in body dissatisfaction ($P < .001$), small to moderate improvements in self-report of depressive symptoms ($P < .001$), and small improvements in total anxiety symptoms ($P < .01$). No demographic or treatment-related characteristics were associated with change over time. Lifetime and follow-up rates were 81% and 39% for suicidal ideation, 16% and 4% for suicide attempt, and 52% and 18% for NSSI, respectively.

**CONCLUSIONS:** Results provide further evidence of the critical role of gender-affirming hormone therapy in reducing body dissatisfaction. Modest initial improvements in mental health were also evident.

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Dr Kuper oversaw data collection, conducted data analysis, and drafted the manuscript; Drs Stewart, Lau, and Lopez conceptualized and designed the study and provided feedback on manuscript drafts; Dr Preston assisted with drafting the manuscript; and all authors contributed to the development of study aims, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

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**WHAT'S KNOWN ON THIS SUBJECT:** Guidelines exist for providing gender-affirming hormone therapy (ie, puberty suppression and masculinizing or feminizing hormone therapy) to transgender youth; however, little research has been conducted on the impact of treatment on body dissatisfaction and mental health and factors that may influence this impact.

**WHAT THIS STUDY ADDS:** One year of receiving gender-affirming hormone therapy resulted in large reductions in youth body dissatisfaction and modest improvements in mental health. No demographic or treatment-related factors were associated with change over time.

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Two influential longitudinal studies from the Netherlands have helped establish guidelines for providing gender-affirming hormone therapy (ie, puberty suppression and masculinizing or feminizing hormone therapy) to transgender youth with gender dysphoria.[1,2] De Vries et al[3] conducted a prospective study with 70 youth who received puberty suppression (ie, medication to stop the progression of puberty). After 2 years, internalizing, externalizing, and depressive symptoms improved along with global functioning, but there was no improvement in body dissatisfaction or anxiety symptoms. A subset of the same cohort ($n$ = 55) was reassessed after masculinizing or feminizing hormone therapy and gender-affirming surgery (vaginoplasty or mastectomy and hysterectomy), at which point there was a sustained improvement in global functioning and most measures of mental health. Gender dysphoria and body dissatisfaction also improved, and self-reported quality of life was similar to the Dutch population.[4] However, patients were not evaluated after masculinizing or feminizing hormone therapy alone.

In the only other longitudinal study of youth, participants seen in a gender clinic in the United Kingdom ($n$ = 35) demonstrated improvement in clinician assessment of psychosocial functioning after 12 months of receiving puberty suppression.[5] Only 1 cross-sectional study has included a subset of transgender youth ($n$ = 82 of 202). In comparison with those who had not started treatment, individuals who received both puberty suppression and/or masculinizing or feminizing hormone therapy as well as surgery had more favorable body image but not those who received puberty suppression and/or masculinizing or feminizing hormone therapy only.[6] Within this study, youth and adults as well as those receiving puberty suppression and/or masculinizing or feminizing hormone therapy were combined.

The benefits of gender-affirming treatment are better described in adults. A recent review of 5 longitudinal and 2 cross-sectional studies found that receipt of masculinizing or feminizing hormone therapy alone was associated with improved depression in 5 of 7 studies, improved anxiety in 2 of 2 studies, and better quality of life in 3 of 3 studies.[7] Two studies also found lower rates of body uneasiness in adults who received masculinizing or feminizing hormone therapy alone (ie, dissatisfaction with body parts and negative body-related experiences, such as avoidance and self-monitoring).[8,9]

Understanding the impact of gender-affirming hormone therapy on the mental health of transgender youth is critical given the health disparities documented in this population. Within samples of transgender youth presenting for gender-affirming hormone therapy, estimates of clinically significant depressive symptoms or diagnoses have averaged in the range of 30% to 60%,[10–13] and estimates of clinically significant anxiety symptoms or diagnoses have averaged in the range of 20% to 30%.[11,14–16] Lifetime history of suicidal ideation (average range 30%–50%),[10,11,16] suicide attempt (average range 15%–30%),[10,11,13] and nonsuicidal self-injury (NSSI) (average range 20%–40%)[12,13,16] also appear common.

There is also some evidence that rates of mental health concerns may vary by gender, but no clear pattern has emerged.[11,14,15,17] Two studies have found higher levels of body dissatisfaction among affirmed females (ie, individuals assigned male at birth who identify as female) in comparison with affirmed males (ie, individuals assigned female at birth who identify as male).[6,18] Changes associated with puberty, as reflected in age and/or Tanner stage (ie, stage of puberty), may exacerbate body dissatisfaction and mental health concerns. Fewer studies have examined differences by age; however, one study found greater symptoms of depression but not anxiety among older adolescents,[16] and one study found higher levels of body dissatisfaction.[4] None have specifically examined the impact of Tanner stage.

Our first aim in this study was to explore how transgender youth baseline body dissatisfaction, depression, and anxiety symptoms vary on the basis of their gender, age at initial assessment, and Tanner stage at first medical visit. Consistent with our earlier article examining differences in mental health functioning using the Child Behavior Checklist and Youth Self-Report,[14] we hypothesized that affirmed males will report greater symptoms of depression and anxiety. We also hypothesized that older age and greater Tanner stage will be associated with higher ratings of body dissatisfaction and more symptoms of depression and anxiety.

Our second aim was to examine how transgender youth body dissatisfaction, depression, and anxiety symptoms change over the first year of receiving gender-affirming hormone therapy. We anticipated improvements in each of these domains but did not have any a priori hypotheses regarding which domains would demonstrate the greatest improvements.

Our third aim was to explore how any changes over time vary by affirmed gender, Tanner stage, age, type of treatment, months on masculinizing or feminizing hormone therapy, mental health treatment received, and whether chest (ie, "top") surgery was also obtained (among those assigned female at birth). We hypothesized that older age, greater Tanner stage,

receipt of puberty suppression only, fewer months on masculinizing or feminizing hormone therapy, and lack of chest surgery will be associated with fewer changes over time. Lastly, for descriptive purposes, we report information on lifetime and follow-up rates of suicidal ideation, suicide attempts, NSSI, and mental health treatment.

## METHODS

### Participants and Procedure

Participants are youth who received gender-affirming hormone therapy with a multidisciplinary program in Dallas, Texas. Before initiating care, participants and their families participated in an initial assessment with the program's psychologist, psychiatrist, and/or clinical therapist after parents completed a phone intake survey and provided a referral letter from a licensed therapist or counselor documenting the presence of gender dysphoria (this letter is no longer required). Approximately 34% of families did not follow-up after the phone intake. Initial assessments occurred between August 2014 and March 2018, with most occurring in 2017 (41%) or 2016 (37%). At home before this visit, participants completed self-report measures of depression, anxiety, and body dissatisfaction. During the visit, clinicians also completed a report of depressive symptoms and collected information regarding lifetime and recent suicidal ideation, suicide attempts, and NSSI as well as current participation in therapy and support groups and use of psychiatric medication(s).

After the assessment, participants were discussed by the multidisciplinary team of providers from psychology, social work, pediatric endocrinology, pediatric and adolescent gynecology, and adolescent medicine. The Endocrine Society Clinical Practice Guidelines[2] guided the initiation of hormone therapy. Chest surgery was not performed within the program, but participants were provided with referrals when requested.

Approximately 1 year after this initial assessment (range: 11–18 months), all patients were asked to participate in a yearly reassessment visit. Participants were readministered self-report measures, and clinicians again completed a report of depressive symptoms and documented information about suicidal ideation, suicide attempts, NSSI, and mental health treatment.

Survey and clinician data were entered into a research database for analysis along with demographic and treatment-related information (ie, Tanner stage at first medical visit, treatment start and end dates, and chest surgery date extracted from physicians' notes). All participants provided consent, or assent with parent consent, to allow this information to be used for research. The study was approved by the institutional review board at the University of Texas Southwestern Medical Center.

### Measures

Participants were asked to self-report their gender identity (all ages) and sexual orientation (age 12 and older). These responses were recorded verbatim by the clinician and entered into the research database. Gender identities were coded into the following categories: (1) male, boy, or man; (2) male spectrum (eg, "trans masculine" or "masculine nonbinary"); (3) female, girl, or woman; (4) female spectrum (eg, "mostly female, slightly nonbinary"); and (5) nonbinary (eg, "agender" or "part girl, part boy").

To assess body dissatisfaction, participants aged 12 years and older rated their degree of dissatisfaction with 29 areas of the body using the Body Image Scale (BIS).[19] Participants of all ages completed the Screen for Child Anxiety Related Emotional Disorders (SCARED), which produces a total score as well as subscale scores for panic-related, social, separation-related, generalized, and school avoidance–related anxiety symptoms,[20] as well as the Quick Inventory of Depressive Symptoms (QIDS)[21] to measure symptoms of depression that reflect the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* criteria for major depressive disorder.[22] The QIDS produces a total score that can also be grouped into clinical categories: not elevated (0–5), mild (6–10), moderate (11–15), and severe (16–27). Clinicians also completed the clinician version of the QIDS. When the percentage of missing values for each total score and subscale score was ≤15%, missing values were imputed by using the mean of nonmissing values.

### Analyses

To examine baseline differences in depression (QIDS self and clinician), anxiety (SCARED), and body dissatisfaction (BIS), bivariate correlation coefficients were first examined by using Pearson's r for age, Spearman's ρ for Tanner stage, and point biserial for gender. Variables with significant correlations were then simultaneously entered into a linear regression for each outcome, and Cohen's $f^2$ was calculated as a measure of effect size (0.1 = small, 0.25 = moderate, and 0.4 = large).[23]

To examine change over time, QIDS (self and clinician), SCARED, and BIS scores were first tested for normality by using the Kolmogorov-Smirnov test. Changes in normally distributed variables were examined by using paired *t* tests, and the Wilcoxon rank test was used when the Kolmogorov-Smirnov value was significant. Cohen's *d* was used as a measure of effect size (0.2 = small, 0.5 = moderate, and 0.8 = large).[23] Changes

in clinical groupings on the QIDS were also examined by using the Wilcoxon rank test. For both baseline and longitudinal analyses, we planned to first examine the SCARED total score then test for differences in subscale scores only if this change was significant.

To test for associations between change scores and demographic and treatment characteristics, change scores were calculated by subtracting baseline scores from follow-up scores for variables that exhibited a significant change over time. Bivariate correlation coefficients were then examined by using Pearson's r for age and months on feminizing or masculinizing hormone therapy, Spearman's ρ for Tanner stage and therapy frequency, and point biserial for gender, treatment type, psychiatric medication use, support group participation, and chest surgery receipt (for those assigned female at birth). We planned to include any variables with significant correlations in a linear regression. $P < .01$ was significant for all statistical tests to help account for the overall number of tests. Confidence intervals (CIs) are reported at the 95% level.

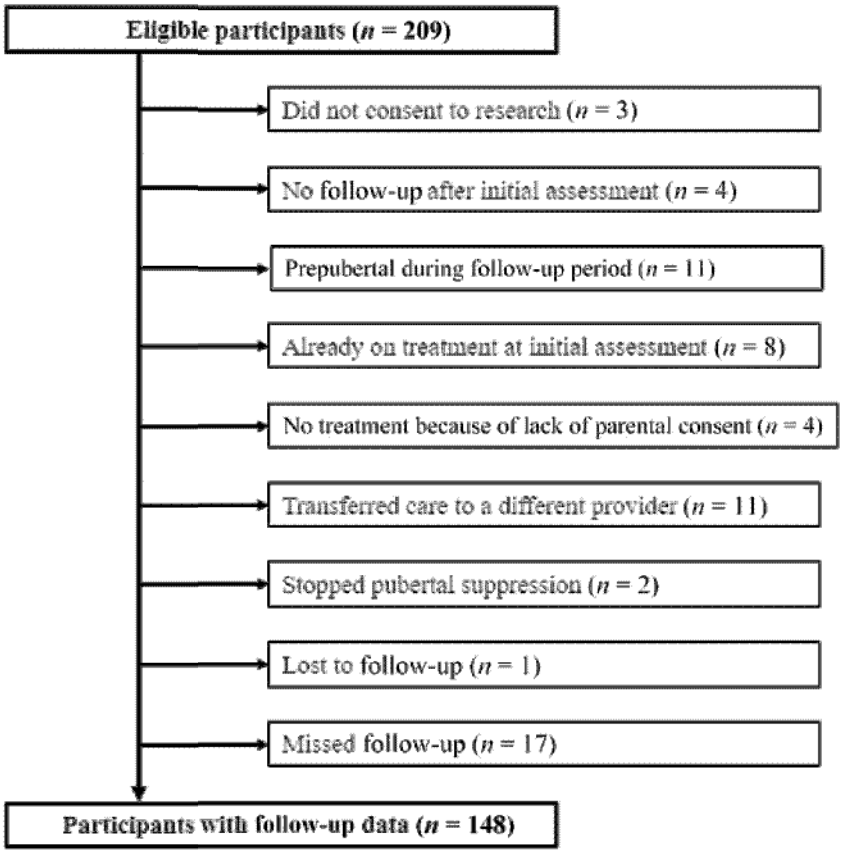


FIGURE 1
Flow diagram.

## RESULTS

Figure 1 presents a flow diagram of participants who were due for follow-up (≥18 months since initial assessment), participants with follow-up data, and the reasons why follow-up data were not available or excluded. The mean number of months between initial assessment and reassessments was 14.9 (SD 2.1). Table 1 presents demographic information on participants. At the initial assessment, patients ranged in age from 9 to 18 years (mean 15.4; SD 2.0). All but 1 participant met *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* criteria for gender dysphoria. This participant subsequently met criteria at a follow-up visit and was started on treatment. Participants who started puberty suppression only did so at a mean age of 13.7 years (range 9.8–14.9; SD 1.5), and participants started feminizing or masculinizing hormone therapy at a mean age of 16.2 years (range 13.2–18.6; SD 1.2). For participants who were on masculinizing or feminizing hormone therapy, the mean length of time receiving treatment before follow-up was 10.9 months (range 1–18; SD 3.3). During the follow-up period, 2 participants stopped puberty suppression without starting masculinizing or feminizing hormone therapy, and no participants stopped masculinizing or feminizing hormone therapy. Fifteen affirmed males obtained chest surgery at an average age of 17.1 years (range 15.2–18.7; SD 1.2) and at an average of 9.2 months from baseline (range 3.0–16.0; SD 3.3).

Table 2 presents means, SDs, and ranges for QIDS, SCARED, and BIS scores at initial assessment and follow-up for the full sample as well as by gender and treatment type. At baseline, affirmed males had greater clinician-reported depressive symptoms (CI −3.76 to −0.81), self-reported depressive symptoms (CI −4.46 to −0.79), total anxiety symptoms (CI −14.94 to −3.99), panic symptoms (CI −5.88 to −1.78), and school avoidance symptoms (CI −1.81, to −0.36) in comparison with affirmed females. However, Cohen's $f^2$ effect sizes were all in the small range (0.07, 0.06, 0.09, 0.10, and 0.07, respectively). No differences were found by age or Tanner stage.

