APA Official Actions

Position Statement on Conversion Therapy and LGBTQ Patients

Approved by the Board of Trustees, December 2018
Approved by the Assembly, November 2018

"Policy documents are approved by the APA Assembly and Board of Trustees. . . These are . . . position statements that define APA official policy on specific subjects. . ." – *APA Operations Manual*

Issue:
Since 1998, the American Psychiatric Association has opposed any psychiatric treatment, such as "reparative" or conversion therapy, which is based upon the assumption that homosexuality per se is a mental disorder or that a patient should change his/her homosexual orientation[1]. This position statement updates and replaces previous position statements about conversion therapy regarding sexual orientation, furthermore it also comments on conversion therapy with gender diverse patients in an attempt to prevent harm to any lesbian, gay, bisexual, transgender, or queer person.

In the past, diversity of sexual orientation and gender identity (e.g. homosexuality, bisexuality, and transgender identities) were seen as a mental illness. This changed in 1973 when the American Psychiatric Association stated that homosexuality per se is not a mental disorder[2]. While Gender Dysphoria remains a part of the DSM-5, there is growing social acceptance that human sexuality and gender identity can present in a variety of ways as part of the human condition[3,4,5,6,7,8,9,10,11,12,13].

The validity, efficacy, and ethics of clinical attempts to change an individual's sexual orientation have been challenged[14,15,16,17,18]. The literature also consists of anecdotal reports of people who claim that attempts to change were harmful to them, and others who claimed to have changed and then later recanted those claims[19,20,21,22,23,24,25,26,27,28,29,30,31]. Along a similar vein, gender diverse patients have been shown to benefit from gender-affirming therapies[32,33,34,35,36,37,38,39,40], and given the documented harm of "reparative" or conversion therapies regarding sexual orientation, it would likely be seen as unethical to research reparative therapy outcomes with gender diverse populations.

While many might identify as questioning, queer, or a variety of other identities, "reparative" or conversion therapy is based on the a priori assumption that diverse sexual orientations and gender identities are mentally ill and should change.

POSITION:

1. **APA reaffirms its recommendation that ethical practitioners refrain from attempts to change individuals' sexual orientation.**
2. **APA recommends that ethical practitioners respect the identities for those with diverse gender expressions.**

3. **APA encourages psychotherapies which affirm individuals' sexual orientations and gender identities.**
4. **APA encourages legislation which would prohibit the practice of "reparative" or conversion therapies that are based on the a priori assumption that diverse sexual orientations and gender identities are mentally ill.**

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Council on Minority Mental Health and Health Disparities

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Do Clinical Data from Transgender Adolescents Support the Phenomenon of "Rapid Onset Gender Dysphoria"?

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Although emergence of gender dysphoria at puberty is long established, a distinct pathway of rapid onset gender dysphoria was recently hypothesized based on parental data. Using adolescent clinical data, we tested a series of associations that would be consistent with this pathway, however, our results did not support the rapid onset gender dysphoria hypothesis. *(J Pediatr 2022;243:224-7).*

Puberty has long been understood as one period when gender dysphoria often first emerges.[1] Although most transgender (trans) older adolescents and adults report needing gender-affirming medical care (hormones and/or surgeries), and also report having been aware of their gender at young ages,[2] only a small proportion receive gender-affirming care as adolescents. Use of hormonal suppression with a gonadotropic-releasing hormone agonist, and hormones such as estrogen and testosterone therapies in trans and gender-diverse adolescents is supported by the American Academy of Pediatrics, the Pediatric Endocrine Society, the Endocrine Society, and the World Professional Association for Transgender Health.[1,3-5] Referrals to adolescent gender clinics have increased internationally, particularly among those assigned female at birth.[6-9]

In 2018, a phenomenon of rapid onset gender dysphoria was hypothesized as a distinct pathway involving social contagion among youth vulnerable due to mental or neurodevelopmental disorders,[10-12] raising public concerns regarding potential for later regret following gender-affirming medical care. This discussion has occurred primarily in the context of data from a single online parental survey.[10,11] Although this parental study has generated controversy,[13] methodologic and social critique,[12,14,15] and calls for additional research,[16,17] its hypotheses have not yet been tested on data from youth themselves. Specifically, rapid onset gender dysphoria is hypothesized as a phenomenon in youth with gender dysphoria emerging at or after puberty, socially influenced through peer contagion, and with contributing factors including poor mental health, neurodevelopmental disabilities, parent-child conflict, and maladaptive coping strategies.[10,11]

If the rapid onset gender dysphoria hypothesis indeed characterizes a distinct clinical phenomenon, and these youth access referrals for hormone suppression or gender-affirming hormones, then we would expect to see differentiation within clinical samples between those with more-recent (ie, rapid-onset) vs more-remote knowledge regarding their gender. Based on the published hypothesis,[10] we would expect more recent gender knowledge to be associated with self-reported mental health measures, mental health and neurodevelopmental disability diagnoses, behaviors consistent with maladaptive coping (eg, self-harm), support from online and/or transgender friends but not parents, and lesser gender dysphoria. We aim to test these hypotheses.

Methods

Baseline data (2017-2019) from the Trans Youth CAN! Cohort included pubertal/postpubertal adolescents age <16 years attending a first referral visit for hormone suppression or gender-affirming hormones at 10 Canadian medical clinics that provide specialized gender-affirming care to adolescents through a range of different care models. Ethics approval was received from all study sites. Years gender was known was missing for 1 participant (excluded), for a final sample of n = 173. Methods and measures are described in detail elsewhere.[18]

Self-reported measures were obtained from baseline interviewer-administered adolescent surveys,[19] and diagnoses from baseline clinical records.[20] Recent gender knowledge was coded by subtracting age in years from age adolescents self-reported they "realized your gender was different from what other people called you." As ages were whole numbers, a difference of 1 could indicate <1 year to just under 2 years. Values ≤1 were coded as recent gender knowledge, with an alternate definition (values ≤2) for sensitivity analysis. Mental health symptoms were assessed with the Overall Anxiety Severity and Impairment Scale,[21] the Modified Depression Scale,[22] and the Kessler-6 scale for psychological distress.[23] Mental health diagnoses extracted from chart included anxiety, depression, personality disorder, eating disorder, and neurodevelopmental disorder diagnoses

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included autism, obsessive compulsive disorder, or attention deficit hyperactivity disorder. Gender dysphoria symptoms were assessed using the Trans Youth CAN! Gender Distress Scale.[24] Self-reported mental health behaviors included self-harm, substance use, and suicidal behavior. Three measures captured social connections to online and trans communities: having gender-supportive online friends was coded if adolescents reported online friends who knew their gender and were "very supportive," and having online or trans friends as general sources of support was indicated in checklist items. Parental support was coded if youth indicated all biological/step/foster parents were "very supportive" of their gender identity or expression.

Statistical analyses were conducted using SAS v 9.4.1 (SAS Institute, Inc), weighted to account for clinics' different recruitment periods due to staggered start dates, to improve generalizability.[18] For analyses of associations between recency of gender knowledge and hypothesized correlates, a series of multiple regressions was conducted, with recency as the independent variable of interest, controlling for age and sex assigned at birth. Linear regressions were used for continuous dependent variables (eg, psychometric scales). For dichotomous dependent variables, modified Poisson regression with robust variance estimation was used.[25] As "rapid-onset" has not been precisely defined, we conducted a sensitivity analysis repeating these analyses using the alternate (value ≤2) definition of recent gender knowledge.

Results

Recency of gender knowledge is presented in the Figure, results of hypothesized associations (recency value ≤ 1) in Table I, and variable means and frequencies in Table II (available at www.jpeds.com). Controlling for age and sex assigned at birth, recent gender knowledge was not significantly associated with depressive symptoms, psychological distress, past diagnoses with mental health issues or neurodevelopmental disorders, gender dysphoria symptoms, self-harm, past-year suicide attempt, having gender-supportive online friends, general support from online friends or transgender friends, or gender support from parents. Recent gender knowledge was associated with lower scores on anxiety severity/impairment (b = −3.272; 95% CI −5.172, −1.373), and lower prevalence of marijuana use (prevalence ratio = 0.11; 95% CI 0.02, 0.82), counter to hypothesized directions of effect. For sensitivity analysis using the alternate (value ≤2) definition of recent gender knowledge, we found all results substantively the same in statistical significance and direction of effect, except past-year marijuana use, which now only approached statistical significance ($P = .0677$).

Discussion

We did not find support within a clinical population for a new etiologic phenomenon of rapid onset gender dysphoria during adolescence. Among adolescents under age 16 years seen in specialized gender clinics, associations between more recent gender knowledge and factors hypothesized to be involved in rapid onset gender dysphoria were either not statistically significant, or were in the opposite direction to what would be hypothesized. This putative phenomenon was posited based on survey data from a convenience sample of parents recruited from websites,[10] and may represent the perceptions or experiences of those parents, rather than of

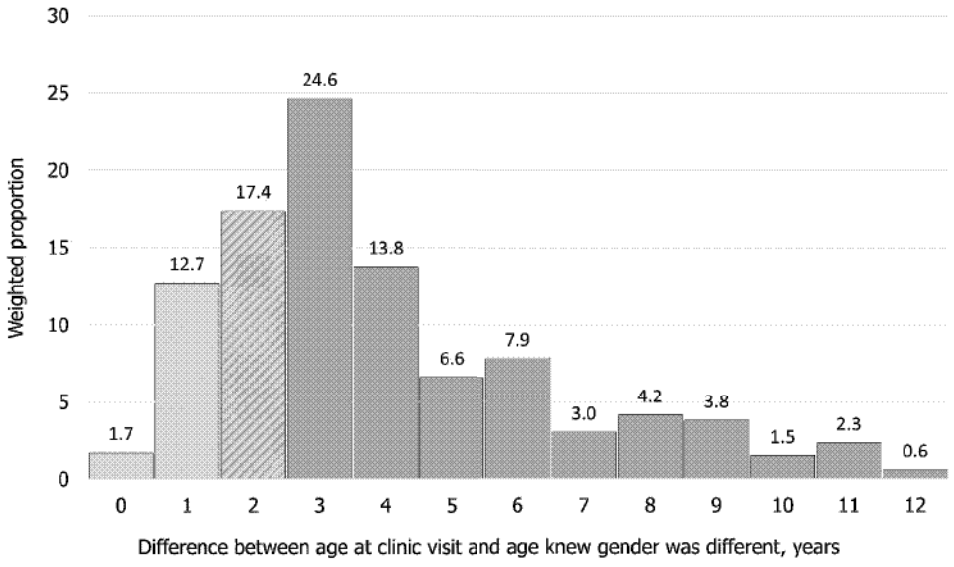

Figure. Recency of gender knowledge among adolescents age <16 years referred to Canadian clinics for hormone suppression or gender-affirming hormones (n = 173). Age at which knew gender was different was subtracted from current age in years; thus, "2 years" could range from more than 1 year to less than 3 years. Lighter gray represents recent gender knowledge in this analysis, with a sensitivity analysis also including the patterned bar.

Table I. Associations between short-term awareness of gender and variables hypothesized to be associated with rapid-onset gender dysphoria, controlling for age and sex assigned at birth

Dependent variables	B*	SE	P	PR*	95% CI†
Mental health scales					
Anxiety severity/impairment (OASIS)	−3.272	0.961	.0008		(−5.172, −1.373)
Depressive symptoms (MDS)	−1.276	0.845	.1328		(−2.944, 0.392)
Psychological distress (K6)	−1.156	1.060	.2771		(−3.248, 0.936)
Record of diagnosis with mental health disorder‡	−0.509	0.315	.1059	0.60	(0.32, 1.11)
Record of diagnosis with neurodevelopmental disorder§	0.066	0.362	.8563	1.07	(0.52, 2.17)
Gender dysphoria/distress (TYC-GDS)	−0.193	0.122	.1139		(−0.434, 0.047)
Mental health related behaviors					
Self-harm, past year	−0.052	0.191	.7833	0.95	(0.65, 1.38)
Marijuana use, past year	−2.178	1.010	.0310	0.11	(0.02, 0.82)
Past-year suicide attempt	−0.592	0.785	.4505	0.55	(0.12, 2.58)
Social connection indicators¶					
Reports having online friends supportive of gender	−0.050	0.157	.7505	0.95	(0.70, 1.29)
Indicates online friends as source of general support	−0.223	0.286	.4366	0.80	(0.46, 1.40)
Indicates trans friends as source of general support	−0.049	0.298	.1016	0.61	(0.34, 1.10)
All parents supportive of gender identity/expression	−0.004	0.202	.9836	1.00	(0.67, 1.48)

B, beta regression; *K6*, Kessler-6 Scale *MDS*, Modified Depression Scale; *OASIS*, Overall Anxiety Severity and Impairment Scale; *PR*, prevalence ratio; *TYC-GDS*, Trans Youth CAN! Gender Distress Scale.
*Estimates adjusted for age in years and sex assigned at birth.
†95% CIs for betas (for linear regressions) or PRs (for modified Poisson regressions).
‡Extracted from medical record: any diagnosis from clinic or referrer of anxiety, depression, personality disorder, eating disorder. Personality disorder diagnoses were uncommon (n = 2) and no youth had a record of eating disorder diagnosis.
§Extracted from medical record: any diagnosis from clinic or referrer of attention deficit hyperactivity disorder, obsessive compulsive disorder, or autism.
¶Hypothesized by other authors based on a survey of parents recruited from websites generally unsupportive of gender-affirming care.[10]

adolescents, particularly those who may enter into clinical care. Similar analyses should be replicated using additional clinical and community data sources. Our finding of lower anxiety severity/impairment scores in adolescents with more recent gender knowledge suggests the potential for longstanding experiences of gender dysphoria (or their social complications) playing a role in development of anxiety, which could also be explored in future research. ■

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50 Years Ago in *The Journal of Pediatrics*

What Changed the Prognosis of Juvenile Dermatomyositis?

Sullivan DB, Cassidy JT, Petty RE, Burt A. Prognosis in childhood dermatomyositis. J Pediatr 1972;80:555-63.

The addition of systemic corticosteroids to the treatment of juvenile dermatomyositis played a pivotal role in changing the outcome of this disease. This commentary published 50 years ago summarized the demographic, clinical, laboratory, pathology, treatment, and outcome of 18 children with dermatomyositis seen between 1960 and 1969 in a single center. The medical treatment consisted of systemic corticosteroids with tapering over 2 years. In a previous classic report from 1964,[1] on which we wrote a commentary in 2014,[2] only 33% were treated with corticosteroids. The outcomes were grim: one-third died, another one-third remained crippled, and only one-third recovered completely. However, in this study merely 8 years later, no deaths from dermatomyositis were recorded. Seventeen of the 18 children were functionally independent after treatment, but 8 of 18 developed calcinosis. Four patients had residual skin scaring, 4 developed mild joint contractures, and 6 had muscle atrophy. It is important to note that most of the cases in this series (13/18) were mild and monophasic, and only 5 patients had dyspnea or dysphagia indicative of a more severe disease, thus contributing to the good prognosis.

Modern aggressive therapy includes corticosteroid-sparing medications. Methotrexate is given as first-line treatment together with corticosteroids. Other medications for severe or chronic disease include intravenous immunoglobulin, calcineurin inhibitors, cyclophosphamide, and biologic modifiers (rituximab and tumor necrosis factor inhibitors). Janus kinase inhibitors have shown promise. Overall, mortality has decreased to 2.5%. However, even today, between 30% and 40% of the patients manifest a chronic disease course with functional impairments and develop calcinosis, and they require long-term immunosuppressive therapy with many potential complications.[3] Thus, despite the improvement in prognosis, there is a still a long way to optimize treatment of this rare disease. Precision medicine, using specific myositis autoantibodies and analysis of immune pathways in individual patients, may further improve the outcome of our patients.[3] In addition, early diagnosis and treatment are key!

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Appendix

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Table II. Weighted frequencies or means for sociodemographic and study variables (n = 173)

Variables	Value
Age, n ($\%_{weighted}$)	
10-11 y	17 (8.5)
12-13 y	37 (22.6)
14-15 y	119 (68.9)
Ethnoracial background,* n ($\%_{weighted}$)	
Indigenous	33 (18.4)
Nonindigenous visible minority†	10 (6.6)
Nonindigenous white	128 (75.0)
Immigration background, n ($\%_{weighted}$)	
1 or more immigrant parent	126 (28.7)
No immigrant parents	44 (71.3)
Living environment, n ($\%_{weighted}$)	
City	87 (55.2)
Suburb	59 (33.9)
Rural	27 (10.9)
Gender identity, n ($\%_{weighted}$)	
Male or primarily a boy	125 (75.7)
Female or primarily a girl	32 (15.9)
Nonbinary‡	14 (8.3)
Mental health scales, $mean_{weighted}$ (SD)	
Anxiety severity/impairment (OASIS)	8.842 (4.548)
Depressive symptoms (MDS)	15.077 (4.030)
Psychological distress (K6)	10.746 (5.100)
Record of diagnosis with mental health disorder,§ n ($\%_{weighted}$)	92 (51.6)
Record of diagnosis with neurodevelopmental disorder,¶ n ($\%_{weighted}$)	44 (25.9)
Gender dysphoria/distress (TYC-GDS), $mean_w$ (SD)	4.048 (0.557)
Mental health related behaviors, n ($\%_{weighted}$)	
Self-harm, past year	110 (67.9)
Marijuana use, past year	29 (20.0)
Past-year suicide attempt	24 (16.9)
Social connection indicators,** n ($\%_{weighted}$)	
Reports having online friends supportive of gender	109 (69.9)
Indicates online friends as source of general support	79 (49.3)
Indicates trans friends as source of general support	92 (55.8)
All parents supportive of gender identity/expression	109 (61.8)

K6, Kessler-6 Scale; *MDS*, Modified Depression Scale; *OASIS*, Overall Anxiety Severity and Impairment Scale; *TYC-GDS*, Trans Youth CAN! Gender Distress Scale.

*Coded to match Statistics Canada categories of Indigenous, visible minority, and white. Nonwhite, nonindigenous ethnoracial backgrounds were indicated by the following numbers of participants: 6 Black Canadian or African American, 2 Black African, 4 Latin American, 4 East Asian, 1 Indo-Caribbean, 3 Black Caribbean, 1 Middle Eastern, and 1 Southeast Asian (participants could indicate more than 1).

†The Canadian government defines visible minorities as "persons, other than Aboriginal peoples, who are non-Caucasian in race or nonwhite in color."[26]

‡Response option was "nonbinary or something other than male or female."

§Extracted from medical record: any diagnosis from clinic or referrer of anxiety, depression, personality disorder, eating disorder. Personality disorder diagnoses were uncommon (n = 2) and no youth had a record of eating disorder diagnosis.

¶Extracted from medical record: any diagnosis from clinic or referrer of attention deficit hyperactivity disorder, obsessive compulsive disorder, or autism.

**Hypothesized by other authors based on a survey of parents.[10]

AMERICAN SOCIETY OF PLASTIC SURGEONS

Advocacy / Advocacy News

State Focus on Gender Affirmation Intensifies

Thursday, February 25, 2021

Policy around transgender care has recently gained considerable attention amid a growing trend of legislation carrying serious professional, financial or criminal penalties for the provision of gender affirmation care. Conversely, although less extensively, efforts to expand coverage for transgender services among both public and third-party payer programs are also taking place.

This period of focused conversation centered on transgender care has been marked by both significant challenges and notable gains in the fight for full access to medically necessary affirming health care.

Background

Gender affirmation is a developing field of medical and surgical practice in which plastic surgeons play a pivotal role, leading the field in many of the physical transformative procedures often involved in gender affirmation.

Like many conditions, gender dysphoria and the process of gender affirmation requires a multidisciplinary approach. Physical, psychological and psychosocial treatment are all components of the gender affirmation process. These components of care – and particularly psychological assessment of gender dysphoria – often begin in childhood and early adolescence. Legislation that seeks to criminalize gender therapy targets this part of the care continuum.

A growing legislative trend

State legislation designed to criminalize gender affirming care first emerged in 2016. The frequency of such bills increased in the years that followed, but 2020 was a particularly active year, seeing six states with bills introduced on the issue. The volume and intent of the legislation between 2016 and 2020 resulted in transgender advocacy groups classifying the bills as "hostile." Last year was also notable because it marked the first instance in which one of the aforementioned bills succe
state legislative chamber.

Pl. Trial Ex. 134

In 2020, the South Dakota House of Representatives passed legislation prohibiting gender-affirming care for minors and leveling serious consequences for physicians found in violation of the law, including possible jail time. The state's Senate ultimately defeated the bill and prevented it from being enacted into law, but the relative success of the legislation was concerning and may have inspired a number of similar bills that would soon follow.

Less than three months into 2021, 11 pieces of legislation attempting to criminalize gender affirmation therapies have been introduced in 10 states. Alabama, Indiana, Iowa, Mississippi, Missouri, Montana, New Hampshire, Oklahoma, Texas and Utah have each introduced bills seeking to regulate the practice of medicine by banning certain procedures for minors and criminalizing the actions of health care providers who elect to administer gender affirmation care.

While the legislative concepts vary by state, the common threads include a prohibition of gender affirmation care for minors, identification of specific procedures and therapies that cannot be performed by the state's health care practitioners and a stipulation that it is illegal for a minor's parents or guardians to consent to the procedures. Penalties for health care providers, guardians and even school counselors found in violation of the laws vary widely and range from a fine of up to $500,000, to notifying child protective services and even classification of the guilty party as a felon.

Efforts to expand coverage

Contrary to the disturbing trend of legislation looking so severely at limiting gender-affirming care that it seeks to make criminals out of some of those involved, concerted efforts are also underway to expand coverage for the transgender community.

In one notable example, Aetna announced in January the expansion of its coverage for gender-affirming surgeries for transgender women. The insurer now covers gender-affirming breast augmentation in most plans, bringing coverage for the procedure into alignment with coverage for other surgeries common in transgender patients, such as breast removal or gender-reassignment.

Additionally, several states have worked to expand gender affirmation coverage. On February 12, ASPS wrote a letter in support of an emergency rule from the Wisconsin Department of Health Services that would repeal current restrictions and expand coverage for transgender Medicaid members. Similar amendments were proposed to the Washington Administrative Code and received the support of the Society via public comment in late January after ASPS involvement in the development of the policy that dates back to 2018.

ASPS involvement

ASPS firmly believes that plastic surgery services can help gender dysphoria patients align their bodies with whom they know themselves to be and improve their overall mental health and well-being. In 2021, the Society has actively opposed legislation seeking to criminalize actions by physicians and guardians when minors receive gender affirmation surgery in Missouri, Montana and Alabama and is readying engagement in other states where the issue has emerged. ASPS will continue its efforts to advocate across state legislatures for full access to medically necessary transition care.

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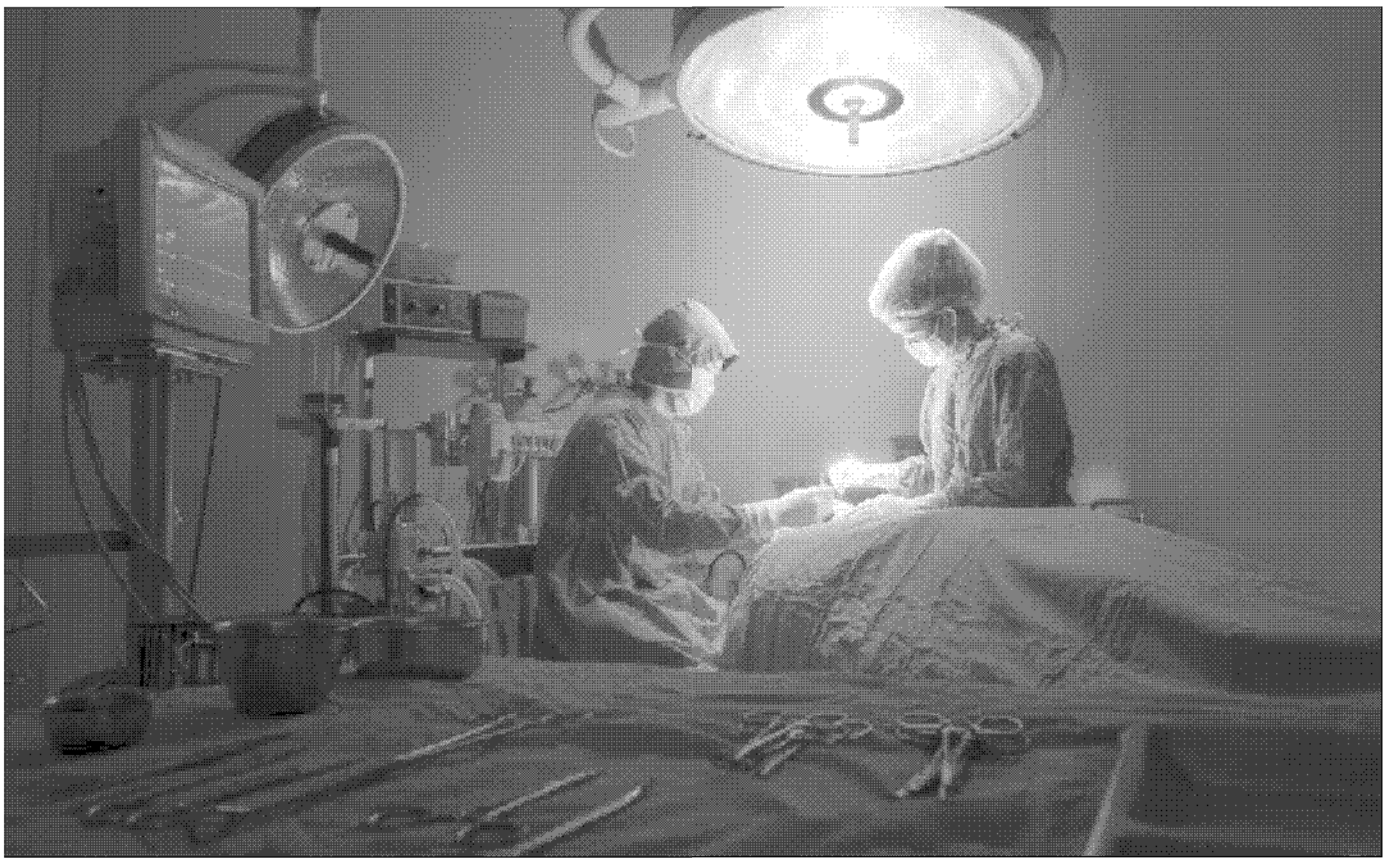
NEWS

Plastic surgeon: Sex-change operation 'utterly unacceptable' and a form of 'child abuse'

Dr. Patrick Lappert, a Catholic deacon in Alabama, says changing a person's sex is a lie and also a moral violation for a physician.



Lisa Bourne

Mon Sep 9, 2019 - 6:42 pm EDT

EDITOR'S NOTE: This story contains explicit content.

September 9, 2019 (LifeSiteNews) – The idea that you can change someone's sex is a lie, an Alabama-based plastic surgeon said, and pursuing this avenue with children amounts to child abuse.

"It's a form of tyranny, exercising a form of tyranny over our own bodies," Dr. Patrick Lappert said. "And in the case of children, it's child abuse."

Appearing on a recent broadcast of Relevant Radio's Trending with Timmerie, Lappert said the view that the human body is something that someone owns, that they can do things in order to provoke happiness in themselves, is a self-reverential view divorced from the objective reality of the human person.

Lappert briefly touched on the negative physical effects of same-sex sexual activity, and he also explained in detail the disturbing reality of what happens when a person undergoes so-called sex-change surgery.

He called it "utterly unacceptable" on moral grounds for a plastic surgeon, because it disregards the surgeon's call to balance respect for both form and function of the body in his or her work.

Regarding children, Lappert said, sexualizing them at a young age with these ideas is grooming them for later abuse.

"It's atrocious," he said. "And no one even knows how that's going to play out. There's no body of scientific evidence to even support the safety of doing that to children. But it's being done."

"Children do not have the capacity to consent to those sorts of treatments," Lappert said of sex-change procedures. "You cannot tell a pre-adolescent child anything about their adult life and expect that they're going to understand what you're telling them."

"Their concept of themselves is in the formative years," he continued. "And to ask a child to think of their sexuality when they're pre-adolescent is utterly insane. And it's in fact another great evil that's being inflicted upon children because it's the sexualization of normal chaste friendships of childhood."

Lappert also explained how suggesting to pre-adolescent children that they may be gay sexualizes chaste friendships and prompts them to think this way.

'They will never be the other sex'

Asked "What is a sex change?" Lappert responded, "Well, to begin with, the idea that you can change someone's sex is a lie."

"Many people have been led to believe by a lot of very clever programs and advertising from plastic surgeons and whatnot that you can actually change a man into a woman or a girl into a boy or anything like that," he said. "You cannot. Essentially all you can do is you can modify people's bodies both with medicines as well as with surgery to make them appear to be the other sex, but they will never be the other sex."

Lappert, a board certified general surgeon and plastic and reconstructive surgeon, is a Navy and Marine veteran, as well as a permanent deacon for the Diocese of Birmingham, Alabama. He is also chaplain for the Courage apostolate in the Birmingham diocese.

Experts have said for years that surgery or hormone treatment for gender-confused individuals, and certainly encouraging transgender ideas in children, is not the solution, and can result in exacerbating their condition.

Nonetheless, sex change surgeries have been on the rise, transgender ideology continues to be pushed in schools, civil government, and healthcare associations and institutions, while gender confused-individuals are also appearing more and more in pop culture, sports, media, and advertising.

The beginning stages

Lappert said gender confused individuals will typically begin by adopting a lifestyle and persona, change their name, hair and other aspects of their looks, and then move onto other identity components such as changing their driver's license and so on. Then hormonal medications are often introduced, and while sometimes these may initially make someone feel better about their gender confusion, this gives the false impression that surgical intervention will result in success, and taking hormones of the opposite sex over time can have a negative physical impact.

Irreversible

Most of the chemical interventions and cosmetic procedures done to alter a person's face or neck are to a degree reversible. However, Lappert warned, more invasive surgeries, such as mastectomy and procedures involving genitalia, are not.

A counterfeit vagina

In the case of men seeking to present as women, after they've had the other initial interventions performed, a definitive genital surgery includes castration, removal of the testicles, and the opening of the penis and removal of the erectile tissue, which is a procedure called penile inversion. This is where the penis is turned inside out and suspended up in the pelvis, turning it into "a receptive structure," Lappert explained.

The tissues of the scrotum are then turned into labia, meaning the external genitalia portions of the phallus itself are used to create the labia minora. In creating the receptive structure, the surgeon is trying to preserve the nerves, so that those parts of the genitalia that provoke erotic sensation can do so.

"Which is a very challenging thing to try to do when you're essentially mutilating the penis," he said, "to try to preserve the neurological support for it, so that the person can have erotic sensation from this counterfeit vagina that you've created."

"The problem is that this counterfeit vagina doesn't want to keep its dimensions," said Lappert. "And so you're constantly having to attend to the dilation of it to try to preserve its dimensions and so on. You also are taking the urethra that was in the penis and shortening it down so that it essentially is just an opening at the top of this counterfeit vaginal orifice that you've created."

This is the most commonly performed operation for males trying to present as female, he said.

A counterfeit penis

In the case of women trying to present as men, it begins with the removal of the ovaries and the uterus, removal of the vagina and the creation of a neo phallus, or a counterfeit penis.

This can be done a couple of different ways, he said, one being a high dose of testosterone, which will produce an enlargement of the clitoris, and then when you have exhausted those very high levels of testosterone, and they've had this effect on the clitoris, an operation is done to lengthen the urethra so that the urethra is extended along the underside of this enlarged clitoris, so that the urine empties at the tip of this structure.

That operation is called a metoidioplasty.

"And essentially what you get there is a small phallus," said Lappert, "and that's usually supplemented by creating a neo scrotum into which are placed two prosthetic testicles."

For women seeking a more developed physique, Lappert continued, a neo phallus is produced by what's called a flap operation.

This is where an area of tissue, typically from the leg, is raised up and surgically turned into a cylindrical structure inside of which is a urethral tube. That urethra tube is then connected to the native urethra, which appears at the base of the clitoris. The clitoris tissue itself is draped over the base of this neo phallus and then, again, a counterfeit scrotum with prosthetic testicles.