Within the full sample, a significant decrease in body dissatisfaction (CI

**TABLE 1** Participant Demographics

| | *n* (%) |
|---|---|
| Gender identity | |
| Male, boy, or guy | 81 (55) |
| Male spectrum | 9 (6) |
| Female, girl, or woman | 52 (35) |
| Female spectrum | 2 (1) |
| Something else[a] | 3 (2) |
| Assigned sex | |
| Male | 55 (37) |
| Female | 94 (63) |
| Sexual orientation[b] | |
| Pansexual | 25 (20) |
| Straight | 24 (19) |
| Bisexual | 15 (12) |
| Gay | 12 (10) |
| Unsure | 12 (10) |
| No label | 11 (9) |
| Asexual | 10 (8) |
| Something else | 10 (8) |
| Lesbian | 6 (5) |
| Race | |
| White | 137 (95) |
| African American | 3 (2) |
| Multiracial | 3 (2) |
| American Indian | 1 (1) |
| Ethnicity | |
| Hispanic | 24 (17) |
| Non-Hispanic | 120 (83) |
| Tanner stage | |
| I | 3 (2) |
| II | 6 (4) |
| III | 5 (4) |
| IV | 32 (23) |
| V | 94 (67) |
| Treatment type[c] | |
| Puberty suppression only | 25 (17) |
| Masculinizing or femininizing therapy only | 93 (63) |
| Both treatments | 30 (20) |

[a] Excluded from gender analyses.
[b] Age 12 and older.
[c] Masculinizing or feminizing therapy only and both treatments were collapsed for analysis by treatment type.

14.74 to 21.90), self-reported depressive symptoms (CI 1.24 to 2.97), and total anxiety symptoms (CI 1.05 to 6.70) was observed during the follow-up period. Decreases in generalized, separation, and school-related anxiety symptoms were significant at the $P < .05$ level but not the $P < .01$ level. No change in clinician report of depressive symptoms was found. Cohen's *d* effect sizes were large for change in BIS scores (1.04), small to moderate for change in QIDS self-report scores (0.44), and small for change in SCARED total scores (0.27). Table 3 reports the percentage of the sample that fell into each clinical category on the QIDS at initial assessment and follow-up. A significant change was also found in self-reported depressive symptom categories ($P < .001$) but not clinician-reported categories. No correlations were found between change scores and demographic and treatment-related characteristics. Although change scores were generally higher for participants who received chest surgery, no correlations were significant.

Table 4 presents descriptive data on mental health treatment, and Table 5 presents data on suicidal ideation, suicide attempt, and NSSI. During the follow-up period, the distribution of therapy frequency was as follows: none (16%), less than every 3 months (15%), every 2 to 3 months (12%), monthly (22%), every other week (21%), and weekly (14%). Of those who experienced suicidal ideation during the follow-up period, 94% had a lifetime history. These figures were 67% for suicide attempt and 87% for NSSI.

## DISCUSSION

Youth reported large improvements in body dissatisfaction during the 1-year follow-up period. The amount of improvement was not related to treatment type. These findings are consistent with a handful of studies that have documented improvements in body dissatisfaction within samples of adults receiving feminizing or masculinizing hormone therapy[8,9] but contrast with the 2 existing studies of youth. Within the longitudinal cohort from Amsterdam, puberty suppression alone was not associated with improvements in body dissatisfaction,[3] and within a cross-sectional study with a mixed sample of youth and adults, puberty suppression and/or feminizing or masculinizing hormone therapy was not associated with more favorable body image.[6] In contrast to the Amsterdam sample, youth in the current study were younger when starting puberty suppression (age: mean 12.5 and range 9.8–14.9 versus mean 13.7 and range 11.1–17.0).

Age, puberty stage, length of time receiving feminizing or masculinizing hormone therapy, and receipt of chest surgery were also not associated with amount of improvement. However, the sample size of participants receiving puberty suppression only and chest surgery were small, and variations in months on feminizing or masculinizing hormone therapy may not have been meaningful enough in the relatively short follow-up period.

**TABLE 2** Body Dissatisfaction, Depression, and Anxiety Symptoms at Baseline and Follow-up

| | *n* | Range[a] | Baseline, Mean (SD) | Follow-up, Mean (SD) |
|---|---|---|---|---|
| Body dissatisfaction (BIS) | | 0–116 | | |
| Full sample[b] | 96 | | 69.9 (15.6) | 51.7 (18.4) |
| Affirmed males | 66 | | 71.1 (13.4) | 52.9 (16.8) |
| Affirmed females | 30 | | 67.5 (19.5) | 49.0 (21.6) |
| Puberty suppression | 10 | | 64.1 (18.2) | 53.8 (20.1) |
| Feminine or masculine hormone therapy | 86 | | 70.7 (15.2) | 51.4 (18.3) |
| Depressive symptoms (QIDS), self report[c] | | 0–27 | | |
| Full sample[b] | 118 | | 9.4 (5.2) | 7.3 (4.6) |
| Affirmed males | 76 | | 10.4 (5.0) | 7.5 (4.5) |
| Affirmed females | 40 | | 7.5 (4.9) | 6.6 (4.4) |
| Puberty suppression | 13 | | 8.2 (6.1) | 7.0 (5.6) |
| Feminine or masculine hormone therapy | 105 | | 9.6 (5.0) | 7.4 (4.5) |
| Depressive symptoms (QIDS), clinician report[c] | | 0–27 | | |
| Full sample | 125 | | 5.8 (4.2) | 5.9 (3.9) |
| Affirmed males | 78 | | 6.7 (4.4) | 6.2 (4.1) |
| Affirmed females | 45 | | 4.2 (3.2) | 5.4 (3.4) |
| Puberty suppression | 19 | | 5.3 (4.9) | 5.5 (4.8) |
| Feminine or masculine hormone therapy | 106 | | 5.9 (4.1) | 6.0 (3.8) |
| Anxiety symptoms (SCARED), total score[c] | | 0–82 | | |
| Full sample[d] | 102 | | 32.4 (16.3) | 28.6 (16.1) |
| Affirmed males | 65 | | 35.4 (16.5) | 29.8 (15.5) |
| Affirmed females | 33 | | 26.4 (14.2) | 24.3 (15.4) |
| Puberty suppression | 22 | | 31.8 (16.6) | 29.3 (17.1) |
| Feminine or masculine hormone therapy | 80 | | 32.6 (16.3) | 28.4 (15.9) |
| Panic symptoms (SCARED)[c] | | 0–26 | | |
| Full sample | 104 | | 8.2 (6.3) | 7.1 (6.3) |
| Affirmed males | 66 | | 9.3 (6.5) | 7.9 (6.5) |
| Affirmed females | 34 | | 5.7 (4.9) | 5.1 (4.9) |
| Puberty suppression | 22 | | 8.7 (6.5) | 7.2 (5.7) |
| Feminine or masculine hormone therapy | 82 | | 8.1 (6.3) | 7.1 (6.5) |
| Generalized anxiety symptoms (SCARED) | | 0–18 | | |
| Full sample | 104 | | 9.7 (5.1) | 8.7 (5.1) |
| Affirmed males | 66 | | 10.4 (5.0) | 9.0 (5.1) |
| Affirmed females | 34 | | 8.6 (5.1) | 8.0 (5.1) |
| Puberty suppression | 22 | | 8.5 (5.2) | 8.2 (5.4) |
| Feminine or masculine hormone therapy | 82 | | 10.0 (5.1) | 8.8 (5.0) |
| Social anxiety symptoms (SCARED) | | 0–14 | | |
| Full sample | 104 | | 8.0 (4.1) | 7.6 (4.3) |
| Affirmed males | 66 | | 8.5 (4.0) | 7.8 (4.1) |
| Affirmed females | 34 | | 7.1 (3.9) | 6.8 (4.4) |
| Puberty suppression | 22 | | 6.3 (3.6) | 7.3 (4.7) |
| Feminine or masculine hormone therapy | 82 | | 8.5 (4.1) | 7.7 (4.2) |
| Separation anxiety symptoms (SCARED)[e] | | 0–16 | | |
| Full sample | 103 | | 4.0 (3.4) | 3.3 (2.7) |
| Affirmed males | 65 | | 4.2 (3.4) | 3.4 (2.6) |
| Affirmed females | 34 | | 3.4 (3.3) | 2.7 (2.3) |
| Puberty suppression | 22 | | 5.8 (4.0) | 4.2 (3.1) |
| Feminine or masculine hormone therapy | 81 | | 3.5 (3.0) | 3.1 (2.5) |
| School avoidance symptoms (SCARED)[c] | | 0–8 | | |
| Full sample | 102 | | 2.6 (2.2) | 2.0 (2.1) |
| Affirmed males | 65 | | 2.9 (2.3) | 2.0 (2.3) |
| Affirmed females | 33 | | 1.8 (1.7) | 1.9 (2.1) |
| Puberty suppression | 22 | | 2.6 (2.7) | 2.4 (2.4) |
| Feminine or masculine hormone therapy | 80 | | 2.6 (2.1) | 2.0 (2.0) |

[a] Absolute range.
[b] Significant change from initial assessment to follow-up ($P < .001$).
[c] Significant difference in baseline scores by gender ($P < .01$).
[d] Significant change from initial assessment to follow-up ($P < .01$).
[e] Significant difference in baseline scores by age ($P < .01$).

**TABLE 3** Depressive Symptoms (QIDS) Scoring Ranges

| | Range | Self-Report[a] | | Clinician Report | |
|---|---|---|---|---|---|
| | | Baseline, *N* (%) | Follow-up, *N* (%) | Baseline, *N* (%) | Follow-up, *N* (%) |
| Not elevated | 0–5 | 33 (25) | 51 (40) | 73 (53) | 67 (49) |
| Mild | 6–10 | 46 (35) | 48 (37) | 44 (32) | 49 (36) |
| Moderate | 11–15 | 29 (22) | 22 (17) | 15 (11) | 16 (12) |
| Severe | 16–27 | 24 (18) | 8 (6) | 5 (4) | 4 (3) |

[a] Significant change from initial assessment to follow-up ($P < .001$).

Most participants (90%) were also in advanced stages of puberty (Tanner stage IV or V) when presenting for care. Limitations associated with collecting data within a busy clinical setting with multiple providers also resulted in missing data. Nonetheless, results suggest that youth receiving gender-affirming hormone therapy experience meaningful short-term improvements in body dissatisfaction, and no participants discontinued feminizing or masculinizing hormone therapy. These results provide additional support for the incorporation of these treatments into the standards of care for transgender youth experiencing gender dysphoria.[1,2]

Youth also reported modest improvements in mental health functioning during the follow-up period. These results are consistent with the existing longitudinal studies of youth.[3–5] Several factors may help explain why improvements were not greater than what was observed. Although physical changes associated with feminizing or masculinizing hormone therapy often start within the first 3 months, changes continue over the course of several years. Furthermore, environmental stressors associated with one's transgender status may not improve after hormone therapy and could potentially worsen should they increase the youth's visibility as a transgender person. Research has consistently documented higher rates of bullying among transgender youth in comparison with nontransgender youth.[24,25] Within the current study, rates of school avoidance–related anxiety did not improve over the follow-up period.

The larger political context is also important to consider. Within Texas, where the current study was conducted, a well-publicized "bathroom bill" was introduced during the study period that prohibited transgender people from using a restroom that was different from the sex on their birth certificate, although the bill ultimately failed to pass.[26] As a whole, the mental health functioning of youth from the present clinic as well as youth from a handful of other US- and European-based clinics appears poorer than the mental health functioning of youth from the Amsterdam clinic.[11,14,17] Previous studies have attributed this difference to Amsterdam's social and political climate, which is known to be more supportive of the lesbian, gay, bisexual, and transgender population.[17]

**TABLE 4** Mental Health Treatment

| | At Initial Assessment, *n* (%) | Follow-up Period, *n* (%) |
|---|---|---|
| Psychiatric medication | 67 (47) | 80 (61) |
| Therapist or counselor | 144 (97) | 114 (84) |
| Support group[a] | 60 (43) | 45 (35) |

[a] Participation by parents and/or youth (eg, transgender family support organization; lesbian, gay, bisexual, and transgender youth center; or school-based Gay-Straight Alliance).

Consistent with our study examining baseline differences in mental health functioning as measured by the Child Behavior Checklist and Youth Self-Report,[14] affirmed males reported greater symptoms of depression and several forms of anxiety in comparison with affirmed females. However, the effect size of these differences was smaller within the current study in comparison with the former. Differences in measurement approach may help explain the mixed findings regarding gender differences in mental health functioning across youth clinics.[11,15,17] Although some research suggests that nonclinic samples of affirmed male youth report more experiences of bullying,[24] affirmed females are thought to experience greater stigma regarding expression of femininity. Consistent with the current sample, the sex ratio of youth presenting to clinics also appears to be shifting from more affirmed females to more affirmed males presenting for care.[27] Although causes of this shift are largely unknown, they may be associated with other shifts in clinical presentations (eg, mental health and psychosocial functioning).

## CONCLUSIONS

The current study is the largest longitudinal study of youth receiving gender-affirming hormone therapy to date and documents important improvements in body dissatisfaction over the first year of treatment. Continued longitudinal study of this

**TABLE 5** Suicidal Ideation, Suicide Attempt, and NSSI

| | Lifetime, *n* (%) | 1–3 mo Before Initial Assessment,[a] *n* (%) | Follow-up Period, *n* (%) |
|---|---|---|---|
| Passive ideation | 105 (81) | 33 (25) | 51 (38) |
| Suicide attempt | 20 (15) | 3 (2) | 6 (5) |
| NSSI | 68 (52) | 13 (10) | 23 (17) |

[a] One month for passive ideation and 3 months for NSSI and suicide attempt(s).

population will increase the field's understanding of the benefits of gender-affirming hormone therapy and assist providers in better anticipating needs. Follow-up periods of several years or more will help document the full impact of the physical changes with feminizing or masculinizing hormone therapy, and larger sample sizes will improve the ability to examine the specific impacts of treatment type and chest surgery. Greater consideration of intersectionality and sociocultural context will further strengthen these efforts.


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## ABBREVIATIONS

BIS: Body Image Scale
CI: confidence interval
NSSI: nonsuicidal self-injury
QIDS: Quick Inventory of Depressive Symptoms
SCARED: Screen for Child Anxiety Related Emotional Disorders


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# Transgender Men Who Experienced Pregnancy After Female-to-Male Gender Transitioning

*Alexis D. Light, MD, MPH, Juno Obedin-Maliver, MD, MPH, Jae M. Sevelius, PhD, and Jennifer L. Kerns, MD, MPH*

**OBJECTIVE:** To conduct a cross-sectional study of transgender men who had been pregnant and delivered after transitioning from female-to-male gender to help guide practice and further investigation.

**MATERIALS AND METHODS:** We administered a web-based survey from March to December 2013 to inquire about demographics, hormone use, fertility, pregnancy experience, and birth outcomes. Participants were not required to have been on hormone therapy to be eligible. We used a mixed-methods approach to evaluate the quantitative and qualitative data.