“And then in that whole apparatus you can also implant malleable or inflatable prosthetics that can produce the appearance of an erection,” explained Lappert. “So that's called a phalloplasty by flap operation.”

The most common flap operation done today is to harvest the skin for the neo phallus from the forearm, said Lappert.

“It's called a radial forearm flap and it's a tremendously disfiguring surgery on the forearm,” he said. “And so these women who are presenting as men will tattoo their forearms to conceal the disfigurement.”

“And then so (ultimately) what you wind up with is a counterfeit phallus or a counterfeit vagina,” stated Lappert.

Why are these counterfeit?

“Because they don't function the way those structures function,” said Lappert. “It’s obviously the case with the reproductive organ that what you're doing is you're robbing the person of an essential human capacity of the reproductive faculty. And that's not reversible or retrievable.”

“You cannot preserve the procreative function when you do these operations,” stated Lappert.

A sterile act

The doctor then touched on the spiritual component with these procedures.

“As Catholics, we recognize the human sexual embrace that's having two aspects, its unity and its procreative,” said Lappert. “It unites the two persons in an emotional-spiritual bond. But it's also a fruitful union.”

“Well, (with sex change procedures) you've robbed it of its fruitfulness,” he said. “It's now become a sterile act.”

The erotic sensation is never fully preserved

"The other thing that people don't understand is that because of the surgeries I've just described the desire to preserve erotic sensation from these structures that you're mutilating is never fully met," said Lappert.

In the nature of our nervous system there is a thing called neural mapping, he continued, meaning even though the physician works to preserve those nerves, the nerves continue to recognize sensations from their original form and function.

"The brain is still thinking that, even though you've turned your penis into a counterfeit vagina, whenever it is stimulated the brain is still thinking that there is a penis down there," said Lappert. "So here's a person trying to live as a woman hoping that they're going to be able to conduct their lives as women, who enters into a relationship with a man, and then in a sexual act is constantly being reminded by their own bodies that they are in fact still men, and that's a hard one to get over."

The malpractice of medicine

Lappert also warned that a whole generation of children is being raised whose psychosexual, physical, and neurological development are being stunted in hopes of supporting this cross-sex idea of themselves – pushed by the transgender industry.

He pointed out that if you took 100 children with cross-sex idea of themselves, 91 percent of them will desist.

"Ninety-one percent of them will stop thinking of themselves as the other sex," said Lappert. "But if you take the same hundred children to a transgender clinic at your local urban center, 100 percent of them will persist in it, which on the face of it tells you that this is this is the malpractice of medicine."

"If 91 percent of them would have gotten over the disease and 100 percent of them persistent and obviously you're doing something wrong here," he added. "But nonetheless that's how it's being presented."

"People are being led to believe that if you have the surgery your sorrows will go away," said Lappert. "But what's called gender dysphoria, this interior sense of sadness that the persons who suffer with transgender feel, they're being told that if they have all of this medical and surgical therapy, that those bad feelings will go away. And the best study looking into that tells us that that is not the case."

After a period of observation beyond some eight to 10 years, the suicide rate goes right back to where it was if nothing had been done for these people.

"If you didn't offer them any care at all, you'd have the same suicide rate that people have now after all of the surgical interventions," said Lappert. "And after the excitement dies down, and eight, 10 years later, they're right back to a 40 to 42 percent suicide rate. So that's a huge misrepresentation of benefit that is just not true."

Advocates for gender-confused individuals continually say these individuals need authentic psychological help that focuses upon the source of the confusion.

This kind of surgery is utterly unacceptable

Lappert called sex change surgery "an intentional destruction of a human faculty," and "so on moral grounds from the perspective of a plastic surgeon this kind of surgery is utterly unacceptable."

The language of slavery

Because these procedures result in sterilization, they are tied to assisted reproductive technology, Lappert explained, with patients asked how they want to "preserve their fertility," donating either sperm or ova, should they want children later.

"Those things will be put aside and for future assisted reproductive technology, essentially turning human persons into commodities," Lappert said.

A huge evil

"Because they will be told, you have a right to have a child even though you're having this transgender surgery," he said. "You have a right to have a child. So we're going to do these things for you. Well, that's the language of slavery, to speak of a person that's having a right to another person is the language of slavery."

"It's leading us to seeing the human person as a commodity that is regulated by the government, by government institutions, universities, and by laboratories," Lappert continued. "And that is a huge evil. It's a huge evil and never forget, that transgender surgery is right at the heart of that evil."

"First of all because it utterly perverts our sense of human sexuality," he said. "It internally divides the human person from their very own bodies. And now it's separating the human community from their reproductive faculties, in the era of assisted reproductive technology. So this is diabolical in every sense of the word. Diabolical."

Rejecting objective truth

Encouraging people to pursue sex-change surgery rejects understanding of who the human person is, said Lappert.

"One of the mistakes that people are making in contemporary life is viewing themselves as sort of a spirit creature and their bodies as something that they own or something that they possess," he said. "They view their own bodies as something that they can do things to in order to provoke happiness in themselves. It's a very self-referential view of the human person and it has at its heart this division of the nature of the human person."

Plastic surgery can never divorce itself from objective reality just as no form of medical care can separate itself from the objective truth of who the human person is, he said.

"So if I aim to be a good surgeon, then the very first thing I have to understand is the subject upon whom I am working," Lappert stated. "If I have met grave misunderstandings about the objective reality of that of the person, I'm going to be making some serious mistakes when I embark on medical or surgical care."

"To view the body as a thing, but somebody that a person owns, to view themselves, their personhood is something separate from their own bodies, is a very grave mistake," he said. "And then to set about modifying the body in ways that you hope will bring about a lasting happiness can't possibly succeed, because it begins with a lie, it begins with an error about the objective truth of who the human person is."

The full interview with Dr. Patrick Lappert is available HERE.

Two positive resources for gender-confused and same-sex attracted individuals featured in the discussion were the Roman Catholic Courage apostolate and Walt Heyer's outreach titled Sex Change Regret. Heyer had transitioned to living as a woman and then returned to living as a man, and now performs outreach for gender-confused people.

Information on Courage is available HERE and HERE.

The Sex Change Regret website can be accessed HERE.

James Shupe, formerly Jamie Shupe, ex-transgender and former non-binary person, writes about his experience and chronicles transgender issues HERE.

The National Suicide Prevention Hotline provides free and confidential help and resources to individuals in distress 24/7. The number is 800-273-8255.

Additional resources are available here, here and here.

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The OXFORD STUDENT

Oxford University's Student Newspaper. Est. 1991

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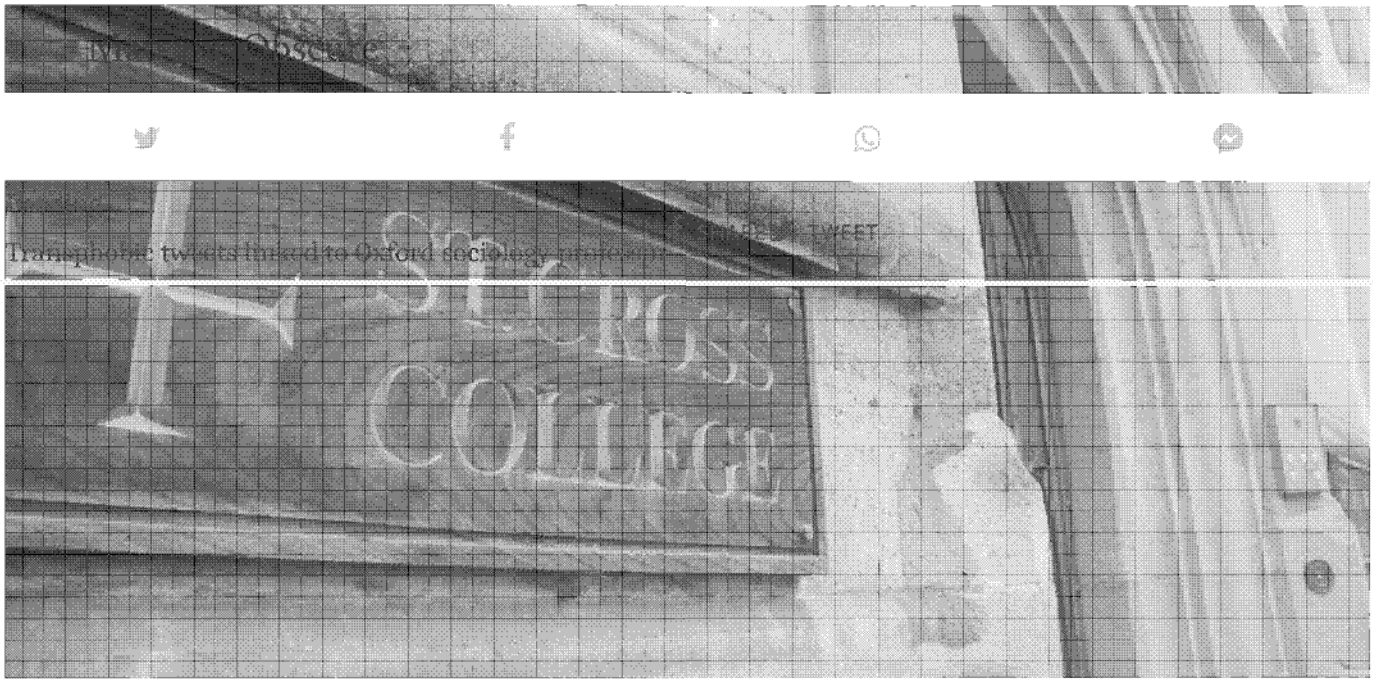


Image Credit: Tom Gould

Investigations · 26th October 2018

Transphobic tweets linked to Oxford sociology professor

James Ashworth and Charlie Willis

Image Credit: Tom Gould. Description: St Cross College.

Please note that this article contains explicit discussion of transphobic statements and images.

Professor of Sociology and Fellow of St Cross College Michael Biggs has been posting transphobic statements online under the Twitter handle @MrHenryWimbush, *The Oxford Student* can reveal.

The Twitter account, named Henry Wimbush and still online at the time of publication, has been tweeting statements such as "transphobia is a word created by fascists, and used by cowards, to manipulate morons" since first Tweeting in January.

In order to substantiate the allegations made that the true identity of the Tweeter was Professor Biggs, it was found that the account in question could be linked to a partial phone number and Yahoo! email using freely available data and by making use of Twitter's various functions. The Yahoo! email itself is also linked to a phone number ending in the same numbers as those previously identified, while also revealing that it is connected to the email address m**********gs@sociology.ox.ac.uk.

When this email is compared to those freely available on the Sociology Department's website, Biggs' is the only name that starts and ends in the correct letters, and also fits the number of characters exactly.

Another tweet states that the person behind the account has gone from "teenage shitlord to Oxford professor" [sic]. While this could refer to Oxford Brookes, the account references an update to their employer's trans policies in a

Biggs has published a number of articles in his own name about transgender issues, including on University servers. One such article was published by Transgender Trend, which has produced literature for schools which states that teachers should not pretend "to believe an idea that contradicts material reality" for children with gender dysphoria, and includes one suggested answer for primary school children asking questions about a transgender classmate is that they "can't actually change from a boy to a girl". In this article, he suggests that suicide in trans children is "not [...] a common occurrence" and that "transgendering organizations [cite evidence] from surveys that recruit respondents haphazardly".

While this article focused on UK-based statistics, it still seems to contradict a study by Becerra-Culqui et al., using a cohort of 1,333 juveniles across California and Georgia. They found that hospitalisation for suicidal ideation before evidence of gender nonconformation could be as high as 29% in transmasculine subjects, though significantly less at 9% in transfeminine individuals. A UK based study by Holt et al., using a smaller cohort of 218 juveniles, saw suicidal ideation placed at 38.3% for transfeminine and 32.8% for transmasculine individuals, while suicide attempts were made by 12.3% of transfeminine and 13.9% of transmasculine individuals. Biggs has also written about his work at the Women's Place UK (WPUK) event in Oxford in April – @MrHenryWimbush mentions attending other WPUK events – described by the Oxford SU LGBTQ+ Campaign in a statement as "predominantly about curtailing transgender people's rights". WPUK described this statement as "containing many inaccuracies".

The account Tweeted 23 June: "If a woman had an unsatisfactory experience at a restaurant, would she get an apology from the city's mayor with 1.5 hours?", apparently in reference to Charlotte Clymer, a trans woman who was removed from a D.C. restaurant when she used the women's bathroom after staff allegedly asked her to show her ID to be allowed in. The incident occurred in the evening, 22 June.

The account also Tweeted that the British medical journal *The Lancet* "endorses eugenics", tagged "#transthegayaway", in response to an article from the journal which states that "based on empirical evidence, clinician consensus, and results of non-randomised and observational studies [...] [hormone] treatment should depend on an individual's ability to make informed decisions, duration of puberty suppression, any coexisting health issues, and the level of family support."

Other Tweets posted by the account include multiple posts misgendering New Zealand weightlifter Laurel Hubbard, asking for an explanation of how "the 2nd and 3rd placed women could have ignored this man", accompanying an image of Hubbard atop a podium with two other weightlifters.

Another states that "gender-critical feminists almost invariably outmatch transactivists" with a suggestion that feminists "always have to argue against orthodoxy" while "transactivists are used to safe spaces where their

ideology is affirmed and never challenged." The last remark is accompanied by a snowflake emoji, with "snowflake" here used as "a disparaging term for a person who is seen as overly sensitive and fragile" (Merriam Webster).

The Handmaid's Tale, which shows four "handmaids" (women forced into sex slavery and resultant involuntary childbirth). The implication appears to be a ridicule of supposing that gender identity would matter in such a situation.

The account's bio states: "AMAB transmasculine non-binary demiboy. Polyam aro/ace. 2 + 2 = 4". This appears to be mocking certain labels of the LGBTQ+ community: "polyam[orous]" – "the practice of engaging in multiple sexual relationships" – and "aro/ace" – short for aromantic, meaning "having no interest in or desire for romantic relationships" alongside asexual, meaning "without sexual feelings or associations" – are clearly intended to sound self-contradictory. "2 + 2 = 4" also appears to be a reference to George Orwell's *1984*.

Further Tweets that have been shown to *The Oxford Student* state that "the odd thing about transitioning is that it makes you LESS attractive", while another states that @MrHenryWimbush can "almost picture your ladydick" in response to Tweets by other accounts. A reply to another Tweet alleges that transgender people are "five times more likely to be tweeting "choke on my ladydick, cuntwipe"".

In addition, both the Oxford LGBTQ+ Society and Dr Clara Barker, a trans woman and vice-chair of the Oxford University LGBTQ+ Advisory Board, have confirmed to *The Oxford Student* that they have passed on complaints about Biggs to the University in June. The account's last activity was on July 1st. Further allegations by Mac Harrison could not be substantiated.

Dr Clara Barker, who is mentioned in the account's Tweets, told *The Oxford Student* that she is "concerned by [Biggs'] personal views. That he may be linked to an account is one thing, but he has since started speaking very publicly as an expert of gender diversity.

"I find it hard to believe that he can say these things [referring to articles and printed comments by Biggs] outside of work, when they are so clearly in opposition to University guidelines and policies, [or] that those views can be left completely outside of a lecture hall. I really worry for any trans students that have to work with him. I would be very uncomfortable around him knowing his views."

St Cross College, of which Biggs is a fellow, referred us to the University Press Office, as did the Sociology Department, where he is a Professor. While stating that they "cannot comment on specific allegations", the University's statement said that "The University aims to create an inclusive trans-friendly culture, workplace and learning environment, free from discrimination, harassment or victimisation, where all transgender people are treated with dignity and respect. We aim to anticipate and respond positively to the needs of prospective, current and former students and staff in relation to gender identity issues, providing a professional and consistent service so that all trans members of the University feel welcome, safe, valued and supported to achieve their potential and contribute as a member of the University. Transphobic abuse, harassment and bullying will be dealt with under the University policy on harassment and bullying."

Ellie Oppenheim, President of the Oxford University LGBTQ+ Society, commented that "Upon hearing about the allegations made against Michael Biggs, the OULGBTQ+ Society were very concerned. Having received complaints


communicated with the vice chair of the OULGBTQ+ Advisory Board (Clara Barker), who supported us in our decision to go through the official university channels of complaint. In terms of our next steps, we will continue working under the guidance of Clara Barker, and remain in close communication with the pro-vice chancellor for equality and diversity."

Biggs, in response to a request for statement on his stance on transphobia, said: "It is not transphobic to discuss the merits of legislation or to debate theories about sex and gender. Dictionary definitions such as 'woman: adult human female' and 'lesbian: female homosexual' are not transphobic. Nor is it transphobic to call the convicted rapist Karen White – who was placed in a women's prison – a man."

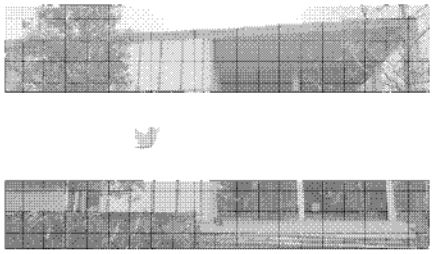
When asked if he supported the University's position on transphobia, he said: "I treat students and colleagues with respect and so would never call a member of the University by a pronoun which he or she found objectionable.

"I do not, however, believe that gender identity supersedes sex, any more than I believe that Jesus was the son of God. Therefore I oppose any attempt by the University to establish an official doctrine on gender, just as I would oppose the imposition of a single religion or one particular position on Israel-Palestine. The enforcement of orthodoxy – often disguised as 'diversity' – would destroy the University's very foundation: academic freedom."

His full statement can be found on his website.

The Oxford Student is currently investigating other claims of harassment and inappropriate comments by staff members of the University. If you have experience of this, and would be happy to be quoted anonymously, please use this anonymous form.

A previous version of this article described polyamory and asexuality as mutually exclusive. We acknowledge that this is not the case and have amended the article accordingly; please get in touch about any further issues with this definition! We have also on recommendation clarified that one quote makes reference to 1984. Thank you to @hans_fowles and @MrsMeadowsweet for clarifying these points. It has also been amended to include further Tweets which have been passed to The Oxford Student.



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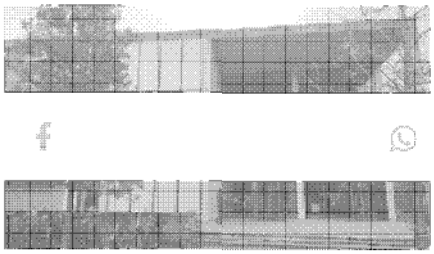

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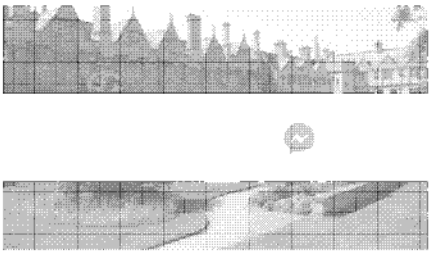

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MANAGEMENT OF ENDOCRINE DISEASE

Long-term outcomes of the treatment of central precocious puberty

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Abstract

GnRH analogues (GnRHa) are the treatment of choice for central precocious puberty (CPP), with the main objective to recover the height potential compromised by the premature fusion of growth cartilages. The aim of this review was to analyze long-term effects of GnRHa on height, body weight, reproductive function, and bone mineral density (BMD) in patients with CPP, as well as the potential predictors of outcome. Because randomized controlled trials on the effectiveness and long-term outcomes of treatment are not available, only qualified conclusions about the efficacy of interventions can be drawn. GnRHa treatment appears to improve adult height in girls with CPP, especially if diagnosed before the age of 6, whereas a real benefit in terms of adult height is still controversial in patients with the onset of puberty between 6 and 8 years of age. No height benefit was shown in patients treated after 8 years. Gonadal function is promptly restored in girls after cessation of treatment, and reproductive potential appears normal in young adulthood. Data are conflicting on the long-term risk of polycystic ovarian syndrome in both treated and untreated women. Fat mass is increased at the start of treatment but normalizes thereafter, and GnRHa itself does not seem to have any long-term effect on BMI. Similarly, analogue treatment does not appear to have a negative impact on BMD. Owing to the paucity of data available, no conclusions can be drawn on the repercussions of CPP and/or its treatment on the timing of menopause and on the health of the offspring.

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Introduction

Puberty results from the reactivation of the hypothalamic–pituitary–gonadal (HPG) axis following the quiescent period occurring during childhood. It is characterized by an increase in the amplitude and frequency of the hypothalamic gonadotropin-releasing hormone (GnRH) pulses, which in turn promote follicle-stimulating hormone and luteinizing hormone secretion by the pituitary, leading to the activation of gonadal function (1).

Precocious puberty is clinically defined by the appearance of secondary sexual characteristics, i.e., Tanner stage II of breast development before the age of 8 in girls and the increase in testicular volume ≥4 ml before 9 years in boys (2, 3). Central precocious puberty (CPP) due to early activation of pulsatile GnRH secretion is the most common form (2). It occurs in ~1:5000–10 000 children, with a female-to-male ratio ranging from 3:1 to 23:1 (3). Females typically present with idiopathic forms, whereas in boys CPP is mostly due to organic lesions such as hypothalamic–pituitary congenital malformations, tumors, infections, infiltrative/inflammatory disorders, and iatrogenic or traumatic injuries (3). Genetic factors (mutations of KISS1, KISS1R, and MKRN3 genes (4)), secular trend, ethnicity, nutritional status, and environmental changes have all been involved in the pathogenesis of CPP (2, 3, 5), although their exact mechanisms of action remain to be elucidated.

Short stature caused by rapid advancement of skeletal maturation driven by premature expo

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the main unfavorable event associated with precocious puberty. Historical data on untreated patients with CPP show mean final heights ranging from 151 to 156 cm in boys and from 150 to 154 cm in girls, being the height loss inversely correlated with the age at the onset of puberty (2, 6).

Treatment is aimed at selectively and effectively suppressing gonadal steroid secretion through medical treatment or removing the underlying cause whenever possible to allow normal sexual maturation and statural growth (2, 3, 6). The avoidance of potential psychosocial problems derived from experiencing precocious puberty and undesirable behaviors like early sexual intercourse and substance abuse reported in some cohorts of patients may also be acknowledged as objectives of the treatment (2, 3, 7). The decision to treat depends on the age at onset of puberty, pace of pubertal development, estimated adult height, and psychological impact of the premature sexual development (2, 3). Treatment is undisputed in rapidly progressive forms, defined on the basis of clinical, radiological, and biochemical criteria (8), for the significant risk of short adult height, while it is not required in patients with nonprogressive or slowly progressive forms who were shown to achieve an adult height within the normal range without treatment (2, 3).

GnRH analogues (GnRHa) are the medical treatment of choice for progressive CPP (2, 3). They derive from a chemical substitution at position 6 and 10 of the native GnRH molecule, which increases its resistance to the enzymatic degradation and affinity to the GnRH–pituitary receptor leading to desensitization of the receptor, ultimately resulting in the inhibition of gonadotropin secretion and return of sex steroids to prepubertal levels (9). Several active principles and formulations are available. Depot formulations are generally preferred because of better patient compliance. Drug choice depends on physician experience, patient needs, and government regulations of drug prescription (6, 7). GnRHa is generally safe and well tolerated. Local events such as bruising, pain, injection reactions, and sterile abscesses are the most common side effects, followed by minor menopausal symptoms – that is, hot flushes, headaches, and nausea (7) – while anaphylaxis is extremely rare (10).

In the last decades, the widespread use of GnRHa has increasingly demonstrated its favorable effects on statural growth, although the net height gain (HG) associated with the treatment and predictors of long-term outcomes remains debated (2, 6, 7, 8), as no randomized controlled trials (RCTs) have been performed and growth estimation suffers from important methodological limitations, which will be discussed later. Moreover, concerns have been raised on the potential negative effects of treatment on weight and metabolic profile, bone mineral density (BMD), and reproductive function in adulthood (2, 3, 6). The aim of our review was to analyze long-term effects of GnRHa on height, body weight, reproductive function, and BMD in patients with CPP, as well as potential predictors of outcome.

A literature search was performed using the PubMed database (http://www.ncbi.nlm.nih.gov/pubmed) and entering the string 'precocious puberty AND (treatment OR GnRH analogues) AND (height OR body mass index OR bone OR fertility OR reproduction OR polycystic ovary syndrome)' with no date limits. Only original studies performed in humans, written in English, reporting data at the beginning and after the completion of treatment were considered for BMI and metabolic parameters, reproductive function, and BMD. Studies focusing on height were considered only if baseline values and adult heights were reported and data expressed as mean (absolute values or SDS) ±S.D. or S.E.M. for study comparison and calculation of treatment efficacy (i.e. HG). Additional articles were identified through a hand search of reference lists in the papers retrieved (Fig. 1).

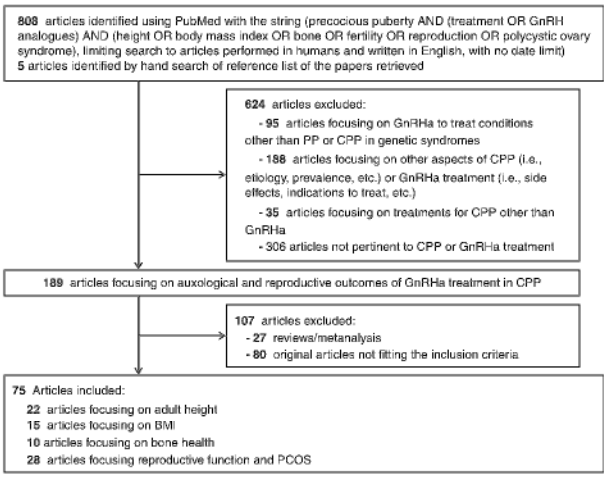

Figure 1

Methodological flow chart summarizing the main steps followed for the identification of articles of interest. CPP, central precocious puberty; GnRHa, gonadotropin-releasing hormone agonists; PCOS, polycystic ovary syndrome; PP, precocious puberty.

European Journal of Endocrinology

Outcomes of GnRHa therapy for CPP

Adult height

GnRHa have been extensively used since the 1980s in children with rapidly progressing CPP with the primary aim to restore genetic growth potential otherwise compromised by sex-hormone-driven premature closure of bone growth plates. The great majority of studies indicate some beneficial effect of treatment on statural growth, with limitations related to the absence of RCTs and the fact that the effects of GnRHa therapy have been traditionally analyzed by comparing the achieved adult height with predicted adult height at initiation of treatment or with adult heights of historical, untreated cohorts.

Bone age (BA) assessment is essential in the management of patients with CPP as it allows the identification of rapidly progressing forms of CPP with compromised predicted adult height requiring treatment. It is also important for monitoring treatment efficacy, as deceleration of BA maturation is a desired effect of treatment. Moreover, BA evaluation is valuable in defining the appropriate time for treatment discontinuation, because the best results in terms of adult height are achieved when treatment is discontinued at around 12–12.5 years in girls and 13.5 years in boys (11), although the optimal age for treatment interruption is not clearly defined by international guidelines. It should be pointed out, however, that BA assessment is affected by a great intra-observer variance, and Bayley and Pinneau tables, the reference standards for height prediction, have been validated for height prediction in normal children (11). In patients with CPP, height prediction based on both 'average' and 'advanced' tables is insufficiently reliable, especially when skeletal maturation is markedly advanced, and it is associated with a systematic overestimation of adult height (3.7–5.9 cm in girls, and even greater in boys in historical series) (2, 3).

The comparison of adult heights of treated CPP patients with those of historical cases is of limited value because data are derived from a small number of patients, usually the most severe, and do not take into account the influence of the secular trend on human growth over the decades. Moreover, studies are heterogeneous for patients – that is, chronological and BA at diagnosis and initiation of treatment and idiopathic vs organic forms of CPP – and treatment characteristics (2, 3).

Predictors of treatment outcomes also remain debated. Treatment efficacy appears to depend mainly on the age of CPP onset and treatment initiation with best outcomes reported in girls with onset of CPP before the age of 6 years and treated soon thereafter. BA advancement at the time of initiation of therapy, duration of therapy, mid-parental height, and height at the end of therapy have also been considered predictors of height outcome but with no definite conclusions reached on their appropriateness. The optimal age for treatment discontinuation is also questionable as several auxologic and treatment characteristics involved in post-treatment HG should be taken into account together with the psychological impact of the resumption of pubertal development on the patient and family (7, 8).

To clarify the impact of GnRHa treatment on statural growth and identify the most reliable predictors of height outcome in treated patients with CPP, 20 articles fitting the above-mentioned inclusion criteria were analyzed (Supplementary Table 1, see section on supplementary data given at the end of this article). For each of them, the following parameters, reported by authors or calculated from raw data, were recorded: number of enrolled patients; treatment type; target height (TH); chronological age, BA, and height at the beginning and end of treatment; HG (computed from the difference between adult and predicted height at diagnosis, according to average and/or advanced BA, as per authors' choice); and the difference between adult and predicted height at the end of treatment. Treatment efficacy was estimated from the comparison of adult height with predicted height at the beginning and end of treatment and/or adult height of historical, untreated patients, as well as the pace of bone maturation progression.

Data analysis demonstrated the efficacy of the various GnRHa formulations in halting BA progression, indicated by the statistically significant difference between BA and chronologic age at the end vs the beginning of treatment (Supplementary Table 1). The great majority of patients was female (female (F):male (M) = 947:90) and treated with triptorelin or leuprolide depot formulations administered monthly. Overall, the mean chronologic age at the start of treatment was 7.5 ± 1.2 years in females and 6.7 ± 1.5 years in males, with a mean BA of 10.3 ± 1.4 years in females and 10.6 ± 2.5 years in males. The mean chronological age at the end of treatment was 11.1 ± 0.9 years in females and 12.2 ± 1.8 years in boys, with a mean BA of 12.4 ± 0.7 and 13.6 ± 1.0 years respectively.

Mean adult height was significantly higher in treated patients than in untreated ones reported in an historical series adjusted for age at diagnosis (12, 13) (mean difference in adult height of 8.3 cm in girls and 13.7 cm in boys) (12) and in age- and sex-matched untreated study

controls (mean difference in adult height ranging from 3.3 to 8.9 cm) (12, 14, 15, 16).

The great majority of patients reached an adult height consistent with the TH (13, 14, 15, 17, 18, 19, 20, 21, 22, 23, 24, 25), a minority of them did not reach the TH (19, 26), and a very small portion of patients remained shorter than the predicted height before treatment (13, 27). Discordant results were obtained when comparing the efficacy of treatment in females and males. According to a study by Bajpai *et al.* (21), in patients treated with monthly triptorelin depot, mean HG was similar in females and males (mean HG: 6.4±2.4 cm vs 7.6±1.0 cm respectively). In contrast, Galluzzi *et al.* (13) reported a higher HG in boys (7.3±3.8 cm; $n=11$) than in girls (3.3±3.0 cm; $n=22$), with an achieved adult height SDS higher in the former than in the latter (0.13±0.91 vs −0.62±0.88; $P<0.001$). In general, HG was highly variable among studies depending on sample characteristics including the progression of pubertal development. Pubertal development was specified as rapidly progressing in some studies (17, 22, 24, 27, 28, 29), whereas in others pubertal progression was not detailed.

Several factors were postulated to influence the effects of GnRH treatment on statural growth. According to the majority of studies, earlier age at start of puberty (i.e. 5 years (15, 22)) and of treatment (i.e. 6 years (18, 20, 21, 23, 24, 25)) are associated with a taller adult stature. In a study by Klein *et al.* (24) performed in 98 patients (F:M=80:18) treated with histrelin or deslorelin, the average adult height and HG (14.5±9.9 cm vs 6.8±6.9 cm; $P<0.001$) were greater in girls with puberty onset <6 years of age than those with onset of puberty between 6 and 8 years of age. Few studies (12, 26) showed no correlation between HG and age at puberty onset or initiation of treatment, suggesting that girls with late onset CPP benefit from treatment similarly to girls with earlier pubertal onset (12). A longer treatment duration appears to be a positive outcome predictor in the majority (19, 20, 21, 24, 30), although not all (15, 23), of the studies, together with a short interval between pubertal onset and the start of treatment (24, 30), a great growth spurt after the end of treatment (12), low pre-treatment estradiol levels (30), and advanced BA at the start of treatment (14, 18, 19, 20, 21, 25). The impact of advanced BA at the start of treatment on adult height was not documented in the study by Brito *et al.* (30), whereas Carel *et al.* (12) found a negative association between the BA/statural age ratio at the onset of treatment and adult height suggesting that treatment is not capable of restoring a full adult height potential if started after an irreversible advancement of BA. This was also confirmed in a study by Kauli *et al.* (26) showing that therapy is more beneficial if started before BA exceeds 12 years.