**RESULTS:** Forty-one self-described transgender men completed the survey. Before pregnancy, 61% (n=25) had used testosterone. Mean age at conception was 28 years with a standard deviation of 6.8 years. Eighty-eight percent of oocytes (n=36) came from participants' own ovaries. Half of the participants received prenatal care from a physician and 78% delivered in a hospital. Qualitative themes included low levels of health care provider awareness and knowledge about the unique needs of pregnant transgender men as well as a desire for resources to support transgender men through their pregnancy.

**CONCLUSION:** Transgender men are achieving pregnancy after having socially, medically, or both transitioned. Themes from this study can be used to develop transgender-appropriate services and interventions that may improve the health and health care experiences of transgender men.

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Transgender individuals often report many barriers in attempting to access health care.[1] The American College of Obstetricians and Gynecologists (the College) recently called on obstetrician–gynecologists to help eliminate these barriers for transgender men (also called female-to-male individuals) by creating nondiscriminatory practices, assisting with gender transition, and providing transgender-appropriate and comprehensive health care.[2] Despite the College's call to action, little systematic attention has been paid to the health and reproductive experiences of transgender men or those individuals who are born with female sexual organs but who identify as male.

Transgender men are individuals who have a male or masculine gender identity but were assigned female at birth. The gender affirmation process may include social, medical, and surgical aspects of transition, although not all transgender men desire medical intervention.[3] Many transgender men desire children[4] and there are anecdotal reports supporting the biological possibility of pregnancy for transgender men who retain a uterus and discontinue testosterone therapy.[5–7] However, there is little scientific literature describing pregnancy experiences among transgender men or the effects of exogenous administration of testosterone on fertility, pregnancy, and neonatal outcomes.[8] Understanding transgender men's experiences with fertility, pregnancy, and birth will allow health care providers to augment pre- and posttransition discussions regarding fertility options, the roles of cross-sex hormones on fecundity, potential birth outcomes, and to support their physical and mental well-being during pregnancy. Expanded knowledge may also help

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health care providers support transgender men in attaining and maintaining healthy pregnancies.

We conducted a mixed-methods study to explore the experiences of transgender men and to contribute to the knowledge base of fertility, conception, pregnancy experience, and birth outcomes among transgender men.

## MATERIALS AND METHODS

We conducted a cross-sectional survey from March to December 2013 of transgender men (assigned female at birth with a masculine, transmasculine, transmale, or female-to-male gender identity) who had been pregnant and delivered a neonate. Inclusion criteria were: age older than 18 years, self-identification as male before pregnancy, pregnancy within the last 10 years, and the ability to fill out the survey in English. Eligibility criteria did not require any type of medical (eg, testosterone use) or surgical (eg, bilateral mastectomy) transition. We recruited study participants through convenience sampling and we collected data using a web-based survey. Participation was not limited by geographic location.

We administered the online survey through REDCap,[9] an encrypted and secure online survey platform. The study contained 47 multiple-choice questions and 24 questions addressing demographics, hormone use, fertility, pregnancy experience, birth experience, and fetal outcomes. The survey concluded with four open-ended questions: "Is there anything you would like medical providers to know about transgender men and pregnancy?" "What was the experience of being pregnant like for you?" "What was the experience of giving birth like for you?" "What was the postpartum experience like for you?" The survey was developed by the authors in consultation with the Center of Excellence for Transgender Health at University of California, San Francisco and other health care providers serving the transgender community.

Initial recruitment occurred through distribution to key stakeholders in lesbian, gay, bisexual, and transgender health centers; transgender community groups; and Internet-based social networking pages created by study authors. We recruited additional participants through initial contacts. We provided interested individuals with a comprehensive study description and links to the study. After accessing the electronic study web site, participants were presented with informed consent documents and participants confirmed their consent through accessing a link to web-based survey. No in-person contact was made with survey participants.

We conducted a mixed-methods analysis to evaluate the quantitative and qualitative data collected from the survey. Using STATA 13.0, we performed unadjusted analyses using $\chi^2$ for method of delivery; *t* tests for pregnancy age, body mass index, and gestational age; and Fisher's exact for all other variables according to testosterone use before pregnancy. As a result of nonresponse, variable totals may not sum to column totals or within category totals. A *P* value of $\leq .05$ was considered statistically significant. We analyzed the qualitative data using grounded theory, identifying iterative themes, and adding new codes as concepts emerged.[10] This study was approved by the University of California, San Francisco Committee on Human Research.

## RESULTS

We excluded nine of the 56 participants who began the survey as a result of insufficient responses for analysis, and six others were excluded because they did not meet study criteria indicating male gender before pregnancy.[11] We included participants who identified as female or preferred "she" or "her" pronouns only if they had more than one validating indicator of a transgender identity (use of testosterone, male identity with female pronouns, or female identity with male pronouns). Forty-one participants remained for final analysis (Table 1). Most of our participants were from the western United States, identified as white, and had completed at least some college. Pronoun preference differed between those who had used testosterone and those who had not ($P=.04$). Participants who had previously used testosterone were more likely to prefer the pronoun "he," whereas those who had not used testosterone were more likely to identify with "they." Although most respondents were primiparous, those who had not used testosterone were more likely to be multiparous ($P=.006$). Four transgender men (10%), all of whom had been on testosterone previously, reported a prior diagnosis of polycystic ovary syndrome.

Twenty-five (61%) transgender men reported using testosterone before pregnancy (Table 2). Among those who had used testosterone, 20 (80%) reported resuming menstruation within 6 months after stopping testosterone. Five participants (20%) conceived while still amenorrheic from testosterone use. After pregnancy, six (38%) participants who had not previously used testosterone before pregnancy initiated use. Ten participants (40%) who had been on previously testosterone reported that they had not yet resumed testosterone use after pregnancy.





**Table 1. Participant Characteristics**

| Characteristic | All (N=41) | Prior Testosterone Use | | P |
|---|---|---|---|---|
| | | Yes (n=25) | No (n=16) | |
| Age (y)* | 28±6.8 | 29±6.9 | 27±6.8 | .5 |
| Gender identity† | | | | .07 |
| Male | 21 (51) | 12 (48) | 9 (56) | |
| Transgender, female-to-male, transman | 10 (24) | 9 (36) | 1 (6) | |
| Bigender, gender fluid, genderqueer | 8 (20) | 3 (12) | 5 (31) | |
| Female | 1 (2) | 1 (4) | 0 | |
| Other | 1 (2) | 0 | 1 (6) | |
| Personal pronoun preference‡ | | | | .04 |
| He | 32 (82) | 21 (88) | 11 (73) | |
| They | 3 (8) | 0 | 3 (20) | |
| She | 2 (5) | 2 (8) | 0 | |
| Ey | 1 (2) | 1 (4) | 0 | |
| No pronouns | 1 (2) | 0 | 1 (7) | |
| Country | | | | .4 |
| United States | 35 (85) | 20 (80) | 15 (94) | |
| Outside United States§ | 6 (15) | 5 (20) | 1 (6) | |
| U.S. region‡‖ | | | | .9 |
| West | 19 (59) | 11 (61) | 8 (57) | |
| Northeast | 5 (16) | 3 (17) | 2 (14) | |
| South | 5 (16) | 2 (11) | 3 (21) | |
| Midwest | 3 (9) | 2 (11) | 1 (7) | |
| Race or ethnicity‡ | | | | 1.0 |
| White | 36 (92) | 21 (88) | 15 (100) | |
| Asian | 1 (3) | 1 (4) | 0 | |
| Asian and black | 1 (3) | 1 (4) | 0 | |
| Native Hawaiian or other Pacific Islander | 1 (3) | 1 (4) | 0 | |
| Education level‡ | | | | .7 |
| High school degree or less | 4 (10) | 3 (12.5) | 1 (7) | |
| Vocational training or some college | 12 (31) | 6 (25) | 6 (40) | |
| Associate or Bachelor's degree | 14 (36) | 10 (42) | 4 (27) | |
| Master's or doctoral degree | 9 (23) | 5 (21) | 4 (27) | |
| Annual household income ($)‡ | | | | .4 |
| Less than 20,000 | 6 (15) | 2 (8) | 4 (25) | |
| 20,000–59,999 | 20 (49) | 12 (50) | 8 (50) | |
| 60,000–100,000 | 8 (20) | 6 (25) | 2 (13) | |
| More than 100,000 | 5 (13) | 4 (17) | 1 (7) | |
| Multiparous (2 or more pregnancies) | 15 (37) | 5 (20) | 10 (63) | .006 |
| Previous PCOS diagnosis | 4 (10) | 4 (16) | 0 | .15 |
| BMI at the start of pregnancy (kg/m$^2$) | 26±6 | 26±6 | 27±6 | .6 |
| Gender-confirming surgical procedure‡¶ | | | | .7 |
| Bilateral mastectomy | 19 (46) | 13 (52) | 6 (38) | |
| Oophorectomy | 2 (5) | 0 | 2 (13) | |
| Hysterectomy | 2 (5) | 2 (8) | 0 | |
| Phalloplasty or metoidioplasty# | 1 (2) | 1 (4) | 0 | |

PCOS, polycystic ovary syndrome/BMI, body mass index.
Data are mean±standard deviation or n (%) unless otherwise specified.
* Age at the beginning of their most recent pregnancy.
† Kuper et al.[28]
‡ Not all the participants answered this question.
§ Canada (n=2), Germany (n=1), England (n=1), Israel (n=1), and Switzerland (n=1).
‖ Regions were defined according to the 2010 U.S. census.
¶ Surgery may have occurred before or after pregnancy.
# Metoidioplasty is procedure that separates the clitoris from the labia to assume a physiologic position similar to a penis (Djordjevic et al[29]).

Two thirds of pregnancies were planned (Table 3). Before the most recent pregnancy, condoms were the most common form of contraception followed by no form of contraception and abstinence (defined as not engaging in penile–vaginal intercourse). Those who had previously used testosterone were more likely to





**Table 2. Findings Among Those Who Used Testosterone Before Pregnancy of Report (n=25)**

| Characteristic | Value |
|---|---|
| Age (y) when testosterone was initiated | 25 (17–35) |
| Length of testosterone use before pregnancy (y) | |
| Less than 1 | 10 (40) |
| 1–2 | 6 (24) |
| 3–10 | 4 (16) |
| More than 10 | 5 (20) |
| Stopped taking testosterone to become pregnant | 17 (68) |
| Duration between stopping testosterone and resumption of menses (mo) | |
| No menses before pregnancy | 5 (20) |
| Less than 1 | 2 (8) |
| 1 | 6 (24) |
| 2 | 7 (28) |
| 3 | 4 (16) |
| 4–6 | 1 (4) |
| Resumed or initiated testosterone after pregnancy* | 20 (48) |

Data are median (range) or n (%).
* Of total respondents in the study (N=41).

report no contraceptive use or abstinence, whereas those who had not used testosterone were more likely to use a hormonal contraceptive method ($P$=.03). The majority of oocytes came from the participants' own ovaries, whereas the majority of sperm came from a significant other or spouse. Most transgender men became pregnant within 4 months of trying, only 15% had a preconception medical consultation, and 7% used fertility drugs to become pregnant.

Pregnancy, delivery, and birth outcomes did not differ according to prior testosterone use (Table 4). Half of the participants received prenatal care from a physician, 40% from an obstetrician, and 10% from a family medicine physician. More than three fourths of the participants began taking prenatal vitamins either before pregnancy or within the first trimester, whereas 15% reported not taking any prenatal vitamins. Participants reported a variety of perinatal complications including hypertension (12%), preterm labor (10%), placental abruption (10%), and anemia (7%). Anemia was not reported by participants who had previously used testosterone. A higher proportion of transgender men who had used testosterone underwent cesarean delivery compared with those who reported no testosterone use (36% compared with 19%, respectively), although this finding was not statistically significant. Among those who underwent a cesarean delivery, 25% cited the indication as elective. Those who had previously used testosterone were statistically less likely to chest (breast) feed their infant than those who had not previously used testosterone ($P$=.04).

Thirty participants (73%) answered at least one of the four open-ended questions. Major themes from these responses were: 1) effect of pregnancy on concepts of family structure; 2) isolation; 3) gender dysphoria and pregnancy; and 4) interactions with health care providers.

Many participants discussed their pregnancy in the context of family structure. For some, pregnancy was a necessary step in creating the family they desired: "I looked at it as something to endure to have a child" (36-year-old, prior testosterone use). Others described the pregnancy in pragmatic terms, possibly as a way to avoid gender dissonance: "Like my body was a workshop, building up this little kid" (35-year-old, prior testosterone use). Another participant found a way to embrace the pregnancy, describing the pregnancy and birth as a bridge to fatherhood: "Pregnancy and childbirth were very male experiences for me. When I birthed my children, I was born into fatherhood" (29-year-old, no prior testosterone use). Participants often used words such as "dad," "carrier," and "gestational parent" to affirm their male gender identity and describe their parenting role.

Feelings of isolation were common. One participant stated, "Pregnancy came with feelings of isolation and limitation" (28-year-old, prior testosterone use). Some identified the source of isolation as stemming from feeling "lonely because I was the only one" (30-year-old, prior testosterone use). These feelings were contextualized by comments about "lack of support" and "lack of resources available to pregnant transgender men." This isolation was also referenced in terms of invisibility: "I passed as 'not pregnant' until my eighth month, because I'm chubby anyways, and because people don't assume that someone who looks like me could be pregnant" (34-year-old, no prior testosterone use). As another participant simply put it: "We exist. And we are different" (35-year-old, prior testosterone use).