Elevated height (or height SDS) before (16, 17, 19, 20, 24, 30) and at the withdrawal of treatment (12, 16, 17, 19, 20, 25, 30), as well as high TH (or TH-SDS) (17, 20, 21, 23, 30), has also been positively associated with adult height, supporting the primary influence of genetic factors in the determination of adult height even in patients treated with GnRHa (20).

Finally, BA at the end of treatment appears to be crucial on adult height, as it determines post-treatment growth potential (7). Indeed, the tallest heights were achieved by patients who stopped treatment at a BA of 12–12.5 years (20) or even <11.5 years (27), whereas continuing treatment after a BA ≥13 years negatively impacted on statural growth (20).

The efficacy of the various GnRHa in terms of HG appeared similar (24, 27, 31), except for a study (32) showing a higher adult height SDS in patients treated with leuprolide depot compared to triptorelin depot.

BMI and correlates of metabolic syndrome

Several studies reported an association between overweight and early/precocious puberty (5, 33) suggesting the involvement of various environmental, genetic, and biochemical factors (5, 7, 17, 34, 35) to explain this association. However, what remains to be clarified is whether it is the high BMI that results in precocious pubertal development or is it the latter that promotes the weight gain (33, 35).

Preliminary studies reported weight gain during treatment with GnRHa in patients with CPP, raising concerns for potential permanent obesity in adulthood (33, 35, 36). According to two independent studies (33, 37) analyzing normal-weight and overweight children separately, BMI–SDS during treatment increased in normal-weight children, whereas it remained stable in overweight subjects. The majority of long-term studies showed an increased prevalence of overweight and obesity in patients with CPP at diagnosis (22, 38), but no significant mean or individual BMI–SDS changes were shown at the end of treatment, irrespective of sex, age at puberty onset and at the start and discontinuation of treatment (15, 17, 22, 23, 24, 25, 30, 32, 39), and type of GnRHa (31). Recently, a study by Colmenares *et al.* (39) evaluated the effects of GnRHa in treated ($n=29$) and untreated ($n=8$) CPP patients and in treated ($n=14$) and untreated ($n=20$) rapidly progressing early puberty (EP), during a 3-year follow-up period. Treatment duration was ≥2 years.

At diagnosis, a higher BMI (*z*-score of 1.1±0.8 vs 0.6±0.7) and a higher prevalence of obesity/overweight (72.9% vs 35.3%) was observed in subjects with CPP when compared to those with EP. BMI *z*-score and obesity/overweight rates did not change significantly in girls with CPP or EP during 3 years of follow-up, regardless of treatment. Weight *z*-scores were higher at 3 years in treated than in untreated girls with CPP, while it was higher in untreated than in GnRHa-treated patients with EP at baseline, 1, 2, and 3 years. Both CPP- and EP-treated patients showed a reduction, although not statistically significant, in BMI *z*-scores and in obesity/overweight rate following treatment discontinuation, supporting the potential, although time limited, detrimental effect of GnRHa on weight. Indexes of glucose and lipid metabolism were in the normal range at diagnosis and remained unchanged during the follow-up period, independent of treatment.

Recently in a case–control study of a historical cohort, Lazar *et al.* (35) assessed the prevalence of obesity, the metabolic outcome (hyperlipidemia, diabetes, and hypertension), and the malignancy rate of former CPP GnRHa-treated and -untreated women between the third and fifth decades of life. The control group comprised women randomly matched for age, year of birth, and community clinic. Weight status of both GnRHa-treated and -untreated former CPP women resembled that of the general population from late adolescence to early-mid adulthood despite their above-average BMI at the onset of puberty. Permanent obesity was detected in women who were already obese in early childhood only. Moreover, weight gain of the treated CPP girls was not aggravated by GnRHa therapy. The incidence of obesity-related complications, such as metabolic dysfunctions and cancer comorbidities, were not increased in former CPP women, reassuring the health status of adult former CPP women.

Results from studies meeting inclusion criteria are summarized in Supplementary Table 2, see section on supplementary data given at the end of this article.

Reproductive function and risk of polycystic ovarian syndrome

The occurrence of menarche, or in some cases resumption of menses, after the discontinuation of either daily or long-acting GnRHa treatment was investigated by follow-up studies of girls in their late teens and women up to 56 years of age (Supplementary Table 3, see section on supplementary data given at the end of this article). The majority of the studies reported a 100% occurrence of menarche, with a few exceptions mostly related to CPP secondary to organic lesions such as hypothalamic hamartoma (40).

Spontaneous menses occurred 0–62 months after the end of treatment (mean 1.1±0.4 years); the mean duration of treatment varied widely among the studies, from 1 to 14 years. It was suggested that the longer time interval to menarche might be related to a longer duration of treatment and/or younger age at the start of therapy (40), but this hypothesis was not confirmed by other authors (41). Age at the discontinuation of treatment, BA, Tanner breast stage, or uterine development at the end of treatment, and the frequency of injections required to suppress the HPG axis function were all proposed as potential predictors of time interval to menarche, without consistency across studies. Interestingly, girls who had experienced menarche prior to GnRHa therapy showed a significantly shorter interval between the last injection and resumption of menses than those who had not experienced menarche before GnRHa treatment (~25 months vs 63 months) (19).

In the last decade, a subcutaneous hydrogel implant releasing histrelin continuously for at least 1 year has become available in the USA. Few reports of follow-up after histrelin implant treatment were published. Gillis *et al.* (31), evaluating a group of CPP patients treated with the monthly GnRHa and one with the histrelin implant showed that the mean time between the removal of the implant or last injection and menarche was shorter in the histrelin implant group. Fisher *et al.* (41) reported the resumption of puberty in 26 of the 30 girls treated with the histrelin implant, with occurrence of menarche 2–36 months after explantation in treatment-naïve and -non-naïve CPP girls, with an older age at explantation correlating with earlier menarche. In a recent study by Silverman *et al.* (43), menarche occurred in two patients, 9 and 2 months after the final explant respectively.

A great variability in the occurrence of regular ovarian cycles was so far reported in CPP-treated patients (44–96%; Supplementary Table 3), probably related to the heterogeneity of the study sample, type and duration of treatment, and follow-up. The highest prevalence of regular cycles (96%) was observed in 87 treated idiopathic-CPP girls during a 7-year follow-up period after the discontinuation of treatment (15). Jay *et al.* (43) described menstrual cycle lengths as becoming increasingly regular, from 41% in the first year post-menarche to 65% at 3 or more years post-menarche (44).

Fertility was reported to be normal in treated CPP girls, in contrast to the untreated ones. Supplementary Table 3 summarizes over 100 pregnancies reported in the

literature, with 97 uneventful pregnancies resulting in healthy children, five elective abortions, and 11 early miscarriages. In a recent study by Lazar *et al.* (45) assessing the reproductive outcome of former CPP women between the third and fifth decades of life, the frequency of pregnancy complications, such as early spontaneous abortion or pre-eclampsia, was comparable in the CPP women and controls. In the same study, spontaneous pregnancy was equally achieved by the treated CPP women and their control groups, while the percentage of women requiring ovulation induction and/or IVF was significantly higher in the untreated CPP group (33%) than in either the control (12.6%) or the CPP-treated groups (11.1%) (45). These findings suggest, according to the authors, a protective role for gonadotropin suppressive treatment on the reproductive outcome of CPP women.

PCO morphology detected by ultrasound (US) was reported in 0–37% of treated CPP girls (median 2%) (21, 36, 46, 47, 48, 49, 50, 51), with different lengths of post-treatment follow-up (up to 20 years), as summarized in Supplementary Table 4, see section on supplementary data given at the end of this article. Feuillan *et al.* (40) described the ovarian volume larger than normal at 4–5 years post-treatment, whereas another study including adult CPP-treated women showed the ovarian volume within normal range (52). Ovarian volume >10 ml was observed in 20% of CPP-treated patients (49, 50), a percentage similar to that found in age-matched, healthy controls (48). CPP patients with regular vs irregular menses showed no differences in the ovarian volume (22).

The development of signs and symptoms of polycystic ovarian syndrome (PCOS) in former CPP women is controversial. Data from the literature are limited, and the criteria used for PCOS diagnosis are not uniform among studies. While Heger *et al.* (22) observed a low incidence of PCOS (2%) based on Franks criteria, one study is supportive of the relationship between CPP and PCOS (48). In this cohort, which did not include a control group of untreated CPP girls, the prevalence of PCOS was 32% using the 2003 Rotterdam criteria and 30% using the Androgen Excess Society (AES) criteria. Moreover, the prevalence of hirsutism and biochemical hyperandrogenism was 23 and 48%, respectively, while irregular menses were present in 15% and PCO morphology in 37% of women. High prevalence of PCO morphology by US is also detected in normal young women (up to 33%) (53). Using the 1990 NIH criteria, Magiakou *et al.* (36) found that PCOS prevalence in CPP-treated young women was not different from that in the untreated ones (17.2 and 30.8% respectively), suggesting that GnRHa treatment does not predispose to PCOS development or menstrual irregularities.

Recently, in a large group of treated and untreated former CPP women aged 25–56 years, Lazar *et al.* (45) evaluated clinical signs potentially related to androgen excess, without performing hormonal assessment or imaging procedures. With these limitations, clinical signs of hyperandrogenism (acne/hirsutism with oligomenorrhea) were more frequent in CPP women than in controls with normal puberty matched for age and year of birth but not for BMI. The relative risk for the development of clinical hyperandrogenism with irregular menses was twofold higher in the untreated than the treated group. Moreover, among the treated women a small number had received cyproterone acetate with outcomes similar to those of GnRHa-treated women, suggesting that pubertal suppression itself may reduce the risk of PCOS rather than the kind of medical treatment. Study findings also suggest an association between CPP and ovarian dysfunction later in life, probably related to the underlying neuroendocrine dysfunction, manifesting as CPP and persisting into adult life. The reproductive outcome in early and mid adulthood was normal in the great majority of the patients studied. A high prevalence of fertility problems was present in the untreated CPP group only, suggesting that gonadotropin-suppressive therapy may have a protective effect on the reproductive outcome.

Limited data are available on the reproductive outcome of male patients treated for CPP (Supplementary Table 3). Three small studies showed normal gonadal function in former CPP male adolescents aged 15–18 years (19, 54, 55). Feuillan *et al.* (54) described a progressive increase in testicular volume, similar to controls after 2 years post-therapy, with normal gonadotropins and testosterone levels 1 year after the discontinuation of treatment. Bertelloni *et al.* (55) confirmed normal testicular function in adolescent boys after GnRHa therapy with full pubertal development and, normal testicular volume, gonadotropins, testosterone, and inhibin B levels into normal adult range. Even though paternity rates have not been reported, sperm analysis, performed in six patients, appeared normal for age (55). Following histrelin implant removal, a spontaneous increase in testicular volume was observed within 1 year of histrelin explantation in five boys with CPP (42).

Bone mineral density

Few studies assessed BMD in CPP during GnRHa treatment, showing minor or no changes in BMD parameters

(56, 57, 58). Boot *et al.* (56) found normal BMD for chronological age but decreased BMD for BA after 2 years of treatment with GnRHa.

Pasquino *et al.* (15) reported that both mean BMD lumbar spine and spine volumetric BMD at the discontinuation of treatment were significantly lower in treated CPP girls than in untreated controls. However, at the complete resumption of gonadal activity, both increased to levels similar to those detected in controls. In a more recent study, Magiakou *et al.* (36) showed BMD values adjusted for height were not different between GnRHa-treated and -untreated girls, evaluated at least 2 years after cessation of treatment. Alessandri *et al.* (59) evaluated bone mass, body composition, and bone remodeling in two groups of girls with idiopathic CPP, namely, one group assessed at diagnosis and a second group 3 years after GnRH agonist treatment. BMD and body composition were not affected by CPP, and GnRHa treatment did not seem to have a detrimental effect on the acquisition of bone mass. Heger *et al.* (22) described normal BMD for age in women after GnRHa treatment, with a 17% prevalence of osteopenia. In a small group of CPP-treated female adolescents, Bertelloni *et al.* (27) showed patients' BMD was not different from that of their mothers. In male patients, evaluated at adult height, BMD was similar to that found in a group of healthy young Italian men with normal pubertal development (55). The highest prevalence of osteopenia (45%) was observed by Tung *et al.* (60) in a small group of Taiwanese women, but a plausible explanation for the finding was not provided by the authors.

Conclusions

GnRHa therapy is efficacious in restoring the growth potential in the majority of children with CPP under the age of 6 years, although the estimate of HG is variable and difficult to assess because of sample heterogeneity, methodological limitations associated with height prediction, and the absence of randomized trials. Age at puberty onset, BA advancement, age at initiation, and duration of treatment are the most important outcome predictors, although their impact on adult height remains to be established. Above-average BMI is present at diagnosis at a high rate among children with CPP, but long-term GnRHa treatment does not appear to cause or aggravate obesity. Long-term data do not support adverse consequences of GnRHa therapy on BMD. Gonadal function is preserved after treatment cessation with normal reproductive potential. An association between CPP and ovarian dysfunction independent of GnRHa treatment was suggested, with a potential protective role of GnRHa therapy on the reproductive outcome. Data on the long-term risk of PCOS in CPP-treated and -untreated patients are conflicting although the majority of studies are not supportive of an association between GnRHa use and PCOS. Further studies to assess whether CPP has long-term implications on the general health status and the risk for premature ovarian failure and premature menopause in late reproductive years and to evaluate the impact of GnRHa therapy on the fertility, fecundity, and health of offspring are warranted.

Supplementary data

This is linked to the online version of the paper at http://dx.doi.org/10.1530/EJE-15-0590.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the review.

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Fertility of Women Treated during Childhood with Triptorelin (Depot Formulation) for Central Precocious Puberty: The PREFER Study

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Keywords
Fertility · Gonadotropin-releasing hormone analogue · Precocious puberty · Pregnancy · Triptorelin (depot formulation)

Abstract
Background: Gonadotropin-releasing hormone analogues (GnRHa) administered as depot formulations are the standard of care for children with central precocious puberty (CPP). Puberty resumes after treatment discontinuation, but little is known concerning fertility in women who have been treated with GnRHa for CPP during childhood. ***Methods:*** The PREFER (PREcocious puberty, FERtility) study prospectively analysed fertility, via a series of questionnaires, in women treated during childhood with triptorelin (depot formulation) for CPP. Co-primary endpoints were the proportion of women wanting a pregnancy any time before study inclusion and during the follow-up period but not pregnant 6 and 12 months after stopping contraception and the waiting time to pregnancy (WTP). ***Results:*** A total of 574 women were identified, and 194 women were included in the analysis. Although there were not enough data for primary endpoint assessment, few women (1.7%) reported issues with fertility or were unable to become pregnant despite trying to conceive. Most pregnancies (84.4%, 95% CI [67.2–94.7%]) occurred within 1 year of trying to conceive, in line with the WTP for women without previous CPP. ***Conclusion:*** The results, based on a limited sample of patients, suggest that CPP treated with triptorelin does not negatively impact women's fertility in adulthood. These results need to be consolidated with a subsequent study performed when these women will have reached their mid-thirties.

Introduction

Precocious puberty (PP) is generally defined as the appearance of the first signs of puberty (breast development in girls and testis enlargement in boys) before the age of 8 years for girls or 9 years for boys [1, 2]. PP can be sub-

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divided into gonadotropin-releasing hormone (GnRH)-dependent and -independent causes. GnRH-dependent PP, also called central precocious puberty (CPP), is due to the early activation of the hypothalamus-pituitary-gonadal axis [3]. Treatment with long-acting GnRH analogues (GnRHa) is the standard of care in children with CPP [4–12]. GnRHa desensitise the pituitary gonadotropic cells to GnRH [13] and decrease FSH and LH secretion and gonadal activation. Their short-term effects on pubertal development are well documented. Long-term effects have been reviewed, but their evaluation is limited by the lack of randomized controlled trials [5, 12].

Discontinuation of GnRHa results in the resumption of puberty [14–16] and in a short post-treatment growth spurt [17–21]. In girls, menarche occurs on average 1 year after treatment discontinuation [17, 22, 23]. There are relatively few data on gonadal function in adolescents and adult women who have been treated for CPP. An increased frequency of signs and symptoms of polycystic ovarian syndrome has been observed in women who had CPP, with potential consequences on fertility, but this remains controversial [5, 12].

The influence of CPP and/or its treatment on reproductive functions is an essential endpoint and is a frequent question asked by parents when GnRHa treatment is discussed. A review of the literature reported that among >100 pregnancies reported in 9 studies in women treated for CPP, there were 97 uneventful pregnancies resulting in healthy children, 5 elective abortions, and 11 early miscarriages [12]. Moreover, the rate of spontaneous pregnancy seems similar between women who have previously been treated with GnRHa for CPP (90.4%; n = 135) and women who did not have CPP during childhood (93.4%; n = 446) [24]. Nevertheless, few large-cohort studies have been published investigating the long-term impact of GnRHa treatment for CPP on fertility in women.

The PREFER (PREcocious puberty, FERtility) study prospectively analysed fertility in a large cohort of women treated during childhood with triptorelin (depot formulation) for CPP. The questionnaire-based study was conducted in France, and the results were compared to those of the general French population.

Methods

The PREFER study was a longitudinal, descriptive, non-comparative, epidemiological study of women treated during childhood with the GnRHa triptorelin (depot formulation; 28-day formulation [3 mg]) for CPP. The study was conducted in 27 centres in France between February 2007 and November 2009. Approval from the French Advisory Committee on the Processing of Information for Medical Research (CCTIRS) was received on June 21, 2006. Approval from the French Data Protection Authority (CNIL) was received on November 3, 2006. The study was carried out in accordance with the Declaration of Helsinki. Written informed consent was obtained from each participant before enrolment in the study.

Participants

Participants were women aged ≥18 years in 2006 (born in 1988 or earlier) who had been treated during childhood with triptorelin (depot formulation) for idiopathic CPP and had initiated triptorelin therapy between 1984 and 1996. Exclusion criteria were CPP secondary to a peripheral production of androgens or oestrogens (e.g., adrenal hyperplasia or gonadal disorder), CPP of neoplastic origin (except hamartomas), and chromosomal abnormality. Women with CPP associated with adoption were included in the study. Enrolling clinical centres identified potential participants by reviewing archives and checking clinical files against the study inclusion criteria to confirm eligibility.

Study Design

The PREFER study examined fertility in women retrospectively during the 2 years before inclusion and prospectively during a 12-month post-inclusion follow-up period. The primary objective was to analyse the fertility of women treated during childhood with triptorelin (monthly depot formulation) for CPP. Fertility was assessed via a series of questionnaires completed by the women. Secondary objectives were to assess the progress and outcome of any pregnancy, ovarian function and biometrics, concomitant description of fertility with the aetiology of PP and its treatment (duration of GnRHa therapy) or any other medical intervention that might have affected puberty (surgery and other additional treatments), and the socioeconomic consequences of CPP (academic level, relationship status, and occupation).

Assessments

A medical questionnaire was completed by participating centres to gather the following data: chronological age, bone age and Tanner stage at the time of diagnosis and treatment of CPP, GnRH stimulation test results, pelvic ultrasound results, and treatments used (GnRHa therapy and other additional treatments, if applicable). Women were contacted, and their agreement to participate was obtained with a signed informed consent form. Women who agreed to participate completed an inclusion questionnaire on their sociodemographic and fertility status. Follow-up questionnaires were sent to participants 6 months and 12 months after inclusion to assess fertility, pregnancy status, and the outcomes of any pregnancy (see online suppl. Table 1; see www.karger.com/doi/10.1159/000513702 for all online suppl. material).

Endpoints

Co-primary endpoints were the proportion of women desiring pregnancy any time before inclusion and during the follow-up period but not pregnant at 6 and 12 months and the waiting time to pregnancy (WTP: time between attempting to conceive and be-

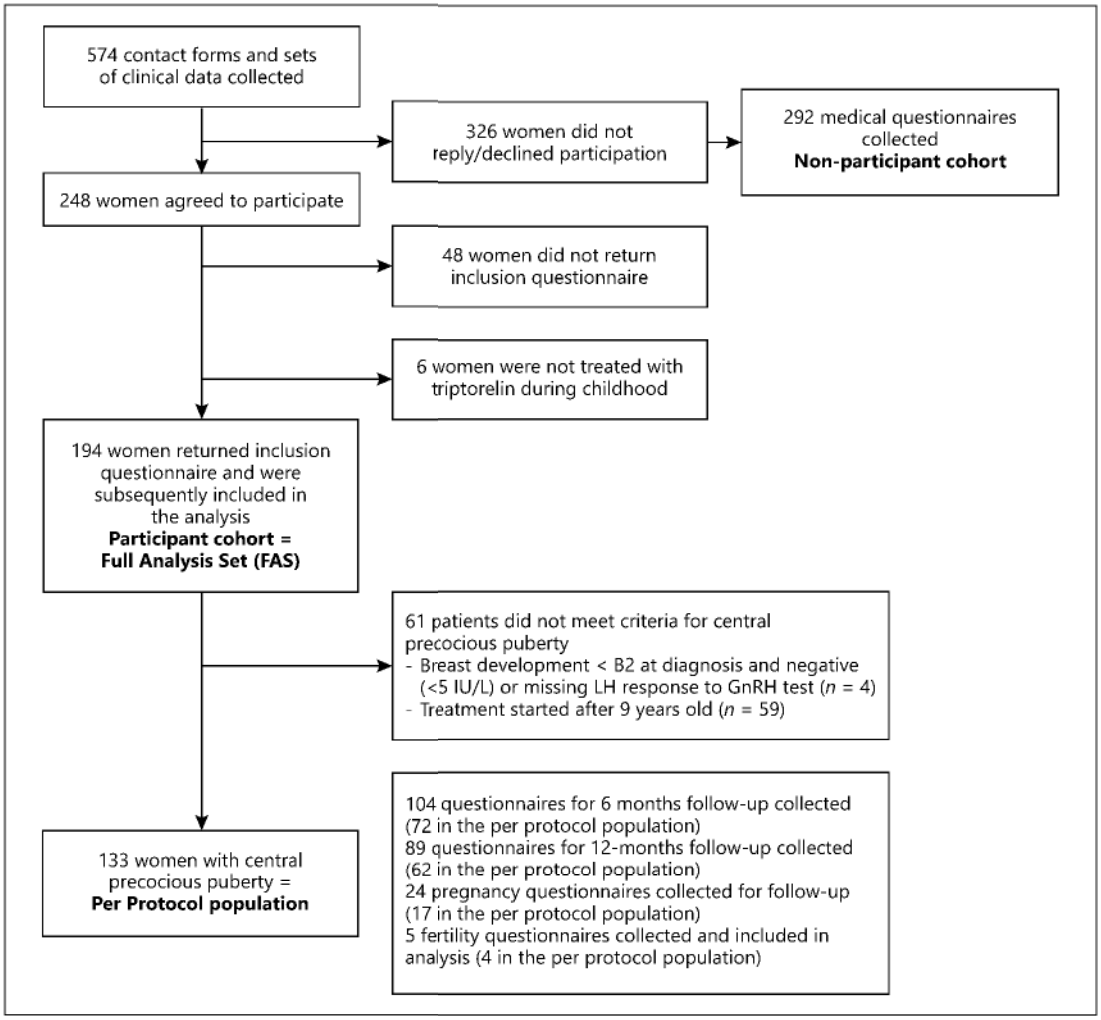


Fig. 1. PREFER study flowchart. FAS, full analysis set; GnRH, gonadotropin-releasing hormone; CPP, central precocious puberty.

coming pregnant) before inclusion. Secondary endpoints (collected at inclusion, 6 months, and 12 months) were the proportion of consultations for infertility or diagnosis of infertility (attempting to conceive for 1 year and no pregnancy or diagnosed during a consultation with a physician) during the 2 years prior to inclusion or during the follow-up period, proportion of unplanned pregnancies prior to the onset of the study, proportion of previous pregnancies and the difficulty in achieving them, proportion of spontaneous abortions and ectopic pregnancies, and the mode of delivery for pregnancies. Only the first pregnancy was considered for all endpoints. Other secondary endpoint data collected at inclusion were age at puberty (defined by onset of menarche), regularity and length of menstrual cycles and menstrual irregularities, current height, weight, and BMI, smoking status, academic level, occupation, and relationship status.

Sample Size and Statistical Analysis

The sample size needed to determine the 1-year pregnancy rate in women was 162. This was based on a 1-year pregnancy rate in the general population of 85% of women attempting pregnancy [25], with a 10% precision rate, an alpha risk of 0.05, and 15% loss of participants to follow-up. Taking into account the age distribution of mothers at the time they give birth [26] and the age distribution of women in France [27], it can be calculated that approximately 27% of women aged 18–30 years will give birth within a 3-year period. Based on these assumptions, a target of 597 patients was set for this study. Assuming that 60% of the patients contacted would be willing to participate (as shown in the feasibility study), 995 women treated for CPP needed to be contacted. Checks for population biases were performed by comparing data (height, weight, chronological age, statural age, bone age, Tanner stage, and proportion of patients with menses) at diagnosis and at the start and end of triptorelin treatment collected from partici-

Table 1. Clinical characteristics of PP in participants and non-participants

Variable	Participants				Non-participants	
	FAS population		per protocol population			
	mean ± SD (range)	*N*	mean ± SD (range)	*N*	mean ± SD*	*N*
Age at diagnosis of CPP, years	8.0±1.5 (1.5–11.3)	186	7.5±1.5 (1.5–9)	129	7.6±1.5	292
Age at initiation of triptorelin therapy, years	8.3±1.4 (1.5–11.3)	178	7.8±1.4 (1.5–9)	122	7.9±1.5	292
Height at initiation of triptorelin therapy, cm	132.7±9.3 (87.5–153.5)	182	130.9±9.8 (87.5–150)	124	132.6±10.7	292
Bone age at initiation of triptorelin therapy, years	10.2±1.5 (3.5–13)	162	9.8±1.6 (3.5–12)	109	10.1±1.6	292
Breast development at initiation of triptorelin (Tanner stage)		165		110		237
B1	2.4%	4	1.8%	2[S]	0%	0
B2	43%	71	37.3%	41	45.6%	108
B3	47.9%	79	55.5%	61	46.4%	110
B4–5	6.7%	11	5.4%	6	8.0%	19
Pubic hair development at initiation of triptorelin (Tanner stage)		173		118		249
P1	25.4%	44	27.1%	32	19.7%	49
P2	48%	83	49.2%	58	55.4%	138
P3	22%	38	21.2%	25	20.9%	52
P4–5	4.6%	8	2.5%	3	4.0%	10
Age at end of triptorelin therapy, years	10.6±0.9 (3.4–12.8)	177	10.4±1.0 (3.4–12.8)	121	10.3±1.2	292
Duration of triptorelin therapy, years	2.4±1.2 (0.5–8.6)	181	2.7±1.3 (0.5–8.6)	124	na	–
Bone age at the end of triptorelin treatment, years	11.7±1.0 (3.5–13.5)	165	11.7±1.1 (3.5–13.5)	111	11.4±1.1	292
Age at menarche, years	11.8±1.4 (7.0–16.0)	174	11.6±1.4 (7.0–16.0)	119	na	–

PP, precocious puberty; na, not available; CPP, central precocious puberty; FAS, full analysis set. * No range was available for the non-participants' data. [S] Two women with Tanner stage B1 were included since they had a peak LH level >5 IU/L.

pants' medical records and also from women who did not reply or declined participation in the study. Data from the questionnaires were entered into an electronic database. However, given the difficulties in retrieving old patient records and chart data, only minimal data monitoring could be performed. Qualitative variables were presented using number of missing data, frequency, and percentage; quantitative variables were presented using frequency of missing and non-missing values, mean, standard deviation, and range (minimum and maximum). Binomial 95% confidence intervals (CI) were computed for proportions. Statistical analysis was performed using SAS® software (v9.4). Inconsistent data were discarded. During the analysis, 2 population of patients were considered, a full analysis set (FAS) population including all participants and a per protocol population excluding patients who did not respect the criteria for CPP, in particular in terms of age at onset (initiating treatment after the age of 9 years, considering a maximum of 1 year between onset and start of treatment), pubertal development (absence of breast development), and GnRH test results (prepubertal) (Fig. 1). A clinical study report was produced in September 2015 and was the basis for an earlier version of this manuscript. However, during the review process, a number of inconsistencies in the analysis were highlighted. Therefore, data analysis was resumed in 2019–2020. The current manuscript and an updated version of the clinical study report are based on this new analysis of the data that had been collected in 2007–2009. The study was approved by the "Comité consultatif sur le traitement de l'information en matière de recherche dans le domaine de la santé" on July 21, 2006 (#06.118), and by the "Commission nationale de l'informatique et des libertés" on November 3, 2006 (#906229).

Results

Participants

Overall, 574 women meeting the inclusion criteria were identified at 27 centres in France between February 2007 and November 2009 (Fig. 1; Table 1). There were 3–97 women per centre and 248 accepted to participate (43%, 0–62% for each centre, median 41%), with a final cohort of 194 women included (FAS population) and 133 women in the per protocol population. The clinical characteristics of participants were very similar to those who did not participate (Table 1). The mean age of participants at study inclusion was approximately 24 years, and their self-reported social characteristics and gynaecological history are presented in Table 2. It is noteworthy that the mean height (162 cm) was close to the national average height (163 cm) [28], and that >50% of participants aged ≥25 years had completed full-length higher education programmes (online suppl. Table 2).

Table 2. Characteristics of participants at inclusion (FAS population and per protocol population)

Variable	FAS population		Per protocol population	
	mean ± SD (range)[a]	N[b]	mean ± SD (range)[a]	N[b]
Age at inclusion, years	24.3±3.0 (18.4–33.3)	187/194	24.3±3.1 (18.4–30.8)	128/133
Proportion with regular menstrual cycles, *n* (%)	126 (68.1)	185/194	86 (67.7)	127/133
Cycle length, days	28.4±1.7 (24–34)	86/126[c]	28.3±1.5 (26–33)	65/86[c]
Age at first sexual intercourse, years	17.5±2.2 (14.0–26.0)	167/173[d]	17.4±2.3 (14.0–26.0)	114/117[d]
Height, cm	161.6±6.1 (145.0–178.0)	188/194	161.9±6.3 (145–178)	128/133
Weight, kg	61.1±13.1 (40.0–147.0)	185/194	61.7±13.6 (43–147)	126/133
BMI, kg/m^2	23.4±4.8 (15.9–50.9)	184/194	23.5±4.8 (15.9–50.9)	125/133
Smoking status, *n* (%)		188/194		128/133
Current smoker	54 (28.7)		37 (28.9)	
Former smoker	23 (12.2)		9 (7.0)	
Non-smoker	111 (59.0)		82 (64.1)	
In a relationship, *n* (%)	123 (68.3)	180/194	81 (66.4)	122/133
Live together	79 (65.3)	121/123[e]	48 (60.8)	79/81[e]
Do not live together	42 (34.7)	121/123[e]	31 (39.2)	79/81[e]
Not in a relationship	57 (31.7)	180/194	41 (33.6)	122/133
Highest academic level, *n* (%)		194		133
None	5 (2.6)		3 (2.3)	
Completed only primary school	1 (0.5)		1 (0.8)	
Completed junior secondary school (up to 15 years)	12 (6.2)		10 (7.6)	
Completed technical college	15 (7.7)		12 (9.0)	
Completed secondary school (baccalaureate)	53 (27.3)		38 (28.6)	
Completed 2-year programme of university studies	28 (14.4)		20 (15.0)	
Achieved full-length university studies	80 (41.2)		49 (36.8)	
Occupation, *n* (%)		192		132
Employed	105 (54.7)		76 (57.6)	
Student or in training	67 (34.9)		44 (33.4)	
Housewife/not working	7 (3.6)		4 (3.0)	
Unemployed	13 (6.8)		8 (6.1)	
Professional category for those employed,[f] *n* (%)		124		87
Employee	78 (62.9)		55 (63.2)	
Senior executive	22 (17.7)		16 (18.4)	
Middle management employee	18 (14.5)		12 (13.8)	
Farmer	2 (1.6)		1 (1.1)	
Self-employed/freelancer	3 (2.4)		2 (2.3)	
Tradeswoman	1 (0.8)		1 (1.1)	

FAS, full analysis set; CPP, central precocious puberty; SD, standard deviation. [a] Unless otherwise stated. [b] Due to the nature of the study, data are not available for all participants for each parameter, and thus the number of participants for which the parameter was available is indicated. [c] Number of women with regular menstrual cycle. [d] Number of women that already had first sexual intercourse at study inclusion. [e] Number of women in a relationship. [f] Excludes participants who responded under professional category that they were students or unemployed.