Another theme that emerged was the relationship between gender dysphoria and pregnancy. Some participants reported improvements in gender dysphoria, feeling new connections with their bodies: "It was relieving to feel comfortable in the body I'd been born with" (20-year-old, no prior testosterone use). Others felt an increase in dysphoria, and for some, that dysphoria continued into the postpartum period: "Heavy time, having a baby, not passing as male, all the changes and a society telling me to just be happy"





**Table 3. Fertility Experiences Surrounding Most Recent Pregnancy by Prior Testosterone Use**

| Characteristic | Total (N=41) | Prior Testosterone Use | | *P* |
|---|---|---|---|---|
| | | Yes (n=25) | No (n=16) | |
| Planned pregnancy | 28 (68) | 19 (76) | 9 (56) | .3 |
| Contraception use before this pregnancy*† | | | | .03 |
| Condoms | 16 (41) | 10 (40) | 6 (43) | |
| None | 15 (38) | 12 (48) | 3 (21) | |
| Abstinence‡ | 3 (7) | 3 (12) | 0 | |
| Fertility awareness | 2 (8) | 0 | 2 (14) | |
| Combined hormonal contraception (OCPs, transdermal patch, vaginal ring) | 1 (3) | 0 | 1 (7) | |
| Injection, intrauterine device, implant | 1 (3) | 0 | 1 (6) | |
| Partner had vasectomy | 1 (3) | 0 | 1 (6) | |
| Time to conception (mo)† | | | | .14 |
| Unplanned pregnancy | 13 (32) | 6 (24) | 7 (44) | |
| Less than 1 | 3 (17) | 1 (20) | 2 (12) | |
| 1–3 | 9 (22) | 8 (32) | 1 (6) | |
| 4–6 | 8 (19) | 5 (20) | 3 (19) | |
| More than 7 | 4 (10) | 1 (4) | 3 (18) | |
| Source of oocyte | | | | .12 |
| Own ovaries | 36 (88) | 21 (84) | 15 (94) | |
| Significant other or spouse | 4 (10) | 4 (16) | 0 | |
| Anonymous donor | 1 (2) | 0 | 1 (6) | |
| Source of sperm | | | | .5 |
| Significant other, spouse, or romantic partner | 31 (76) | 17 (68) | 14 (88) | |
| Known donor | 4 (10) | 3 (12) | 1 (6) | |
| Anonymous donor or sperm bank | 6 (15) | 5 (20) | 1 (6) | |
| Medical intervention to become pregnant§ | | | | |
| Consultation | 6 (15) | 4 (16) | 2 (12) | |
| Fertility drugs | 3 (7) | 2 (8) | 1 (6) | |
| Assisted reproductive technology‖ | 5 (12) | 5 (20) | 0 | |

OCP, oral contraceptive pill.
Data are n (%) unless otherwise specified.
* Participants were given the option to identify with more than one, so total exceeds 100%.
† Not all the participants answered this question.
‡ Defined as not having penile–vaginal intercourse.
§ Participants could mark more than one, therefore not comparing the results statistically.
‖ Includes artificial insemination, in vitro fertilization, and gamete intrafallopian transfer.

(35-year-old, prior testosterone use). Combined with feelings of isolation postpartum, many participants specifically mentioned having postpartum depression. "Began to show symptoms of postpartum depression long before anyone discussed symptoms to watch for… Began researching and working through postpartum depression issues independently; found no professional with familiarity with 'trans/genderqueer' gestational parents" (28-year-old, prior testosterone use). As mentioned, the depression seemed amplified by a lack of gender-sensitive resources for postpartum depression.

In response to queries interactions with health care providers, some participants mentioned positive interactions with their health care teams regarding their gender identity. "I was always called 'he,' I was always called 'dad,' and my body parts were called by the words I used" (34-year-old, prior testosterone use). As previously, positive experiences often focused on proper use of gender-related language. Other participants mentioned negative experiences that ranged from improper pronoun use and rude treatment to being turned away from medical practices and denied treatment. In one extreme experience, a participant reported that "Child Protection Services was alerted to the fact a 'tranny' had a baby" (21-year-old, prior testosterone use). Many participants called for better treatment from the health care system through acknowledging the unique identities of pregnant transgender men and grounding health care provider–patient interactions in compassion and respect. As one participant said, "treat us as if we are normal human beings with normal bodies" (37-year-old, no prior testosterone use). Additionally, participants





**Table 4. Pregnancy Experience and Neonatal Outcomes**

| Characteristic | Total (N=41) | Prior Testosterone Use | | P |
|---|---|---|---|---|
| | | Yes (n=25) | No (n=16) | |
| Source of prenatal care* | | | | 1.0 |
| Obstetrician | 16 (40) | 9 (38) | 7 (44) | |
| Certified nurse midwife | 11 (28) | 7 (29) | 4 (25) | |
| Lay midwife | 7 (18) | 4 (17) | 3 (19) | |
| Family practice doctor | 4 (10) | 3 (13) | 1 (6) | |
| No prenatal care | 2 (5) | 1 (4) | 1 (6) | |
| Perinatal complications† | | | | |
| Hypertension | 5 (12) | 4 (16) | 1 (6) | |
| Preterm labor | 4 (10) | 3 (12) | 1 (6) | |
| Placental abruption | 4 (10) | 2 (8) | 2 (12) | |
| Anemia | 3 (7) | 0 | 3 (19) | |
| Gestational diabetes | 2 (5) | 2 (8) | 0 | |
| Multiple pregnancy‡ | 2 (5) | 2 (8) | 0 | |
| Postpartum infection | 2 (5) | 1 (4) | 1 (6) | |
| Premature rupture of membranes | 1 (2) | 0 | 1 (6) | |
| Pyelonephritis | 1 (2) | 1 (4) | 0 | |
| Uterine rupture | 1 (2) | 1 (4) | 0 | |
| Substance use§ | | | | |
| Cigarettes | 3 (7) | 2 (8) | 1 (6) | 1.0 |
| Alcohol | 1 (2) | 1 (4) | 0 | 1.0 |
| Recreational drugs | 1 (2) | 0 | 1 (6) | .6 |
| Gestational age at delivery (wk±d) | 38±6 | 37±9 | 39±5 | .4 |
| Location of birth | | | | .6 |
| Hospital | 32 (78) | 18 (72) | 14 (88) | |
| Home | 7 (17) | 5 (20) | 2 (13) | |
| Independent birth center | 2 (5) | 2 (8) | 0 | |
| Underwent labor induction | 9 (22) | 7 (28) | 2 (12) | .3 |
| Method of delivery | | | | .5 |
| Vaginal | 29 (71) | 16 (64) | 13 (81) | |
| Cesarean | 12 (30) | 9 (36) | 3 (19) | |
| Reason for cesarean delivery | | | | .6 |
| Previous cesarean delivery | 1 (8) | 1 (11) | 0 | |
| Breech presentation | 1 (8) | 1 (11) | 0 | |
| Placenta previa | 1 (8) | 1 (11) | 0 | |
| Arrest of labor | 2 (17) | 1 (11) | 1 (33) | |
| Multiple pregnancy (twins) | 1 (8) | 1 (11) | 0 | |
| Requested cesarean delivery | 3 (25) | 3 (33) | 0 | |
| Other‖ | 3 (25) | 1 (11) | 2 (66) | |
| Birth weight (g)¶ | 3,146±1,671 | 2,914±1,276 | 3,490±625 | .2 |
| Neonate admitted to the NICU* | 5 (14) | 4 (20) | 1 (7) | .4 |
| Neonate diagnosed with an anomaly or developmental disorder*# | 3 (9) | 1 (5) | 2 (14) | .7 |
| Neonate diagnosed with a disorder of sexual development** | 2 (6) | 1 (5) | 1 (7) | .8 |
| Chest (breast) fed | 21 (51) | 10 (40) | 11 (69) | .04 |

NICU, neonatal intensive care unit.
Data are n (%) or mean±standard deviation unless otherwise specified.
* Not all the participants answered this question.
† Includes complications occurring in the preconception, antepartum, intrapartum, and postpartum periods.
‡ Both sets of multiples were twins.
§ Survey question stated: "Once you knew you were pregnant, did you regularly: _ drink alcohol, _ smoke cigarettes, _ use recreational drugs, _ none of the above."
‖ Other reasons for cesarean delivery: placental abruption (n=1), preeclampsia (n=1), none specified (n=1).
¶ N=42 neonates resulting from a set of twins.
# Ventricular septal defect (n=1), bone cancer (n=1), sensory integration disorder (n=1).
** Intersex (n=1), micropenis (n=1).





noted that although their specific health care provider(s) may have been transgender-friendly, this was not necessarily the case with the office staff, nurses, and other health care workers.

## DISCUSSION

The College has highlighted the need for obstetrician–gynecologists to help eliminate barriers to care for transgender men.[2] Our results demonstrate that transgender men desire children[4] and are willing and able to conceive, carry a pregnancy, and give birth. Participants repeatedly expressed a desire for more information regarding fertility options and access to reproductive health care providers who respect, support, and understand their gender identity.

Studies suggest that amenorrhea commonly occurs within 6 months of initiating testosterone therapy.[12,13] However, timeframe for resumption of menses after cessation of testosterone is unclear, and some have stated amenorrhea may be irreversible.[14] Participants who discontinued testosterone to attempt pregnancy reported resumption of menses within 6 months, with the majority within 3 months. Some conceived before return of menses. Despite small sample size, the timeline for menses resumption is consistent with that of literature on women who became amenorrheic with Sertoli-Leydig tumors and resumed menses after tumor resection.[15]

Although most transgender men in this study received prenatal care from a physician and delivered in a hospital, participants used nonphysician providers and nonhospital birth locations more frequently than the general public. In 2009, 99% of U.S. births occurred in hospitals,[16] compared with 78% of our participants. It is possible that health care provider choice and delivery location were responses to actual or anticipated negative experiences as suggested from many qualitative reports of suboptimal interactions with health care providers. However, health care provider and birth location may have resulted from other barriers such as access to health insurance.[17–20] Further research to clarify the experiences of transgender men with peripartum service provision will provide guidance for meeting their needs.

There is a 12% prevalence of major depressive disorders surrounding pregnancy, including postpartum depression, for women in the United States.[21] Although we did not specifically ask about depressive disorders, many of our participants reported experiences with peripartum depression in the narrative responses. A Canadian study of mental health among transgender men (n=207) found that depression was common.[22] Our findings suggest that transgender men may represent a high-risk population for postpartum depression and, although further research is warranted, future recommendations should emphasize assessment of peripartum depression in this population.

Nearly half of the transgender men who had not used testosterone had an unplanned pregnancy, a proportion comparable to that of the U.S. population.[23] Comparatively, one fourth of those previously on testosterone had unplanned pregnancies. By design this study cannot speak to incidence or prevalence of unplanned pregnancies among transgender men. However, given the financial burden[24] and risk of increased morbidity[25] from unintended pregnancy as well as the contraindication of testosterone use during pregnancy,[26,27] these findings suggest a potential unmet need for contraceptive services for transgender men.

Limitations to this study include those inherent with an online, cross-sectional survey, including not allowing for follow-up clarification from participants, decreasing responses from those with low literacy or other barriers to taking an online survey, and self-reported data raising concern for recall bias. The limited socioeconomic and racial diversity in respondents reduces immediate generalizability. Lastly, our eligibility criteria screened for transgender men who had a successful birth, impeding generalizable to those who attempt to get pregnant and cannot and those who do not carry to term. Strengths include the novelty of reporting transgender men's pregnancy experiences, inclusion of those who had socially and medically transitioned, and the mixed-methods format that allows insight into experiences.

Through demonstrating that transgender men are becoming pregnant and having babies, regardless of prior testosterone use, this preliminary study contributes data to emerging discussions regarding their reproductive health experiences. Respondents highlight the need for health care providers to partner with this community and develop gender-appropriate resources and support. Simple but meaningful steps for health care providers include establishing rapport by using patients' preferred names and pronouns, validating gender identity, and reflecting their individual relationships to their pregnancies. Counseling with transgender men should include discussions of reproductive goals, including fertility desires, and the role of contraception. We also suggest all health care providers discuss fertility preservation options with patients before initiating testosterone use in accordance with international standards of care.[26,27] More





clinical and investigational work is needed to understand the physical and emotional needs of transgender men during pregnancy and birth so that health care providers may partner with this underserved community to improve care. As we respond to calls for increased access to reproductive health care for transgender men, we must ensure that we can provide evidence-based, comprehensive services befitting their unique needs and concerns.[2]

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ORIGINAL ARTICLE

# Psychosocial assessment in transgender adolescents☆

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**KEYWORDS**
Transgender;
Adolescent;
Gender dysphoria;
Gender identity

**Abstract**
*Objectives:* To evaluate the psychosocial status of the patients who attend a paediatric endocrinology clinic due to gender incongruity (GI), and to establish the impact on this after one-year of cross hormonal therapy (CHT).
*Material and methods:* An analytical and prospective study conducted on adolescents between 14 and 18 years old with GI, and who attended the Endocrinology Clinic during 2018–2019. The sample included 23 transgender cases (16 male and 7 female cases) and 30 cisgender controls. Study variables were collected at T0 (pre-treatment) and T1 (after one year of CHT) and included sociodemographic data, Utrecht test, SDQ-Cas test, family APGAR test, STAI scale-anxiety Grade, and BDI-II depression assessment test.
*Results:* A significant improvement ($P < .05$) was found between T0 and T1 in the transgender group in terms of emotional symptoms, behaviour problems, hyperactivity symptoms, pro-social conduct, as well as in the degree of anxiety and depression measured by the SDQ-Cas test, the STAI and the BDI-II scale. There were significant differences in these scales between the transgender group and the controls at T0, however, the scores equalised at T1. The families in this sample of transgender patients provided a very favourable environment according to the scores obtained on the family APGAR scale.

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*Conclusions:* The rates of anxiety, emotional and behaviour distress, depressive symptomatology, as well as the feeling of gender dysphoria of these transgender patients were similar to those of non-transsexual population of the same age after one year of CHT initiated at ages between 14 and 18 years old.


**PALABRAS CLAVE**
Transgénero;
Adolescente;
Disforia de género;
Identidad de género

**Evaluación psicosocial en adolescentes transgénero**

**Resumen**
*Objetivos:* Evaluar el estado psicosocial de los pacientes que acudan a consulta de endocrinología pediátrica por incongruencia de género y determinar el impacto en este sentido de la terapia hormonal cruzada (THC) después de un año.
*Material y métodos:* Se trata de un estudio analítico, prospectivo realizado en adolescentes con incongruencia de género de entre 14 y 18 años que acuden a endocrinología infantil durante 2018-2019. Tamaño muestral: 23 casos transgénero (16 masculinos y 7 femeninos) y 30 controles cis. Variables del estudio en T0 (pretratamiento) y T1 (tras un año de THC): datos sociodemográficos, Test de Utrecht, Test SDQ-Cas, APGAR familiar, Escala STAI, Test de evaluación de depresión BDI-II.
*Resultados:* Se encuentra mejoría significativa ($p < 0,05$) entre T0 y T1 en el grupo trans en cuanto a los síntomas emocionales, los problemas de conducta, los síntomas de hiperactividad y la conducta prosocial, así como en el grado de ansiedad y depresión. Existen diferencias significativas entre el grupo trans y los controles en T0 igualándose las puntuaciones en T1 en las escalas evaluadas. Las familias de nuestra muestra de pacientes transgénero proporcionan un entorno muy favorable según las puntuaciones obtenidas en la escala del APGAR familiar.
*Conclusiones:* Los índices de ansiedad, distrés emocional y comportamental, sintomatología depresiva, así como el sentimiento de disforia de género de nuestra muestra de pacientes transgénero fueron similares a los de población no transexual de su misma edad tras un año de THC iniciada en edades comprendidas entre los 14-18 años.