Pregnancy

At inclusion, 142 women in the FAS population (97 in the per protocol population) had never been pregnant (Table 3). Of these women, 85.2% in the FAS population and 85.6% in the per protocol population declared they did not want to become pregnant, and 2.1 and 3.1%, respectively, declared that they had been unable to become pregnant. At inclusion, 43 women in the FAS population (31 in the per protocol population) declared they had been pregnant and 4/42 (9.5%) reported difficulties to conceive (3/30 [10.0%] in the per protocol population). These 43 women in the FAS population reported 62 past pregnancies (30 [69.8%] 1 pregnancy, 9 [20.9%] 2 pregnancies, and 4 [9.3%] 3 or 4 pregnancies). Similar numbers of pregnancies were observed in the per protocol population. During the study, primigravida pregnancies

Table 3. Participants' desire for pregnancy and pregnancy outcomes before inclusion in the study

Variable	FAS population (N = 194) n (%)	Per protocol population (N = 133) n (%)
Did not want to become pregnant	121/142[a] (85.2)	83/133[a] (85.6)
Unable to become pregnant	3/142[a] (2.1)	3/97[a] (3.1)
Women pregnant prior to inclusion, n	43/194 (22.2)	31/133 (23.3)
Pregnancies prior to inclusion, n	62	46
Wanted	22 (52.4)	16 (53.3)
Unexpected	16 (38.1)	11 (36.7)
Occurred despite using contraception	4 (9.5)	3 (10.0)
Data missing	1	1
Pregnancy outcomes for pregnancies before inclusion or ongoing at time of inclusion	45	32
Delivery	28[b] (62.2)	21[b] (65.6)
Elective abortion	13 (28.9)	8 (25.0)
Abortion for medical reasons[c]	3 (6.7)	2 (6.3)
Miscarriage	1 (2.2)	1 (3.1)

FAS, full analysis set. [a] Denominator is all women never having been pregnant at inclusion in the FAS/per protocol population. [b] Including 1 twin birth. [c] The high number of medical abortions is likely due to a misunderstanding of respondents with elective abortion.

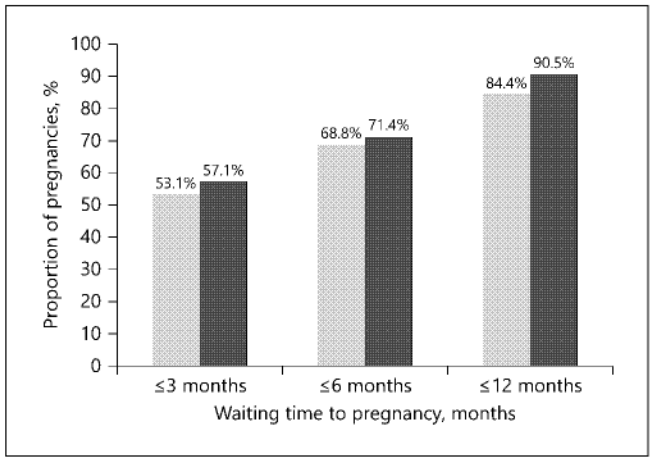


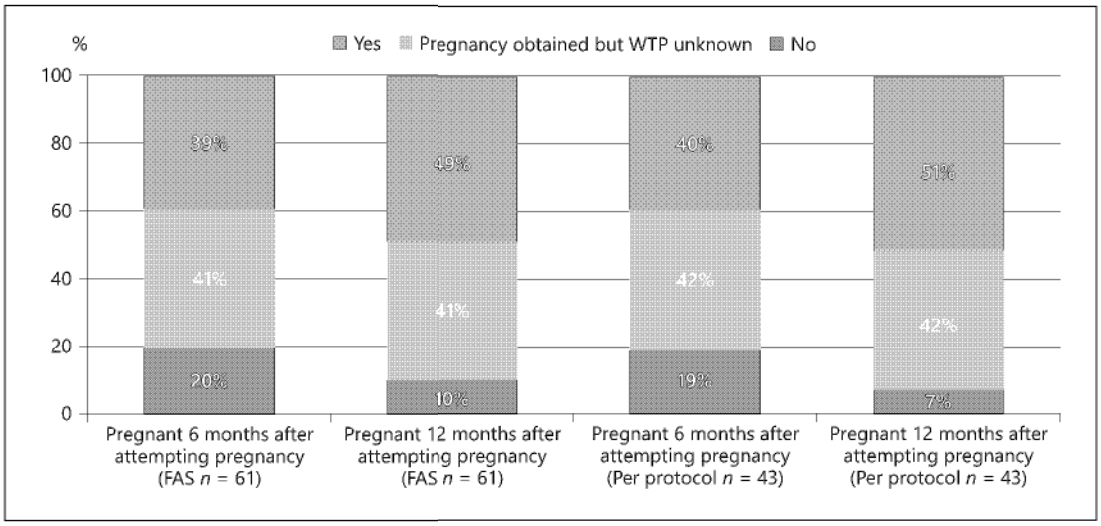
Fig. 2. WTP for pregnancies occurring before inclusion in the PREFER study. The proportion of women with various WTP is represented for the pregnancies with this information available in the FAS population (n = 32, black boxes) and in the per protocol population (n = 21, grey boxes). WTP, waiting time to pregnancy; FAS, full analysis set.

were reported by 6 women at inclusion, 4 at 6 months, and 2 at 12 months of follow-up in the FAS population. Therefore, at least 55/194 (28.4%) participants (37/133 [27.8%] in the per protocol population) had at least 1 pregnancy before or during study follow-up. WTP was available for 32 pregnancies that occurred prior to inclusion in the study and 21 pregnancies in the per protocol population and showed that a pregnancy was achieved within 12 months for 27/32 (84.4%) women (95% CI [67.2–94.7%]) in the FAS population and 19/21 (90.5%) women in the per protocol population (95% CI [69.6–98.8%]) (Fig. 2).

Fertility

At 6 and 12 months in the study, 78/92 (84.8%) and 66/73 (90.4%), respectively, of participants in the FAS population reported using contraception, therefore limiting the number of patients who were eligible for the infertility and pregnancy questionnaires. At inclusion in the study, among the women in the FAS population with available data, 1/132 (0.8%) reported having a fertility problem, 25/132 (18.9%) reported having no fertility problem, 35/132 (26.5%) did not know whether they had a fertility problem, and 71/132 (53.8%) felt that the question did not apply to them. Results were similar in the per protocol population. Three women had sought advice for infertility before participation in the study, 1 of whom had also reported having a fertility problem.

At 6 months and 12 months in the study, 5/85 (5.9%) and 0/52, respectively, of the participants in the FAS population had consulted a physician during the previous 6 months for difficulties in conceiving. Finally, among the women in the FAS population who had stopped contra-



Color version available online

Fig. 3. Proportion of women with pregnancy among those desiring pregnancy 6 and 12 months after having stopped contraception methods. The analysis was performed on women pregnant at least once or trying to get pregnant and having stopped all contraception methods. Modality "unknown" concerns women with unexpected pregnancies or missing dates to calculate WTP. All pregnancies or pregnancy attempts were considered including those before the study, at study inclusion, and at 6-month and 12-month follow-up. WTP, waiting time to pregnancy; FAS, full analysis set.

ception and were trying to conceive during the study, 12/61 (19.7%) and 6/61 (9.8%) were not pregnant after attempting pregnancy for 6 and 12 months, respectively (Fig. 3).

Discussion

In the PREFER study, few (1.7%) women reported problems with fertility or were unable to become pregnant despite trying to conceive. Most pregnancies (84.4%, 95% CI [67.2–94.7%]) in the PREFER study cohort occurred within 1 year of trying to conceive, and the 12-month WTP was similar to that previously published for women without CPP trying to conceive (~85%) [25, 29–31]. Most women who had not been pregnant up to the day of inclusion or during the study declared they did not want a pregnancy. Our results support those from previous studies in patients treated during childhood with GnRHa for CPP [24, 32, 33] and highlight the fact that fertility outcomes are better evaluated in women in their late 20s than mid-20s, given the median age of 28 years at first pregnancy in France 2007 (INED) [34].

The proportion of women who reported a fertility problem in our study (1.7%) was particularly low and needs to be compared with results from other similar studies and from the general population. Lazar et al. [24] reported higher prevalence of fertility problems of 11.1 and 10.9% of women who had received triptorelin treatment for CPP or early puberty, respectively. In the general population, an international review of 25 population surveys sampling 172,413 women reported a median prevalence of infertility of 9% [35]. In a US cross-sectional cohort study of 4,558 women, 623 (13.7%) and 328 (7.2%) reported seeking an infertility evaluation and undergoing subsequent infertility treatment, respectively [36]. The younger age of the population included in the PREFER study (mean 24 years) compared with the Lazar study (mean 33 years) could have contributed to these differences; moreover, fertility mostly declines after the age of 35 years [37].

Interestingly, the PREFER study participants had a higher level of education than expected in the general population, which possibly had an influence on the study results. Over half of the respondents who were 25 years or over had completed full-length higher education programmes, compared with only 18% of 25- to 49-year old women in the general population in France [38]. The proportion of women with an occupation was higher in the PREFER study than in the French general population. There were more senior management executives, employees, and students and less inactive persons in the PREFER study population than in the general population [38]. This may result from selection

biases, either from increased awareness of CPP in families with a higher level of education or from increased willingness to complete the questionnaire in those with a higher educational/professional status. In contrast, Lazar et al. [24] reported that the educational level of women with CPP (whether treated or untreated) was similar to that of the general population. In addition, early puberty in general (i.e., not associated with CPP per se) has been reported to detrimentally affect academic performance and subsequent academic achievement, including the lesser likelihood of pursuing a college education and the tendency to be employed in lower-paying, less prestigious jobs [39]. Although the design of the PREFER study does not allow us to explain why its patient population has such a high level of education, it is clear that this affects our analysis of fertility in this cohort, given the association between age at first pregnancy and level of education with a mean of 29 years for high versus 26 years for intermediate and 24 years for low educational levels in France [40].

The PREFER study has several limitations. The primary objective was to analyse prospectively the fertility of women treated during childhood with triptorelin (depot formulation) for CPP. However, once all the questionnaires had been collected, there were insufficient data to conclude on the primary endpoint (i.e., the proportion of women desiring a pregnancy but not pregnant 6 and 12 months after having stopped all contraception methods). Therefore, the proportion of women achieving pregnancy after 12 months (84.4%) was calculated on a small sample of 32 pregnancies leading to wide confidence intervals (95% CI [67.2–94.7%]). The design of the questionnaires also meant that certain parameters could not be fully documented (e.g., although data on total number of pregnancies were collected, most detailed information was collected on a maximum of 3 pregnancies per woman, but some women were pregnant >3 times). Consequently, some planned analyses could not be performed, and some aberrant values were discarded. Data that could not be presented were duration of pregnancy, distribution of birth weight and sex ratio, rate of preterm births and macrosomy, rate of stillbirths and birth defects, episodes of amenorrhoea or menstrual irregularities, acne and body hair, hormonal treatments initiated before or since puberty, hormone monitoring and abnormal hormone levels, characterisation of CPP, any episodes of triptorelin treatment suspension, and concomitant treatments.

In addition, a high proportion of patients declined to participate or did not respond to the invitation to participate. We were able to compare height, weight, chronological age, bone age, and Tanner stage at the time of diagnosis of CPP and at the beginning and end of treatment with triptorelin for the 292 non-participants and the 194 women included in the study. No statistically significant difference was found between participants and non-participants. While this suggests that there was no selection bias based on these parameters, the educational status of women differed, however, between the PREFER study cohort and populations in other studies and in the general population. This may have resulted from patient- or centre-selection bias. Nevertheless, the method of data collection in the PREFER study allowed a large cohort to be studied with the use of standardized questionnaires.

Conclusion

The PREFER study showed that the WTP and pregnancy rate for women treated during childhood with triptorelin (depot formulation) for CPP was consistent with that reported for the general population in France, although with a wide confidence interval. Women in the PREFER study cohort had a low prevalence of infertility. These results, based on a limited sample of patients, suggest that CPP treated during childhood with the GnRHa triptorelin does not negatively impact women's fertility in adulthood. Given the age profile of the PREFER cohort, these results need to be consolidated with a subsequent study performed 10 years later to assess, retrospectively, fertility and infertility rates when these women will have reached their mid-thirties.

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Statement of Ethics

The study was carried out in accordance with the Declaration of Helsinki. Written informed consent was obtained from each participant before enrolment in the study. Approval for use of medical records and data was obtained from the French Advisory Committee on the Processing of Information for Medical Research (CCTIRS) and the French Data Protection Authority (CNIL).

Conflict of Interest Statement

Jean-Claude Carel is a co-ordinating investigator for a study sponsored by Ipsen Pharma. Jacques de Mouzon had a contract as a scientific advisor for Ipsen Pharma, performed the statistical analyses, and created a study report for the initial PREFER study. Laetitia Martinerie has received lecture fees from Ipsen Pharma and has been invited by Ipsen Pharma to attend international scientific meetings. Joelle Blumberg, Luigi di Nicola, and Pascal Maisonobe are present or former employees of Ipsen Pharma.

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REVIEW ARTICLE

Gender dysphoria in childhood

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ABSTRACT

Gender dysphoria (GD) in childhood is a complex phenomenon characterized by clinically significant distress due to the incongruence between assigned gender at birth and experienced gender. The clinical presentation of children who present with gender identity issues can be highly variable; the psychosexual development and future psychosexual outcome can be unclear, and consensus about the best clinical practice is currently under debate.

In this paper a clinical picture is provided of children who are referred to gender identity clinics. The clinical criteria are described including what is known about the prevalence of childhood GD. In addition, an overview is presented of the literature on the psychological functioning of children with GD, the current knowledge on the psychosexual development and factors associated with the persistence of GD, and explanatory models for psychopathology in children with GD together with other co-existing problems that are characteristic for children referred for their gender. In light of this, currently used treatment and counselling approaches are summarized and discussed, including the integration of the literature detailed above.

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Gender identity; gender dysphoria; childhood; psychosexual development; persistence; treatment

Introduction

Children can vary in the extent to which they show gender role expressions, behaviours, interests, and preferences. For most children these expressions are largely congruent with their experience of being male or female – their gender identity – and in line with the gender assigned at birth. This is in contrast to children who experience gender dysphoria (GD). These children show extreme and enduring forms of gender nonconforming/gender variant behaviours, preferences, and interests because they do not identify with their birth-assigned gender. Because of the incongruence between their assigned gender and experienced gender, these children may experience clinically significant distress and are consequently often in need of clinical attention (American Psychiatric Association, 2013).

Although there has been much opposition against diagnosing GD in prepubescent children, primarily due to the stigmatizing effect of having a mental disorder (e.g. Drescher, 2013), the condition is included in the current edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) (American Psychiatric Association, 2013) as well as in the *International Classification of Diseases* (ICD-10; World Health Organization, 1992). The World Health Organization (WHO) is, however, in the process of revising the tenth version of the ICD; but instead of removal of the childhood diagnosis the terminology will most likely be changed from 'gender identity disorder of childhood' into 'gender incongruence of childhood' (Drescher, Cohen-Kettenis, & Winter, 2012).