## Introduction

Transgender individuals are individuals whose gender identity or gender expression does not conform to that typically associated with the sex to which they were at birth, in the absence of an underlying mental disorder or chromosomal abnormality that could be the cause of this experience. The concept of gender dysphoria featured in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and the International Classification of Diseases, Tenth Revision (ICD-10)[1,2] refers to the distress caused by this incongruence between gender identity and the sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics),[3,4] and not all transgender individuals experience it. During the development of the International Classification of Diseases, Eleventh Revision (ICD-11), the World Health Organization (WHO) redefined gender identity-related health, replacing categories like ''transsexualism'' and introducing the concept of ''gender incongruence''. This category is included in the so-called Z codes, which are codes used to define a variety of psychosocial factors or life events and do not fit into a diagnostic category.[5]

In transgender adolescents, puberty suppression at an early age (Tanner stages 2 and 3) seeks to alleviate the suffering caused by the development of secondary sex characteristics, to widen the temporal window for decision-making, as at this stage the treatment is still reversible, and to facilitate social transition to the new gender role.[6,7] Thus, a study conducted in the Netherlands by Cohen-Kettenis et al in transgender youth that had undergone puberty suppression analysed behavioural problems, depression, anxiety and overall functioning and found considerable improvement in every scale following treatment.[8,9]

In a study published in *Pediatrics*, Spack et al. reported similar outcomes applying the 'Dutch model' to those found by De Vries and Cohen-Kettenis in 2014.[10]

Outside the works we have just mentioned, the literature on the psychosocial impact of hormone therapy in transgender youth is scarce. More specifically, no such study has been conducted in Spain, and none of those conducted elsewhere included a control group. For this reason, the objectives of our study were to assess the psychosocial status of patients seeking care in the paediatric endocrinology clinic for gender incongruence and the impact on psychosocial status of cross-sex hormone therapy (CSHT) at 1 year of treatment.

## Materials and methods

### Study design

We conducted a prospective analytical study in adolescents with gender incongruence aged 14–18 years managed as new patients in the paediatric endocrinology clinic of the Hospital Clínico San Carlos. In our unit, the hormone therapy approach used for male-to-female (MTF) transition starts with gonadotropin-releasing hormone (GnRH) analogues in the intermediate pubertal stages (Tanner 2–3), adding CSHT with oral estradiol starting from age 14 years, with the specific timing determined on a case-by-case basis. The approach to female-to-male (FTM) transition starts with GnRH analogues in the intermediate pubertal stages with addition of CSHT with intramuscular testosterone starting from age 14 years. We analysed the cases of 23 trans patients (16 FTM and 7 MTF) and 30 cisgender controls matched for age, ethnicity and socioeconomic status. We recruited both cases and controls in the paediatric endocrinology clinic of the Hospital Clínico San Carlos simply by requesting that they volunteer to participate in the study. We followed up patients in both groups for a year after initiation of CHST in the trans cases.

### Variables under study at T0 (before hormone therapy) and T1 (1 year after initiation of cross-sex hormone therapy)

1. *Sociodemographic characteristics*. Family: age, country of origin, ethnicity, educational attainment and income level.
   Personal: age, country of origin, ethnicity, sexual orientation and past use of mental health services.
2. *Severity of gender dysphoria – Utrecht Gender Dysphoria Scale* (*UGDS*).[11] Filled out for the sex assigned at birth at T0 and the self-identified gender at T1.
3. *Patient strengths and difficulties – Strengths and Difficulties Questionnaire, Spanish Version* (*SDQ*-Cas).[12] This questionnaire detects potential emotional and behavioural problems in children and adolescents. A score of more than 20 is considered indicative of risk of having a disorder (normal: 0–15; borderline: 16–19, abnormal: 20–40).
4. *Family functioning – Family APGAR test*.[13] The family APGAR test assesses how family members perceive overall family functioning. It is interpreted as follows: functional, 17–20 points; mildly dysfunctional, 16–13 points; moderately dysfunctional, 12–10 point; severely dysfunctional, <9 points.
5. *Level of anxiety – State-Trait Anxiety Inventory*.[14] This instrument is based on a theoretical model with 2 components: state anxiety and trait anxiety. It is composed of 2 separate self-report subscales, each with 20 items, to assess these components. Specific cut-off points have not been established for its interpretation, and instead the result is reported as the percentile corresponding to the raw score.
6. *Mood – Beck Depression Inventory II* (*BDI*-II).[15] The 21 items of the inventory describe the most frequent symptoms found in patients with depression (psychological or affective-cognitive items, and somatic-vegetative items). The instrument was developed mainly for use in clinical practice as a means to assess severity of depression in adolescent and adult patients. The ranges used to interpret the score are: no depression, 0–9; mild depression, 10–18; moderate depression, 19–29; severe depression, >30.

### Inclusion criteria

- Adolescents with gender incongruence at a stage of pubertal development of Tanner 2 or higher that were willing to participate.
- Absence of psychiatric comorbidity that could affect the experience of gender dysphoria.
- Having demonstrated an understanding of the potential risks and benefits of CSHT.

### Ethical considerations

We obtained the written informed consent of the parents and the assent of the minor as a requisite for participation in the study. We provided an informational document and explained the protocol in detail to all participants. We did not include any personally identifiable information in the study dataset. Thus, the study adhered to international regulations for data protection and current Spanish law on personal data protection. The protocol was approved by the Ethics and Clinical Research Committee of the Hospital Clínico San Carlos de Madrid.

### Statistical analysis

We did a descriptive analysis of all study variables, using measures of central tendency and dispersion for quantitative variables and absolute and relative frequency distributions for quantitative variables. We used the mean and standard deviation (SD) to summarise quantitative variables. We compared the mean scores at baseline (T0) in both groups using the two-sample t test and the changes in scores between baseline (T0) and 1 year of treatment (T1) by one-way repeated measures analysis of variance (ANOVA), introducing the group variable as an intergroup factor and the T0 and T1 timepoints as an intragroup factor. We set a level of significance of 5% for all tests. Data were handled and analysed with the software SPSS 23.0.

## Results

We analysed data for 53 participants aged 14–18 years, of who 23 were trans gender (16 [69%] trans male and 7 [31%] trans female) and 30 were healthy cisgender controls (12 [40%] female and 18 [60%] male). All were Caucasian of Spanish descent except for 2 trans participants, 1 Asian participant of Chinese descent and 1 black participant from Colombia. We did not find significant differences in the socioeconomic status between the trans participants and the cis controls ($P = .2$). Approximately 40% to 50% of participants in each group were of middle socioeconomic status and had parents with a university education (Table 1).

**Table 1** Sociodemographic characteristics.

| | Trans group | Cis group | |
|---|---|---|---|
| Mean age (range) | 16 (14–18 years) | 16 (14–18 years) | NS |
| Sex assigned at birth | Female (69%), male (31%) | Female (60%), male (40%) | NS |
| Caucasian and of Spanish descent | 91% | 100% | NS |
| Parents with university education | 52% | 40% | NS |
| Previous use of mental health services | 30.4% | 30% | NS |
| Sexual orientation | Heterosexual (65%), homosexual (13%), bisexual (21%) | Heterosexual (90%), homosexual (10%), bisexual (0%) | $P < .05$ |

**Table 2** Results of the Strengths and Difficulties Questionnaire in trans adolescents and the control group before hormone therapy (T0) and at 1 year of cross-sex hormone therapy (T1).

| Variable | Trans | | | | | Cis | | | | | Group comparison | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | T0 | | T1 | | | T0 | | T1 | | | T0 | T1 |
| | Mean | SD | Mean | SD | *P* | Mean | SD | Mean | SD | *P* | *P* | *P* |
| Prosocial | 8 | 1.6 | 9 | 1.2 | <0.001 | 7.7 | 1.2 | 7.5 | 1.2 | .3 | .4 | <.001 |
| Emotional symptoms | 5.2 | 1.6 | 3.4 | 1.2 | <0.001 | 3.7 | 1 | 3.7 | 1 | 1 | <.001 | .3 |
| Conduct problems | 2.7 | 0.8 | 1.8 | 1 | <0.001 | 2.3 | 1.2 | 2.6 | 1.6 | .1 | .1 | .05 |
| Hyperactivity | 4 | 1.9 | 2.6 | 1.8 | <0.001 | 3.8 | 0.9 | 3.9 | 0.8 | .8 | .5 | .002 |
| Peer problems | 2.6 | 1.3 | 2.3 | 0.8 | 0.1 | 1.3 | 0.4 | 1 | 0.2 | .07 | <.001 | <.001 |
| Total difficulties | 14.7 | 3.3 | 10.3 | 2.9 | <0.001 | 11.3 | 2.3 | 11.3 | 2.3 | .9 | <.001 | .1 |

Cis, cisgender control group; SD, standard deviation; Trans, transgender case group.

We found that 30.4% of the trans participants ($n = 7$) and 30% of the cis controls ($n = 9$) had previously used mental health services, while only 1 trans participant (4.3%) had ever received psychiatric medication (Table 1).

The trans participants had a supportive social environment, as 100% had disclosed their transgender identity to their parents and 82% (19 out of 22) had disclosed it in their respective schools. In addition, 95% (22 out of 23) reported being addressed by their chosen names at home and 82% in their school.

## Severity of Gender Dysphoria-Utrecht Scale

Participants in the trans group had a mean score in the UGDS of $57.1 \pm 4.1$ at T0 (the cut-off point to identify dysphoria is 40 points, out of a total possible maximum of 60 points) compared to a mean score of $14.7 \pm 3.2$ at T1, which evinced significant improvement at 12 months of treatment ($P < .001$). Every trans participant had gender dysphoria at T0 and none had gender dysphoria at T1 applying the cut-off point established for definition of gender dysphoria in this scale.

## Strengths and Difficulties Questionnaire

The mean overall score in the trans group was in the upper range of normal at T0 ($14.7 \pm 3.3$), with a significant improvement at T1 ($10.3 \pm 2.8$ DE) ($P < .001$). When we compared the trans and cis groups at T0, we found significant differences, with a mean difference in the questionnaire score of $3.3 \pm 0.7$ ($P < .001$), a difference that was nearly reversed after 1 year of treatment ($-1.0 \pm 0.7$; $P = .153$), so that emotional symptoms and conduct problems had both become comparable to those of the control group at T1. Tables 2 and 3 summarise the scores in the SDQ.

When we analysed each of the 5 groups of difficulties that compose the SDQ, we found significant improvement between T0 and T1 in the trans group in the areas of emotional symptoms, conduct problems, hyperactivity and prosocial behaviour ($P < .001$), with no significant change in the area of peer relationship problems, with similar scores at T0 and T1.

**Table 3** Percentage of trans participants with SDQ scores in the normal, borderline and abnormal range at T0 and T1.

| SDQ in trans group | T0 | T1 |
|---|---|---|
| Normal (0–15 points) | 61% ($n = 14$) | 95.6% ($n = 22$) |
| Borderline (16–19 points) | 34.7% ($n = 8$) | 4.3% ($n = 1$) |
| Abnormal (20–40 points) | 4.3% ($n = 1$) | 0% |

**Table 4** Results of the State-Trait Anxiety Inventory (STAI) in the trans adolescent group and the cis adolescent control group before hormone therapy (T0) and at 1 year of cross-sex hormone therapy (T1).

| Variable | Trans | | | | | Cis | | | | | Group comparison | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | T0 | | T1 | | | T0 | | T1 | | | T0 | T1 |
| | Mean | SD | Mean | SD | *P* | Mean | SD | Mean | SD | *P* | *P* | *P* |
| STAI-S | 33.3 | 9.1 | 16.8 | 8.1 | <0.001 | 11.8 | 3.8 | 12.3 | 3.8 | 0.6 | < 0.001 | 0.008 |
| STAI-T | 33 | 7.2 | 18.5 | 8.4 | <0.001 | 14.2 | 4.8 | 14.2 | 4.8 | 0.9 | < 0.001 | 0.02 |

Cis, cisgender control group; SD, standard deviation; STAI-S, STAI state anxiety subscale; STAI-T, STAI trait anxiety subscale; Trans, transgender case group.

**Table 5** State anxiety subscale percentiles in the trans group.

| STAI-State in trans group | Mean (SD) | Percentile |
|---|---|---|
| T0 | 33.3 (9.1) | 75th–85th |
| T1 | 16.8 (8.1) | <50th |

SD, standard deviation; STAI, State-Trait Anxiety Inventory.

**Table 6** Trait anxiety subscale percentiles in the trans group.

| STAI-Trait in trans group | Mean (SD) | Percentile |
|---|---|---|
| T0 | 33.0 (7.2) | p 85–95 |
| T1 | 18.5 (8.4) | <p50 |

SD, standard deviation; STAI, State-Trait Anxiety Inventory.

### Family environment: Family Apgar test

We found a mean score of 17.9 at T0 and of 18 at T1 in the trans group, both within the normal range. We did not find differences between T0 and T1 or between the case and control groups.

### Anxiety assessment: State-Trait Anxiety Inventory

State anxiety in the trans group improved significantly, with the mean score decreasing by $16.5 \pm 1.1$ points ($P < .001$), corresponding to a decrease from the 75th to 85th percentile at T0 to below the 50th percentile at T1. On the other hand, participants in the control group had similar scores at T0 and T1 (Tables 4 and 5).

Comparing the trans and cis groups at T0, we found a difference in the mean score of $21.5 \pm 1.8$ ($P < .001$), and there was still a mean difference at T1, in this case of $4.6 \pm 1.6$ points ($P < .008$), which indicated a higher level of anxiety in cases compared to controls at 1 year despite treatment (Table 4).

Trait anxiety decreased by a mean of $14.5 \pm 0.9$ points between T0 and T1 in the trans group ($P < .001$), with no difference between time points in the control group. We found a decrease from the 85th to 90th percentile at T0 to below the 50th percentile at T1. In contrast, controls had similar scores at T0 and T1, as was also the case with the state anxiety.

Comparing the trans and cis groups at T0, we found a mean difference of $18.8 \pm 1.6$ points ($P < .001$), and we also found differences between groups at T1, with a mean difference of $4.3 \pm 1.8$ points ($P < .02$). As was the case with state anxiety, while there was improvement in the score for trait anxiety, the level of anxiety continued to be higher in the trans group compared to the control group at T1 (Tables 4–6).

### Assessment of depression: Beck Depression Inventory II

We found a decrease in symptoms of depression between T0 and T1 in the trans group, with a mean difference in the BDI-II score of $9.5 \pm 0.6$ points ($P < .001$), while there were no differences in the control group (Table 7). The mean score at T0 was 19.3 (at the lower limit of moderate depression) and decreased to 9.7 at T1 (at the lower limit of mild depression). In the cis control group, the mean at T0 was within the normal range and it remained normal at T1 (Table 7). In the trans group, we observed clear improvement at T1 at every level of depression (Table 8).

Comparing the trans and cis groups at T0, we found a mean difference of $12.0 \pm 1.3$ points in the score ($P < .001$) that had decreased to $2.4 \pm 0.7$ points at T1 ($P < .034$). Trans participants had more depression symptoms compared to controls at T0 and, despite improvement, also at T1 (Table 7).

## Discussion

In many cases, both families and the health professionals that habitually work with trans adolescents need to make decisions without the support of clear scientific evidence. But, as any professional that works with trans youth and their families knows, in a population that faces this level of discrimination[16–18] and in which self-harm, suicidal ideation, anxiety and other problems are so prevalent, the risk associated with not performing any kind of intervention is very high.[19–21]

Medical treatment of transgender adolescents has been a controversial issue since it was first reported in the Netherlands in 1998.[22] Since 2013, our paediatric endocrinology clinic offers multidisciplinary treatment to patients with adolescent-onset gender dysphoria, with collaboration of social workers, psychologists, psychiatrists, gynaecologists, dermatologists, paediatricians and endocrinologists. At

**Table 7** Results of the Beck Depression Inventory II in the trans and cis groups, before hormone therapy (T0) and at 1 year of cross-sex hormone therapy (T1).

| Variable | Trans | | | | | Cis | | | | | Group comparison | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | T0 | | T1 | | | T0 | | T1 | | | T0 | T1 |
| | Mean | SD | Mean | SD | *P* | Mean | SD | Mean | SD | *P* | *P* | *P* |
| BDI-II | 19.3 | 5.5 | 9.7 | 3.9 | <.001 | 7.2 | 3.9 | 7.4 | 3.6 | .7 | <.001 | .034 |

BDI, Beck Depression Inventory; SD, standard deviation.

**Table 8** Percentage of trans participants with BDI-II scores in the normal, mild depression, moderate depression and severe depression range at T0 and T1.

| BDI-II in trans group | T0 | T1 |
|---|---|---|
| Normal (0–9) | 0% | 69.5% |
| Mild (10–18) | 60.8% | 26.0% |
| Moderate (19–29) | 34.7% | 4.3% |
| Severe (>30) | 4.3% | 0% |

present, our clinic manages 50 patients receiving hormone therapy for this indication, mostly following the latest recommendations of the World Professional Association for Transgender Health,[3] with a model similar to the one recommended by Hembree[4] and the Cohen-Kettenis group.[8] That is, patients that have reached a stage of pubertal development of at least Tanner 2 or 3, without psychiatric comorbidity that could play a role in gender dysphoria, with adequate social, family and psychological support and that have demonstrated an understanding of the risks and benefits of hormone therapy.

At present, the scientific community does not consider transgender identities pathological. Removing transgender identities from the classification of psychiatric disorders and placing related problems in the Z codes is a solution that allows their depathologisation, including them in the classification criteria related to factors that have an impact on health status.[5] Until recently, the few manuals available to guide the management of trans patients mainly focused on the incongruence between the sex assigned at birth and the gender identity of the individual, and particularly on the distress caused by this discrepancy.[2] This distress may or may not be directly associated with the possibility of freely expressing gender identity, being able to transition if so desired, the support received by the family and the general social environment and the degree of transphobia experienced. In our study, all trans participants experienced gender dysphoria at T0, which had resolved in all at 1 year of CSHT, which demonstrates that this dysphoria is not a necessary condition in transgender individuals and is not always present in transgender youth.

In our sample, the families of transgender participants provided a highly supportive environment, as demonstrated by the family APGAR scores. This could explain the highly favourable outcomes observed at 1 year of treatment with CSHT. The support of families and physicians is essential to the adequate and healthy neuropsychological development of transgender adolescents.[6,7,23] Initiation of CSHT and the associated physical changes at younger ages than currently recommended in management protocols (16 years) may have psychological benefits, given the particular importance of fitting in the peer group during adolescence. In fact, we found excellent results in the SDQ, with a significant improvement between T0 and T1 in the trans group in emotional symptoms, conduct problems, hyperactivity and prosocial behaviour, which were comparable to those of the control group at T1 (Tables 2 and 3).

We know that a high proportion of transgender youth experience anxiety and depression, and there is evidence in the literature on the mental health of trans children and youth whose desired identities are affirmed and supported by their families. In this sense, the family plays an essential role in improving the lives of these minors, acting as a protective factor against depression, which is why it is important to implement strategies that promote the support of families due to their impact on mental health.[24–31]

We found substantial improvement in the mean scores and percentiles in the STAI state anxiety and trait anxiety scales in the trans group after 1 year of CSHT. We also found differences at T0 compared to the control group that had improved at T1, as the differences had decreased, although not disappeared (Tables 4 and 5). We also found substantial improvement in the BDI-II scores. Before initiation of hormone therapy, all trans participants had scores corresponding to some level of depression. After 1 year of CSHT, 70% had scores in the normal range. These findings suggest that initiation of CSHT at earlier ages than recommended at present, with adequate family support in general or specifically expressed in the decision of allowing an early social transition, may be associated with better mental health outcomes in transgender children.

Our findings are consistent with those of the longitudinal study published in *Pediatrics* by Annelou de Vries in 2014.[8] The levels of anxiety, emotional distress and behavioural disturbances and depressive symptoms and the experience of gender dysphoria in transgender participants were similar or better compared to those of their cisgender peers matched for age at 1 year of CSHT. Based on this body of evidence, it is essential for paediatric providers to have updated knowledge and an unbiased attitude on this reality, the concerns regarding the future impact of these interventions and the lack of evidence on their long-term adverse effects.[32] We ought to mention the recent position statement of the Asociación Española de Pediatría (Spanish Association of Paediatrics) on the approach to gender diverse and transgender identities in children and adolescents.[33] This document does not simply adopt the depathologising perspective that is increasingly espoused by health professionals, but pushes

beyond, calling for a necessary shift in social perception, as it considers that diversity in gender identity and expression enriches humankind.

Keeping in mind that age should not be the main criterion for initiation of hormone therapy in transgender minors, we, as other authors before us, hope for the development of more flexible management protocols.[34]

## Limitations of the study

Selection bias: the selected sample is a key element in any study, and use of an inadequate sampling method is one of the most frequent sources of error in designing a study, as most statistical methods in use assume that the data source is a random sample. The simplest and most appropriate way of selecting a sample is completely random selection, but under real world conditions this is nearly impossible to do. We resorted to obtaining a convenience sample of individuals that volunteered to participate. Without forgetting that the sample in our study may not be representative of the general adolescent transgender population, as many transgender adolescents do not have a supportive family and many others do not need referral to a paediatric endocrinology clinic, we do not believe that the internal validity of our study was affected by the sampling method.

## Conflicts of interest

The authors have no conflicts of interest to declare.

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# Conversion Therapy and LGBT Youth Update

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## EXECUTIVE SUMMARY

Conversion therapy, also known as sexual orientation or gender identity change efforts, is a practice grounded in the belief that being LGBT is abnormal. It is intended to change the sexual orientation, gender identity, or gender expression of LGBT people.[1] Conversion therapy is practiced by some licensed professionals in the context of providing health care and by some clergy or other spiritual advisors in the context of religious practice.[2] Efforts to change someone's sexual orientation or gender identity are associated with poor mental health,[3] including suicidality.[4] As of June 2019, 18 states, the District of Columbia, and a number of localities have banned health care professionals from using conversion therapy on youth.

The Williams Institute estimates that:

- 698,000 LGBT adults (ages 18-59)[5] in the U.S. have received conversion therapy, including about 350,000 LGBT adults who were subjected to the practice as adolescents.[6]
- 16,000 LGBT youth (ages 13-17) will receive conversion therapy from a licensed health care professional before they reach the age of 18 in the 32 states that currently do not ban the practice.[7]
- 10,000 LGBT youth (ages 13-17) live in states that ban conversion therapy and have been protected from receiving conversion therapy from a licensed health care professional before age 18.[8]
- An estimated 57,000 youth (ages 13-17) across all states will receive conversion therapy from religious or spiritual advisors before they reach the age of 18.[9]

This report updates conversion therapy estimates published by the Williams Institute in January 2018.[10]

# HISTORY

Conversion therapy has been practiced in the U.S. for over a century. Academic literature has documented instances of conversion therapy being used as early as the 1890s and continuing through the present day.[11] Throughout the history of conversion therapy, a range of techniques have been used by both health care professionals and religious figures seeking to change people's sexual orientation or gender identity. Currently, talk therapy is the most commonly used therapy technique.[12] Some practitioners have also used "aversion treatments, such as inducing nausea, vomiting, or paralysis; providing electric shocks; or having the individual snap an elastic band around the wrist when the individual became aroused to same-sex erotic images or thoughts."[13] Other practitioners have used non-aversive techniques such as attempting to "change thought patterns by reframing desires, redirecting thoughts, or using hypnosis."[14]

*An estimated 698,000 LGBT adults in the U.S have received conversion therapy at some point in their lives.*

An estimated 698,000 LGBT adults in the U.S have received conversion therapy either from a licensed professional or a religious advisor or from both at some point in their lives,[15] including about 350,000 LGBT adults who received conversion therapy as adolescents.[16]

# CURRENT PERSPECTIVES

## PROFESSIONAL HEALTH ASSOCIATIONS

A number of prominent national professional health associations—including the American Medical Association, the American Psychological Association, and the American Academy of Pediatrics, among others—have issued public statements opposing the use of conversion therapy because it is harmful and ineffective.[17] Several of these associations have called on Congress and state legislatures to pass laws that ban conversion therapy. For example, the CEO of the American Counseling Association (ACA) submitted testimony to the Illinois House and Senate in support of the state's conversion therapy ban bill in 2015.[18] In addition, ACA members sent 79 letters to the Governor and 84 letters to state legislators in support of the bill.[19] Also, several professional health associations endorsed the Therapeutic Fraud Prevention Act, a federal bill that would have prohibited the practice of conversion therapy, including the National Association of School Psychologists, the American Psychoanalytic Association, the American Counseling Association, and the American Academy of Pediatrics.[20]

# PUBLIC OPINION

Public opinion polls at the national level and in several states have found majority support for ending the use of conversion therapy on youth. A 2019 national poll conducted by Ipsos/Reuters found that 56% of US adults support making conversion therapy on youth by mental health practitioners illegal as compared to a minority (18%) who think that it should be legal.[21] Majority support for making conversion therapy on youth illegal was observed across all age groups, regions of the US, and rural/urban residence.[22]

**Table 1. Public support for laws banning conversion therapy on minors in US**

Question: Conversion therapy is when mental health practitioners try to change an LGBTQ person's sexual orientation or gender identity. Do you think conversion therapy should be illegal or legal to use on LGBTQ children under age 18?

| | | Age | | | Region | | | | Residence | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | All | 18-34 | 35-54 | 55+ | Northeast | Midwest | South | West | Urban | Suburban | Rural |
| Conversion therapy on LGBTQ children should be illegal | 56% | 56% | 56% | 55% | 58% | 51% | 53% | 62% | 53% | 59% | 52% |
| Conversion therapy on LGBTQ children should be legal | 18% | 22% | 18% | 16% | 13% | 19% | 20% | 19% | 21% | 16% | 18% |
| Don't know | 26% | 21% | 26% | 30% | 29% | 30% | 27% | 19% | 25% | 25% | 30% |

Source: Ipsos Poll Conducted for Reuters, Stonewall Anniversary Poll, June 6, 2019.

Recent polls in six states have also found strong support for laws that ban licensed health care professionals from using conversion therapy on youth.

**Table 2. Public support for laws banning conversion therapy on minors in six states**

| Jurisdiction | Support for law banning conversion therapy | Year |
|---|---|---|
| Arizona[23] | 59% | 2017 |
| Florida[24] | 71% | 2017 |
| New Mexico[25] | 60% | 2016 |
| North Carolina[26] | 80% | 2019 |
| Pennsylvania[27] | 54% | 2017 |
| Pennsylvania's 18th Congressional District[28] | 63% | 2018 |
| Virginia[29] | 64% | 2016 |

Polling also indicates that many people do not think conversion therapy is effective; only 8% of respondents to a 2014 national poll said they thought conversion therapy could change a person's sexual orientation from gay to straight.[30]

# CURRENT LAWS

## CONVERSION THERAPY BY LICENSED HEALTH CARE PROFESSIONALS

As of June 2019, 18 states and the District of Columbia had passed statutes limiting the use of conversion therapy: California, Colorado, Connecticut, Delaware, D.C., Hawaii, Illinois, Maine, Maryland, Massachusetts, Nevada, New

Hampshire, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, and Washington.[31] The laws protect youth under age 18 from receiving conversion therapy from licensed mental health care providers.[32] California was the first state to pass a conversion therapy ban in 2012.[33] Four states—Colorado, Maine, Massachusetts, and New York—passed bans in 2019.[34] In addition, a number of cities and counties in states without statewide bans have passed bans at the local level.[35]

All of the state statutory bans allow licensing entities to discipline health care providers who use conversion therapy on youth under age 18.[36] Under Connecticut, Illinois, and New Hampshire laws, the use of conversion therapy on youth is also considered an unfair business practice, and the laws allow for enforcement and penalties consistent with other state laws against such practices.[37] In addition, in 2015, a New Jersey court held that providing conversion therapy in exchange for payment constitutes a fraudulent business practice, regardless of whether it is used on youth or adults.[38]

16,000 LGBT youth (ages 13-17) will receive conversion therapy from a licensed health care professional before they reach the age of 18 in the 32 states that currently do not ban the practice, unless additional states pass conversion therapy bans.[39] Approximately 10,000 LGBT youth (ages 13-17) who live in states with bans have been protected from receiving conversion therapy from a licensed health care professional before age 18 because their states have banned the practice.[40]

In addition to state bans, members of Congress have introduced federal legislation aimed at limiting conversion therapy. The Therapeutic Fraud Prevention Act, introduced in both the House and Senate in 2017[41] and 2015[42], would have classified conversion therapy provided in exchange for payment as a form of consumer fraud.[43] The law would have allowed state attorneys general and the Federal Trade Commission to bring enforcement actions against individuals who are providing conversion therapy for payment or advertising such services.[44] Additionally, the Prohibition of Medicaid Funding for Conversion Therapy Act and the Every Child Deserves a Family Act would limit the practice of conversion therapy by prohibiting payments under the Medicaid and Social Security programs for conversion therapy.[45] Both of these bills have been introduced in Congress in 2019.[46]

### CONVERSION THERAPY BY RELIGIOUS AND SPIRITUAL ADVISORS

The state statutory conversion therapy bans apply to licensed mental health care professionals and sometimes more broadly to others who seek to provide conversion therapy in exchange for payment.[47] The laws generally do not apply to religious or spiritual advisors who engage in sexual orientation or gender identity change efforts within their pastoral or religious capacities.

These exclusions for therapy provided by religious or spiritual advisors leave many youth vulnerable to conversion therapy even in states with bans. An estimated 57,000 youth (ages 13-17) across all states will receive conversion therapy from religious or spiritual advisors before they reach the age of 18.[48] This includes approximately 38,000 youth (ages 13-17) who will receive conversion therapy from religious or spiritual advisors, but not a licensed health care professional before they reach the age of 18.[49] Some youth will receive conversion therapy from both a licensed health care provider and a religious or spiritual advisor before they reach age 18.

## CONCLUSION

Conversion therapy continues to be used in the U.S. despite support for ending the practice among prominent medical and mental health associations and the public. An estimated 698,000 LGBT adults in the U.S. have received

treatment to change their sexual orientation or gender identity at some point in their lives, including about 350,000 who received treatment as adolescents. As of June 2019, 18 states, the District of Columbia, and a number of localities had enacted laws banning licensed professionals from using conversion therapy on youth. An estimated 16,000 LGBT youth will receive conversion therapy from a licensed professional before they reach the age of 18 in the 32 states that currently do not ban the practice. In addition, an estimated 57,000 LGBT youth across all states will receive conversion therapy from religious or spiritual advisors. Because of the large number of youth who may be vulnerable to conversion therapy, individuals who have contact with minors should be aware that the American Psychological Association has issued a resolution "advising parents, guardians, young people, and their families to avoid sexual orientation change efforts that portray homosexuality as a mental illness or developmental disorder and to seek psychotherapy, social support and educational services that provide accurate information on sexual orientation and sexuality, increase family and school support, and reduce rejection of sexual minority youth[.]"[50]

# ABOUT THE WILLIAMS INSTITUTE

The Williams Institute on Sexual Orientation and Gender Identity Law and Public Policy at UCLA School of Law advances law and public policy through rigorous, independent research and scholarship, and disseminates its work through a variety of education programs and media to judges, legislators, lawyers, other policymakers and the public. These studies can be accessed at the Williams Institute website.

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# ENDNOTES

[1] Judith M. Glassgold et al., Am. Psych. Assoc., Report of the Am. Psych. Assoc. Task Force on Appropriate Therapeutic Responses to Sexual Orientation 22 (2009).

[2] Susan L. Morrow & A. Lee Beckstead, Conversion Therapies for Same-Sex Attracted Clients in Religious Conflict: Context, Predisposing Factors, Experiences, and Implications for Therapy, 32 Counseling Psychologist 641, 642 (2004).

[3] *E.g.*, Annesa Flentje, Nicholas C. Heck & Bryan N. Cochran, *Sexual Reorientation Therapy Interventions: Perspectives of Ex-Ex-Gay Individuals*, 17 J. Gay & Lesbian Mental Health 256 (2013); Elizabeth M. Weiss et al., *A Qualitative Study of Ex-Gay and Ex-Ex-Gay Experiences*, 14 J. Gay & Lesbian Mental Health 291 (2010); Ariel Shidlo & Michael Schroeder, *Changing Sexual Orientation: A Consumer's Report*, 33 Prof. Psych.: Research & Practice 249 (2002).

[4] Sandy E. James et al., Nat'l Ctr. for Transgender Equality, The Report of the 2015 U.S. Transgender Survey (2016); Caitlin Ryan et al., *Parent-Initiated Sexual Orientation Change Efforts with LGBT Adolescents: Implications for Young Adult Mental Health and Adjustment*, J. Homosexuality (Nov. 7, 2018) (online).

[5] 698,000 US LGBT adults ages 18 to 59 are estimated to have received treatment to change their sexual orientation or gender identity [range 572,000 to 857,000]. This figure was calculated by adding estimates for LGB and transgender adults and rounding them to the nearest 1,000. In order to determine an estimate for the number of LGB adults who have received conversion therapy, we started with the proportion of LGB adults ages 18 to 59 who report having received treatment to change their sexual orientation (6.7%) from the Generations Study*, a national probability study of LGB individuals supported by the Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health under Award Number R01HD078526 (Ilan H. Meyer, PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The proportion who received conversion therapy across three age cohorts (18-25, 34-41, and 52-59) did not statistically significantly differ across cohorts and is assumed to be consistent for those ages 18 through 59 years (Williams Institute unpublished analyses). That proportion was then multiplied by the proportion of adults ages 18 to 59 who identify as LGBT (5.3%) in the 2015-2017 Gallup Daily Tracking Survey (Williams Institute unpublished analyses) and the proportion of LGBT individuals ages 18 to 59 who are cisgender (87.7%) among LGBT-identified respondents to the 2014-2015 BRFSS (Williams Institute unpublished analyses), and then applied to the number of adults ages 18 to 59 in the U.S. (180,757,997), according to 2016 population estimates from the 2010 U.S. Census. For total 18-59 population estimates: search American FactFinder, (last visited Dec. 15, 2017) (select advanced search, enter "Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States, States, and Puerto Rico Commonwealth: April 1, 2010 to July 1, 2016" under topic or table name, and select "Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States, States, and Puerto Rico Commonwealth: April 1, 2010 to July 1, 2016" 2016 Population Estimates). The same steps were followed with 95% confidence intervals to calculate a range for each estimate.

In order to determine an estimate for the number of transgender adults who have received conversion therapy, we started with the proportion of transgender adults who report that one or more professionals tried to make them identify only with their sex assigned at birth or try to stop them from being transgender (13.0%), as observed in the U.S. Transgender Survey—the largest purposive sample study of transgender adults to date and reported in James et al., *supra* note 4. The proportion who received conversion therapy was multiplied by the proportion of adults ages 18 and older who are estimated to be transgender (0.6%) and then applied to the number of adults ages 18 to 59 in the U.S. (180,757,997). This estimate is likely to be somewhat conservative given that slightly larger proportions of the population identify as transgender among younger age cohorts. For transgender population estimates see Andrew R. Flores et al., The Williams Institute, How Many Adults Identify as Transgender in the United States? (2016).

***About the Generations Study.** *Generations* participants were recruited by Gallup, Inc., a survey research consulting company (http://www.gallup.com/) using the Gallup Daily Tracking Survey as initial contact. *Generations* baseline participants were screened and enrolled in the study between March 28, 2016 – March 30, 2017. The Daily Tracking Survey is a telephone interview of a national probability sample of 1,000 adults ages 18 and older that is conducted daily (350 days a year) to inquire about topics including the respondents' politics, economics and general well-being. Respondents include English and Spanish-speaking individuals from all 50 U.S. states and the District of Columbia. Gallup uses a dual-frame sampling procedure, which includes random-digit dialing (RDD) to reach both landline and cellphone users, as well as an additional random selection method for choosing respondents with landlines. Gallup stratifies the RDD list to ensure that the unweighted samples are proportionate by U.S. Census region and time zone. Gallup weights the data daily to compensate for disproportionalities in non-response and selection probabilities.

The *Generations* study used a 2-step recruitment procedure. In the first step, utilizing a question asked of all Gallup respondents, all LGBT individuals were identified. The Gallup question to assess sexual orientation and gender identity asked by the phone interviewer is "I

have one final question we are asking only for statistical purposes. Do you, personally, identify as lesbian, gay, bisexual, or transgender?" In the second step, Gallup respondents who were identified as LGBT were assessed for eligibility for participation in the *Generations* study and those eligible were invited to participate in *Generations*. Respondents were eligible if they identified as LGB (and not transgender) in response to a *Generations* question that asked if they were *lesbian, gay, bisexual, queer, or same-gender loving,* if they were in the age and race/ethnicity groups targeted for the 3 cohorts under investigation in *Generations*: ages 18-25, 34–41, or 52–59; Black, Latino, or White; completed 6th grade at least, and if they spoke English well enough to conduct the phone interview in English. Transgender respondents were recruited into a contemporary TransPop study.

Respondents who were eligible for participation in Generations were invited to participate in the study. If they agreed, they were emailed or mailed a survey questionnaire to complete by self- administration (via a web link or printed questionnaire, respectively). Respondents were sent $25 gift certificate with their invitation to participate in the study, which they could redeem at any time. Prior to completing the survey, respondents reviewed an information sheet about the study and their rights and responsibilities as research participants. Respondents who agreed to participate then submitted the web survey online or returned the printed questionnaires for data entry using a provided addressed envelope.

In total, 366,644 participants were screened by Gallup for inclusion in the Generations study. Of them, 3.5% were identified as LGBT and 27.5% of them were eligible for Generations based on the eligibility criteria. Of these, 80% agreed to participate in the survey and of those, 48% completed the survey. The final Generations baseline sample size was 1,345. Generations is funded by a grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD grant 1R01HD078526) and through supplemental grants from the National Institutes of Health, Office of Behavioral and Social Sciences Research and the Office of Research on Women's Health.

Generations Survey Items about Conversion Therapy

133 Did you ever receive treatment from someone who tried to change your sexual orientation (such as try to make you straight/heterosexual)? *If yes, please mark all that apply.*

- ☐ No → ***Skip to the text before Question 135***
- ☐ Yes, from a healthcare professional (such as a psychologist or counselor who was not religious-focused)
- ☐ Yes, from a religious leader (such as a pastor, religious counselor, priest)

134 About how old were you the last time you received treatment to change your sexual orientation?

☐☐ *Your best estimate is fine.*

***Continue*** ⇨

[6] Among adults who have received conversion therapy, approximately 49.9% of LGB adults in the Generations Study and 51.0% of transgender adults in the U.S. Trans Survey are estimated to have received treatment at or before the age of 18. These proportions are applied to the number of LGB and transgender adults ages 18 to 59 who are estimated to have received conversion therapy, as described above. Thus, we estimate that 350,000 LGBT adults [range 287,000 to 429,000] received treatment as adolescents. We believe that our estimate of conversion therapy among cisgender LGB adolescents is, if anything, an underestimate because the Generations Study survey asked about age at which last conversion therapy was received versus the age at which conversion therapy first began. It is possible that some youth received conversion therapy that did not end until age 18 or later and that these individuals are missing in our estimates of the percentage of LGB youth who received conversion therapy. This would lead to an underestimate of the number of current LGB youth currently at risk of conversion therapy.

[7] 16,000 LGBT youth ages 13 to 17 [range 10,000 to 26,000] are estimated to live in states without state-wide conversion therapy bans and will receive conversion therapy from a professional before the age of 18. This figure was calculated by adding estimates for LGB and transgender youth. In order to determine an estimate for the number of LGB youth who will receive conversion therapy before age 18, we multiplied the proportion of LGB adults ages 18 to 59 who report having received treatment from a health care professional to change their sexual orientation that began and ended before the age of 18 (1.2%) from the Generations Study (Williams Institute unpublished analyses) by the proportion of youth in grades 9 through 12 who identify as LGB (8.0%) in the 2015 YRBS and by the proportion of LGB young adults ages 18 to 24 who are cisgender (95.7%) among LGB-identified respondents to the 2014-2015 BRFSS (Williams Institute unpublished analyses), and then applied this proportion to the number of youth ages 13 to 17 in the U.S. (20,870,650), according to 2016 population estimates from the 2010 U.S. Census. For total 13-17 population estimates: search American FactFinder, (last visited Dec. 15, 2017) (select advanced search, enter "Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States, States, and Puerto Rico Commonwealth: April 1, 2010 to July 1, 2016" under topic or table name, and select "Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States, States, and Puerto Rico Commonwealth: April 1, 2010 to July 1, 2016" 2016 Population Estimates). For estimates of the proportion of youth who identify as lesbian, gay, or bisexual see Laura Kann et al., Sexual Identity, Sex of Sexual Contacts, and Health-Related Behaviors among Students in Grades 9-12 – United States and Selected Sites,

2015 (2016). Note: The proportion who received conversion therapy from a health care professional to change their sexual orientation that began and ended before the age of 18, was not significantly different across the three age cohorts (18-25, 34-41, and 52-59) where receipt of conversion therapy is assumed to be consistent for those ages 26 to 33 and 42 to 51 (Williams Institute unpublished analyses).

In order to determine an estimate for the number of transgender youth who have received conversion therapy we multiplied the proportion of transgender adults who report that a professional (nonreligious or spiritual) tried to make them identify only with their sex assigned at birth or stop them from being transgender (9.0%) by the proportion for whom this had happened at or before age 18 (51%), as observed in the U.S. Transgender Survey and reported in James et al., *supra* note 4. This proportion (4.6%), those who received conversion therapy at or before age 18, was multiplied by the proportion of youth ages 13 to 17 who are estimated to be transgender (0.73%) and then applied to the number of youth ages 13 to 17 in the U.S. (20,870,650). For transgender population proportion estimates see JODY L. HERMAN ET AL., THE WILLIAMS INSTITUTE, AGE OF INDIVIDUALS WHO IDENTIFY AS TRANSGENDER IN THE UNITED STATES (2017).

For a list of the states that have banned conversion therapy state-wide see note 33, *infra*. Although some cities and counties have enacted local bans on conversion therapy, the population of these localities is not large and would not have an appreciable impact on state estimates.

[8] Following the same approach described above, we estimate that approximately 10,000 LGBT youth [range 6,000 to 16,000] live in states that have banned conversion therapy state-wide by licensed professionals.

[9] 57,000 LGBT youth ages 13-17 [range 37,000 to 94,000] are estimated to be at risk of receiving treatment to change their sexual orientation or gender identity from a religious leader, advisor or counselor at or before age 18. This figure was calculated by adding estimates for LGB and transgender youth. In order to determine an estimate for the number of LGB youth who will receive conversion therapy, we multiplied the proportion of LGB adults ages 18 to 25 who report having received treatment from a religious leader (pastor, religious counselor, priest) to change their sexual orientation that began and ended before the age of 18 (3.4%) from the Generations Study (Williams Institute unpublished analyses) by the proportion of youth in grades 9 through 12 who identify as LGB (8.0%) in the 2015 YRBS and by the proportion of LGB young adults ages 18 to 24 who are cisgender (95.7%) in the 2014-2015 BRFSS (Williams Institute unpublished analyses), and then applied this proportion to the number of youth ages 13 to 17 in the U.S. (20,870,650), according to 2016 population estimates from the 2010 U.S. Census. For total 13-17 population estimates: search American FactFinder, (last visited Dec. 15, 2017) (select advanced search, enter "Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States, States, and Puerto Rico Commonwealth: April 1, 2010 to July 1, 2016" under topic or table name, and select "Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States, States, and Puerto Rico Commonwealth: April 1, 2010 to July 1, 2016" 2016 Population Estimates). For estimates of the proportion of youth who identify as lesbian, gay, or bisexual see KANN ET AL., *supra* note 7.

In order to determine an estimate for the number of transgender youth who received conversion therapy from a religious or spiritual counselor/advisor, we multiplied the proportion of transgender adults who report that such a person tried to make them identify only with their sex assigned at birth or stop them from being transgender (4.0%) by the proportion for whom this had happened at or before age 18 (51%), as observed in the U.S. Transgender Survey and reported James et al., *supra* note 4. This proportion (2.0%), those who received conversion therapy at or before age 18, was then multiplied by the proportion of youth ages 13 to 17 who are estimated to be transgender (0.73%) and then applied to the number of youth ages 13 to 17 in the U.S. (20,870,650). For transgender population proportion estimates see HERMAN ET AL., *supra* note 7.

[10] In our prior report, the Williams Institute estimated that approximately 20,000 LGBT youth (ages 13-17) would receive conversion therapy from a licensed health care professional before they reached the age of 18 in the 41 states that had not banned the practice as of January 2018. The report further estimated that approximately 6,000 LGBT youth (ages 13-17) who lived in states that had bans in place in January 2018 would have received conversion therapy from a licensed health care professional before they reached the age of 18 had their states not banned the practice. This report considers the impact on those numbers of the nine state-level conversion therapy bans that were enacted between January 2018 and June 2019.

[11] *See, e.g.*, Prince Morton, *Sexual Perversion or Vice? A Pathological and Therapeutic Inquiry*, 25 J. NERVOUS AND MENTAL DISEASES 237 (1898); William Stekel, *Is Homosexuality Curable?* 7 PSYCHOANALYTIC REVIEW 443 (1930); FRANK S. CAPRIO, FEMALE HOMOSEXUALITY: A PSYCHODYNAMICS STUDY OF LESBIANISM 299 (1954); IRVING BIEBER ET AL., HOMOSEXUALITY: A PSYCHOANALYTIC STUDY (1962); Jolande Jacobi, *Case of Homosexuality*, 154 J. ANALYTICAL PSYCHOLOGY 48 (1969); Lee Birk, *The Myth of Classic Homosexuality: Views of a Behavioral Psychotherapist* in HOMOSEXUAL BEHAVIOR 376 (J. Marmor, ed., 1980); Robert L. Sptizer, *Can Gay Men and Lesbians Change Their Sexual Orientation? 200 Participants Reporting a Change from Homosexual to Heterosexual Orientation*, 32 ARCHIVES OF SEXUAL BEHAVIOR 403 (2003).

[12] Nat'l Ctr. for Lesbian Rights, #BornPerfect: The Facts About Conversion Therapy, http://www.nclrights.org/bornperfect-the-facts-about-conversion-therapy/ (last visited Jan. 2, 2018).

[13] GLASSGOLD ET AL., *supra* note 1 at 22.

[14] *Id.* at 33.

[15] For methodology, see note 5, *supra*.

[16] For methodology, see note 6, *supra*.

[17] American professional organizations that have issued statements opposing the use of conversion therapy on youth include: American Academy of Child and Adolescent Psychiatry, American Academy of Pediatrics, American Association for Marriage and Family Therapy, American College of Physicians, American Counseling Association, American Medical Association, American School Health Association, American Psychoanalytic Association, American Psychiatric Association, American Psychological Association, American School Counselor Association, and National Association of Social Workers Stewart L. Adelson, *Practice Parameter on Gay, Lesbian, or Bisexual Sexual Orientation, Gender Nonconformity, and Gender Discordance in Children and Adolescents*, 51 J. AM. ACAD. CHILD & ADOLESCENT PSYCHIATRY 957 (2012); Am. Acad. of Pediatrics, *Homosexuality and Adolescence*, 92 PEDIATRICS 631 (1993); Am. Assoc. for Marriage and Family Therapy, Positions on Couples and Families: Reparative/Conversion Therapy (Mar. 25, 2009), http://www.aamft.org/iMIS15/AAMFT/Content/about_aamft/position_on_couples.aspx; Hilary Daniel & Renee Butkis, *Lesbian, Gay, Bisexual, and Transgender Health Disparities: Executive Summary of a Policy Position Paper from the American College of Physicians*, 163 ANNALS OF INTERNAL MEDICINE 135 (2015); Am. Counseling Assoc., Ethical Issues Related to Conversion or Reparative Therapy (Jan. 16, 2013), https://www.counseling.org/news/updates/2013/01/16/ethical-issues-related-to-conversion-or-reparative-therapy; Am. Med. Assoc., Policies on Lesbian, Gay, Bisexual, Transgender & Queer (LGBTQ) Issues, H-160.991 Health Care Needs of the Homosexual Population, https://www.ama-assn.org/delivering-care/policies-lesbian-gay-bisexual-transgender-queer-lgbtq-issues (last visited Dec. 1, 2017); Am. Psychoanalytic Assoc., Position Statement on Attempts to Change Sexual Orientation, Gender Identity, or Gender Expression (June 2012), *available at* http://www.apsa.org/content/2012-position-statement-attempts-change-sexual-orientation-gender-identity-or-gender; Am. Psychiatric Assoc.; Position Statement on Therapies Focused on Attempts to Change Sexual Orientation (Reparative or Conversion Therapies) (2000); Barry S. Anton, *Proceedings of the Am. Psychological Assoc. for the Legislative Year 2009: Minutes of the Annual Meeting of the Council of Representatives and Minutes of the Meetings of the Board of Directors*, 65 AM. PSYCHOLOGIST 385 (2010); Am. Psychological Assoc., Resolution on Appropriate Affirmative Responses to Sexual Orientation Distress and Change Efforts (2009); Am. School Counselor Assoc., The Professional School Counselor and LGBTQ Youth (revised 2016), *available at* https://www.schoolcounselor.org/asca/media/asca/PositionStatements/PS_LGBTQ.pdf; Nat'l Assoc. of Social Workers, Nat'l Comm. on Lesbian, Gay, Bisexual, and Transgender Issues, Position Statement: Sexual Orientation Change Efforts (SOCE) and Conversion Therapy with Lesbians, Gay Men, Bisexuals, and Transgender Persons (2015), https://www.socialworkers.org/LinkClick.aspx?fileticket=yH3UsGQQmYI%3d&portalid=0;

[18] Press Release, Am. Counseling Assoc., ACA Advocacy Efforts Assist in Prohibiting 'Conversion Therapy' for Minors in Illinois (Aug. 21, 2015), *available at* https://www.counseling.org/news/news-release-archives/by-year/2015/2015/08/21/aca-advocacy-efforts-assist-in-prohibiting-conversion-therapy-for-minors-in-illinois.

[19] *Id.*

[20] Press Release, U.S. Rep. Ted Lieu, Rep. Lieu Introduces the Therapeutic Fraud Prevention Act of 2017, https://lieu.house.gov/media-center/press-releases/rep-lieu-introduces-therapeutic-fraud-prevention-act-2017.

[21] Reuters/Ipsos Poll Data, Ipsos Poll Conducted for Reuters: Stonewall Anniversary Poll 06.06.2019, https://www.ipsos.com/sites/default/files/ct/news/documents/2019-06/2019_reuters_tracking_-_stonewall_anniversary_poll_06_07_2019.pdf (last visited June 11, 2019).

[22] Williams Institute analysis of Reuters/Ispos poll data collected May 29-30, 2019 and June 5-6, 2019. Reuters/Ipsos Poll Data, Ipsos Poll Conducted for Reuters: Stonewall Anniversary Poll 06.06.2019, https://www.ipsos.com/sites/default/files/ct/news/documents/2019-06/2019_reuters_tracking_-_stonewall_anniversary_poll_06_07_2019.pdf (last visited June 11, 2019).

[23] Respondents were asked if they supported a range of protections for LGBTQ people in the state, including a ban on conversion therapy on youth; non-discrimination protections in employment, housing, and public accommodations; and non-discrimination protections for prospective parents and kids in the child welfare system. Fifty-four percent of respondents supported all protections. It is not possible to determine the level of support for each individual type of protection from available data. Hart Research Assoc., Key Findings from the Arizona Survey on LGBT Equality (Dec. 8, 2017), https://assets2.hrc.org/files/documents/Hart-Polling-Memo-_Arizona.pdf?_ga=2.2178288.1323628615.1559927537-706045989.1558542516.

[24] Doug Kaplan, Political Climate Forecast for Florida in 2018 Looks Positive for John Morgan, Negative for Gay Conversion Therapy, and Uncertain on the Future of American Involvement in Syria, ORLANDO POLITICAL OBSERVER, Apr. 3, 2017, http://orlando-politics.

com/2017/04/13/political-climate-forecast-for-florida-in-2018-looks-positive-for-john-morgan-negative-for-gay-conversion-therapy-and-uncertain-on-the-future-of-american-involvement-in-syria/.

[25] Ctr. for Civil Policy, 2017 Landscape Poll (Jan. 15, 2017), https://civicpolicy.com/2017-landscape-poll/.

[26] In response to the poll, 80% of respondents immediately said that they think conversion therapy should be illegal on children under 18. Half of the remaining 20% of respondents (those who initially agreed or had no opinion) agreed that the practice should be banned when they had a better understanding of what the practice entails. Born Perfect N.C., Protecting LGBT Youth in North Carolina from Conversion Therapy, https://southernequality.org/wp-content/uploads/2019/04/BornPerfectNCPolling.pdf (last visited June 8, 2019).

[27] Respondents were asked if they supported a range of protections for LGBTQ people in the state, including a ban on conversion therapy on youth; non-discrimination protections in employment, housing, and public accommodations; and non-discrimination protections for prospective parents and kids in the child welfare system. Fifty-four percent of respondents supported all protections. It is not possible to determine the level of support for each individual type of protection from available data. Hart Research Assoc., Key Findings from Pennsylvania Survey on LGBTQ Equality (Dec. 14, 2017), https://assets2.hrc.org/files/documents/Hart-Polling-Memo-Pennsylvania.pdf?_ga=2.204736336.1323628615.1559927537-706045989.1558542516.

[28] Gravis Marketing, Pennsylvania Polling (Jan. 6, 2018), https://www.realclearpolitics.com/docs/Gravis_PA_18_Special_Election_January_6_2018.pdf.

[29] Gravis Marketing, Virginia Election Poll (May 26, 2017), http://www.gravismarketing.com/polling-and-market-research/virginia-election-poll052016/.

[30] Peter Moore, *Only 8% of Americans Think Gay Conversion Therapy Works*, YouGov.com, June 12, 2014, https://today.yougov.com/news/2014/06/12/gay-conversion-therapy/.

[31] Cal. Bus. & Prof. Code § 865 (2017); 2017 Conn. Pub. Acts 5 (Reg. Sess.); H.B. 19-1129, 72nd Gen. Assemb., Reg. Sess. (Colo. 2019) (enacted); S.B. 65, 149th Gen. Assemb., Reg. Sess. (Del. 2018) (enacted); D.C. Code § 7-1231.14 (2017); S.B. 270, 29th Leg., Reg. Sess. (Haw. 2018) (enacted); 405 Ill. Comp. Stat. 48/1 (2017); H.P. 755, 129th Leg., Reg. Sess. (Me. 2019); H.B. 140, 191st Gen. Court, Reg. Sess. (Mass. 2019) (enacted); S.B. 1028, 2018 Gen. Assemb., Reg. Sess. (Md. 2018) (enacted); S.B. 201, 79th Leg., Reg. Sess. (Nev. 2017); H.B. 587, 2018 Gen. Ct., Reg. Sess. (N.H. 2018) (enacted); N.J. Rev. Stat. § 45:1-54 (2016); S.B. 121, 2017 Leg., Reg. Sess. (N.M. 2017); S.B. S1026, 2019-2020 Gen. Assemb., Reg. Sess. (N.Y. 2019) (enacted); Or. Rev. Stat. §§ 675.070; 675.300; 675.336; 675.540; 675.745 (2016); H. 5277, 2017 Gen. Assem., Reg. Sess. (R.I. 2017); Vt. Stat. Ann. tit. 18, § 8351; Vt. Stat. Ann. tit. 26, §§ 1354(a), 1842(b), 3016, 3210(a), 3271(a), 4042(a), 4062(a), 4132(a); S.B. 5722, 65th Leg., Reg. Sess. (Wash. 2018) (enacted).

[32] Some laws apply to other types of health professionals as well. For example, New Mexico's conversion therapy ban applies to nurses and doctors of osteopathic medicine. S.B. 121, 2017 Leg., Reg. Sess. (N.M. 2017)

[33] Cal. Bus. & Prof. Code § 865.

[34] S.B. 65, 149th Gen. Assemb., Reg. Sess. (Del. 2018) (enacted); S.B. 270, 29th Leg., Reg. Sess. (Haw. 2018) (enacted); S.B. 1028, 2018 Gen. Assemb., Reg. Sess. (Md. 2018) (enacted); H.B. 587, 2018 Gen. Ct., Reg. Sess. (N.H. 2018) (enacted); S.B. 5722, 65th Leg., Reg. Sess. (Wash. 2018) (enacted).

[35] Trevor Project, Progress Map, https://www.thetrevorproject.org/get-involved/trevor-advocacy/50-bills-50-states/progress-map/?location=fl-br (last visited June 8, 2019).

[36] See note, *supra*.

[37] 2017 Conn. Pub. Acts 5 (Reg. Sess.); 405 Ill. Comp. Stat. 48/1 (2017); H.B. 587, 2018 Gen. Ct., Reg. Sess. (N.H. 2018) (enacted).

[38] Ferguson v. JONAH, No. L-5473-12 (N.J. Sup. Ct. Dec. 18, 2015).

[39] For methodology, see note 7, *supra*.

[40] For methodology, see note 8, *supra*.

[41] H.R. 2119, 115th Cong. (2017); S. 928, 115th Cong. (2017).

[42] H.R. 2450, 114th Cong. (2015); S. 2880, 114th Cong. (2015).

[43] *Id.*

[44] *Id.*

[45] H.R. 1981, 116th Cong. (2019); H.R. __, 116th Cong. (2019).

[46] *Id.*

[47] See note 33, *supra*.

[48] For methodology, see note 9, *supra*.

[49] 38,000 LGBT youth ages 13-17 [range 24,000 to 61,000] are estimated to be at risk of receiving treatment to change their sexual orientation or gender identity from a religious leader, advisor or counselor only at or before age 18. This figure was calculated by adding estimates for LGB and transgender youth and rounding them to the nearest 1,000. In order to determine an estimate for the number of LGB youth who will receive conversion therapy, we multiplied the proportion of LGB adults ages 18 to 59 who report having received treatment from a religious leader (pastor, religious counselor, priest) to change their sexual orientation that began and ended before the age of 18 (2.2%), and who did not also receive conversation therapy from a health care professional, from the Generations Study (Williams Institute unpublished analyses) by the proportion of youth in grades 9 through 12 who identify as LGB (8.0%) in the 2015 YRBS and by the proportion of LGB young adults ages 18 to 24 who are cisgender (95.7%) in the 2014-2015 BRFSS (Williams Institute unpublished analyses), and then applied this proportion to the number of youth ages 13 to 17 in the U.S. (20,870,650), according to 2016 population estimates from the 2010 U.S. Census. For total 13-17 population estimates: search American FactFinder, (last visited Dec. 15, 2017) (select advanced search, enter "Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States, States, and Puerto Rico Commonwealth: April 1, 2010 to July 1, 2016" under topic or table name, and select "Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States, States, and Puerto Rico Commonwealth: April 1, 2010 to July 1, 2016" 2016 Population Estimates). For estimates of the proportion of youth who identify as lesbian, gay, or bisexual see KANN ET AL., *supra* note 7. The proportion who received conversion therapy from a religious leader only did not statistically significantly differ across age cohorts (18-25, 34-41, and 52-59) (Williams Institute unpublished analyses).

In order to determine an estimate for the number of transgender youth who received conversion therapy from a religious or spiritual counselor/advisor, we multiplied the proportion of transgender adults who report that such a person tried to make them identify only with their sex assigned at birth or stop them from being transgender (4.0%) by the proportion for whom this had happened at or before age 18 (51.0%), as observed in the U.S. Transgender Survey and reported JAMES ET AL., *supra* note 4. This proportion (2.0%), those who received conversion therapy at or before age 18, was then multiplied by the proportion of youth ages 13 to 17 who are estimated to be transgender (0.73%) and then applied to the number of youth ages 13 to 17 in the U.S. (20,870,650). For transgender population proportion estimates see HERMAN ET AL., *supra* note 7.

[50] Am. Psych. Assoc., Resolution on Appropriate Affirmative Responses to Sexual Orientation Distress and Change Efforts, http://www.apa.org/about/policy/sexual-orientation.aspx (last visited Dec. 18, 2017).