According to the DSM-5, a diagnosis of GD of childhood can be made if a child experiences a marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by six out of eight criteria. One *sine qua non* criterion must be the experience of a strong desire to be of another gender or an insistence to be another gender. In addition to this, there are two criteria focusing on anatomic dysphoria; a dislike of one's sexual anatomy and the desire for primary/secondary sex characteristics of the experienced gender. In addition there are five behavioural criteria. The behavioural criteria concern the preference for cross-dressing; adopting cross-gender roles in fantasy play; a strong preference for toys, games and activities of the other gender; a preference for playmates of the other gender; and a strong aversion or rejection of typically gender congruent roles, interests, preferences and behaviours. Furthermore, the condition is associated with clinically

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significant distress or impairment in social, school, or other important areas of functioning (American Psychiatric Association, 2013).

Valid information on the prevalence of childhood GD is not available yet due to the absence of formal prevalence studies. An estimate of the prevalence of gender nonconforming/gender variant behaviours can, however, be made on the basis of studies where the Child Behavior Checklist (CBCL) (Achenbach & Edelbrock, 1983) was used. On the CBCL – a parent-report questionnaire on behavioural problems – two items are related to gender variance: Item 5 ('Behaves like opposite sex') and item 110 ('Wishes to be of opposite sex'). Information from the Dutch normative sample of the CBCL shows that in children, both items are more frequently endorsed by parents of girls than of boys; 'Behaves like opposite sex' in 2.6% of the boys and 5.0% of the girls, 'Wishes to be of opposite sex' in 1.4% of the boys and 2.0% of the girls (Verhulst, van der Ende, & Koot, 1996). These findings are in concordance with data from the normative sample of the CBCL in North-America (Achenbach & Edelbrock, 1981; Zucker, Bradley, & Sanikhani, 1997), and are largely replicated in a study of Dutch twins (N = 23,393) at ages 7 and 10 (Van Beijsterveldt, Hudziak, & Boomsma, 2006). Therefore, gender variance/gender nonconformity seems to be present in a small percentage of children and is more prominent in girls than in boys.

Interestingly, from what we know about the referrals to specialized gender identity clinics, the sex ratios for referred prepubescent children have always been in favour of natal men, which may be a direct effect of a difference in increased acceptance of masculinity in girls compared to femininity in boys (e.g. Blakemore, 2003; Cohen-Kettenis et al., 2003; Steensma et al., 2014; Wallien, Veenstra, Kreukels, & Cohen-Kettenis, 2010; Zucker, Wilson-Smith, Kurita, & Stern, 1995). Over the last decades the reported sex ratios have, however, gradually changed. For example, in the period before 2000 the ratio between boys and girls was 5.75:1 in Canada and 2.93:1 in the Netherlands (Cohen-Kettenis et al., 2003). In the period after 2000, the sex ratios decreased in Canada to 3.41:1 (2008–2011) for boys and girls respectively (Wood et al., 2013); and a similar pattern was observed in the Netherlands with a sex ratio of 1.68:1 between 2008 and 2011 (Steensma, 2013). For both countries this change in ratios is caused by fewer referrals of boys. Although empirical evidence is currently not available, the decrease of referrals in boys may indicate an increasing tolerance over time towards gender nonconforming behaviours in both countries.

Psychological functioning, social tolerance, and other co-existing problems

Besides the gender nonconforming presentation, children with GD who are referred to clinical settings have been shown to be more psychologically vulnerable in comparison to non-referred controls (Bates, Bentler, & Thompson, 1973, 1979) and in comparison to the general population (e.g. Cohen-Kettenis et al., 2003; Singh, Bradley, & Zucker, 2011; Steensma et al., 2014). Furthermore, these studies show that these psychological problems are more of an internalized nature (such as depression, social withdrawal, and anxiety), instead of an externalizing nature (such as aggression) (Bates et al., 1973, 1979; Coates & Person, 1985; Rekers & Morey, 1989; Zucker & Bradley, 1995; Cohen-Kettenis et al., 2003; Steensma et al., 2014). However, as Zucker, Wood, and VanderLaan (2014) recently concluded from their summary of studies reporting on the psychological functioning of gender-referred children, there is a considerable variability across the different studies. For example, the percentage of clinical-range cases reported in studies using the total behaviour problem score of the CBCL, ranged from 12.5% up to 84% of the described children over the different studies (for an overview see Zucker et al., 2014).

To understand this association between GD and the variability of psychological functioning within the population of children with GD, the empirical literature indicates the effect is largely mediated through social (in)tolerance towards gender nonconformity/gender variance. Indeed, a wide range of studies in children from the general population showed that gender nonconforming behaviour is often evaluated negatively by other children (e.g. Carter & McCloskey, 1984; Levy, Taylor, & Gelman, 1995; Ruble et al., 2007; Signorella, Bigler, & Liben, 1993; Stoddart & Turiel, 1985). Peer relations in general are therefore poorer for clinically referred children with GD than for non-referred children/youth (e.g. Cohen-Kettenis et al., 2003; Zucker et al., 1997, 2012); and, as we might expect, poor peer relations are associated with a negative well-being and poor psychological functioning in children with GD (e.g. Cohen-Kettenis et al. 2003; Steensma et al., 2014). Consequently the variability in psychological functioning detailed within the literature is likely inversely correlated with the intensity of social intolerance experienced by the children with GD. For example, a cross-national study between children referred for their gender from Canada and from the Netherlands showed a much higher prevalence of emotional and behavioural problems in the Canadian children than in the Dutch children. Interestingly, quality of peer relations rather

than IQ, parental social class, marital status, or ethnicity, turned out to be the strongest predictor in both countries. Furthermore, the quality of peer relations was lower in Canada than in the Netherlands. This indicates that psychological functioning is highly dependent upon how gender nonconformity is accepted within a certain culture or environment (Steensma et al., 2014).

However, this may not be the only factor that results in poorer psychological functioning. Over the years other models postulated in the literature focused, for example, upon generic risk factors for psychopathology and behavioural problems (such as parental psychopathology, social class background) in relation to GD; and considered them as an inherent cause of psychological problems in children with GD. Evidence for these relations is, however, still scarce and both models are under-studied in comparison to other factors such as social (in)tolerance (Zucker et al., 2014).

As far as co-occurring problems in children with GD are concerned, the relationship between Autistic Spectrum Disorders (ASD) and GD is important to mention. Although there are few studies investigating the relationship between the two, one study by de Vries, Noens, Cohen-Kettenis, van Berckelaer-Onnes, & Doreleijers (2010) showed that in a sample of 108 gender-referred children ASD was present in 6.4% of the children. This is significantly higher than the prevalence of 0.6–1% of ASD in the general population (Fombonne, 2005). Corresponding with these findings, a study by VanderLaan et al. (2015) of children referred for gender studied obsessional interests – which may be an indication of ASD – and showed that obsessions were more frequently reported by children referred for their gender in comparison with the general population. With regard to how ASD and GD are related, the question arises as to whether GD is an expression of ASD, or whether ASD is a symptom of GD; alternatively, of course, the two may be present without being related to each other (see van der Miessen et al., this issue).

Psychosexual development and related factors for persistence of GD

A central question in the counselling of children with GD is what their psychosexual outcome will be. Will the child grow up and identify as a gay man, lesbian woman, bisexual man or woman, or heterosexual man or woman without experiencing feelings of gender incongruence which require any intervention; or will the child need medical treatment in the future because the gender dysphoric feelings will persist and further intensify?

To date, there are 10 prospective follow-up studies described in the literature, together reporting on 317 gender nonconforming children who were followed-up in adolescence or early adulthood. The follow-up information in Zucker & Bradley (1995) is not included in this summary. In personal correspondence with Dr. Zucker it became clear that the 45 cases described are also included in the samples of Drummond, Bradley, Peterson-Badali, & Zucker (2008) (5 natal girls) and Singh (2012) (40 natal boys).

The conclusion from these studies is that childhood GD is strongly associated with a lesbian, gay, or bisexual outcome and that for the majority of the children (85.2%; 270 out of 317) the gender dysphoric feelings remitted around or after puberty (see Table 1).

However, there may be a number of arguments to nuance this high percentage of desistence. As is shown in Table 1 there is much variation in the reported persistence rates between the studies, ranging from 2% to 39%. Interestingly the studies before the year 2000 reported much lower persistence rates in comparison to the more recent studies after the year 2000. Furthermore, the persistence rates reported in two Canadian studies (Drummond et al., 2008; Singh, 2012) were identical (12%) but clearly lower in comparison to the follow-up study by Wallien & Cohen-Kettenis (2008) from the Netherlands. The explanation for these differences may be threefold:

First, the variation in intensity of GD in the children included differs across studies: The lower persistence rates in the earlier studies, compared to the more recent studies after 2000, may be the result of the inclusion of less extreme cases in the earlier studies than in later studies. For example, before the publication of DSM-III in 1980 there was no formal diagnosis of GD for children (Drescher, 2014). It could therefore be that the children included in the studies before 1980 would in retrospect not meet the full criteria for a diagnosis. Also, the recent

Table 1. Follow-up studies in children with GD.

Study	Sample	Age at follow-up (range)	Persistence rate
Bakwin (1968) Lebovitz (1972) Zuger (1984) Money & Russo (1979) Davenport (1986) Kosky (1987)	55 natal boys	(13–36)	9% (5 out of 55)
Green (1987)	44 natal boys	19 (14–24)	2% (1 out of 44)
Drummond et al. (2008)	25 natal girls	23 (15–37)	12% (3 out of 25)
Wallien & Cohen-Kettenis (2008)	40 natal boys 14 natal girls	19 (16–28)	39% (21 out of 54)
Singh (2012)	139 natal boys	21 (13–39)	12% (17 out of 139)

studies consisted of clinically referred samples of children, which was not the case for the earlier studies. For example, in the study by Green (1987) the sample of feminine boys was recruited through advertisement.

Secondly, and in line with the intensity explanation, there are possible cultural differences in referral: As described earlier, the sex ratios of child referrals in Canada are historically in greater favour of boys than girls as compared to the Netherlands. This may indicate that femininity in boys is experienced as more problematic in Canada –resulting in more referrals of boys with less extreme GD than in the Netherlands. As a result, the persistence rates are higher in the Netherlands compared to Canada.

Thirdly, we can consider the time of follow-up: As can be seen in Table 1, the time of follow-up differed across the studies and one could hypothesize that the studies with a later follow-up age (of older adolescents or adults) and those having a longer follow-up time, would report higher persistence rates than the studies where the follow-up took place at a younger age (i.e. shorter follow-up time). This trend is however not observed over the reported studies. To test this hypothesis, Steensma & Cohen-Kettenis (2015) recently published a report on the first 150 childhood cases from Amsterdam, the Netherlands, and checked whether a longer follow-up period would result in higher persistence rates. The children were at the time of first assessment – between 5 to 12 years old and between 19 to 38 years of age at the time of follow-up. Out of the 150 cases, 40 re-entered the clinic during adolescence (12–18 years of age) and turned out to be persisters (26.7%). However, after checking the files of the adult clinic (which sees nearly all adults with gender dysphoria in the Netherlands), it appeared that five individuals applied for treatment after the age of 18, raising the persistence rate to 30% and showing the importance of long-term follow-ups. Based on this information, it seems reasonable to conclude that the persistence of GD may well be higher than 15%. However, desistence of GD still seems to be the case in the majority of children with GD.

Two other clinically relevant questions are (1) whether we know anything with regard to the factors that are associated with the persistence or desistence of childhood GD and (2) how the process of persistence or desistence is experienced.

As to the factors associated with the persistence of GD, knowledge is still limited but fortunately slowly increasing. A central finding from all quantitative studies focusing on the topic is that the persistence of GD is most closely linked to the intensity of the GD in childhood and the amount of reported cross-gendered behaviour; in other words the more intense GD is in childhood, and the more cross-gendered behaviour is reported by parents or through self-report, the higher the chance that the GD persists (Drummond et al., 2008; Singh, 2012; Steensma, McGuire, Kreukels, Beekman, & Cohen-Kettenis, 2013; Wallien & Cohen-Kettenis, 2008). In addition to this, several other factors are linked to persistence of GD: For example, Steensma et al. (2013) and Wallien & Cohen-Kettenis (2008) showed that the persistence rate is generally higher in natal girls than in natal boys; And Steensma et al. (2013) and Singh (2012) found that the assessment age in childhood was higher in children where the GD persisted than for desisters; Further, Singh (2012) reported a higher social class in the parents of desisters compared to the parents of persisters.

In addition, Steensma et al. (2013) found that a social transition in childhood, especially in natal boys, and verbal identification with the desired/experienced gender was predictive for the persistence of GD. Interestingly, the identification finding was reported in an earlier qualitative study by Steensma, Biemond, de Boer & Cohen-Kettenis (2011) who observed differences in reported experiences of GD between persisters and desisters who were interviewed. For example, the persisters explicitly indicated that they felt they *were* the 'other' sex and the desisters indicated that they only *wished* they were the 'other' sex. The primary aim of the Steensma et al. (2011) study was to get a better understanding of the processes that contribute to the persistence and desistence of childhood GD. By interviewing adolescents (14 persisters, 11 desisters) who all fulfilled the DSM-IV or DSM-IV-TR criteria of a gender identity diagnosis in childhood (APA, 1994, 2000), it became clear that the period between 10 and 13 years was considered crucial. Both persisters and desisters stated that the changes in their social environment, the anticipated and actual feminization or masculinization of their bodies, and the first experiences of falling in love and sexual attraction in this period, contributed to an increase (in the persisters) or decrease (in the desisters) of their gender related interests, behaviours, and feelings of gender discomfort.

Treatment and counselling of children with GD

Over the last decade, the care for prepubescent children with GD has been rapidly changing and there is a growing number of specialized gender clinics for young people (Hsieh & Leininger, 2014; Khatchadourian, Ahmed, & Metzger, 2014; Riittakerttu, Sumia, Työläjärvi, & Lindberg, 2015). Best clinical practice in gender referred children is still controversial and raises debates among dedicated professionals. General agreement does, however, exist that the care for children with

GD should be focused on reducing the child's distress related to their GD; on help with other psychological difficulties; and optimizing psychological adjustment and wellbeing (e.g. Byne et al., 2012; Coleman et al., 2011). As for the counselling of the gender dysphoric feelings in children with GD; empirical treatment models do not exist and general consensus between clinicians is not always easy to obtain (Byne et al., 2012). In the current professional literature, three treatment models for the care of gender variant children can be distinguished (e.g. Byne et al., 2012; Drescher, 2013) and it is these to which we now turn.

The first approach focuses on working with the child and caregivers to lessen cross-gender behaviour and identification, to persuade the child that the 'right gender' is the one assigned at birth (Giordano, 2012), to decrease the likelihood that GD will persist into adolescence, and prevent adult transsexualism. Critics of this approach have linked it to 'reparative therapy', a term more commonly used to describe efforts to change same sex attraction to heterosexuality in gay adults or 'pre-homosexual' children (Drescher, 2013). In the past, such behavioural and psychodynamic therapies to lessen the GD have been largely used in children with GD with overall unsatisfactory results (Byne et al., 2012; Möller, Schreier, Li, & Romer, 2009). Instead, children often seem to become distressed if their preferences and/or behaviours are blocked (Richardson, 1999). At present, interventions aimed to lessen GD are referred to as unethical by the World Professional Association for Transgendered Health (WPATH: Coleman et al., 2011) and many other international professional organizations. The American Academy of Child & Adolescent Psychiatry, for example, has explicitly formulated their position against any psychological treatment aimed to change gender nonconforming behaviours (Adelson, 2012).

The second approach is focused on dealing with the potential social risks for the child (Byne et al., 2012). Because its aim is to allow the progress of the GD in the child to unfold in a natural way, it is often referred to as 'watchful waiting' (Drescher, 2013). Counselling based on this approach may include interventions that focus on the co-existing problems of the child and/or the family; helping parents and the child to bear the uncertainty of the child's psychosexual outcome; and providing psycho-education to help the child and the family to make balanced decisions regarding topics such as the child's coming out, early social transitioning, and/or how to handle peer rejection or social ostracism. In practice, the child and parents are encouraged to find a balance between an accepting and supportive attitude toward GD, while at the same time protecting the child against any negative reactions and remaining realistic about the chance that GD feelings may desist in the future. Parents are encouraged to provide enough space for their child to explore their gender dysphoric feelings, while at the same time keeping all future outcomes open (e.g., de Vries & Cohen-Kettenis, 2012; Di Ceglie, 1998, 2014).

The third approach is focused on affirming the child's (trans)gender identification and helps the child to build a positive self-identity and gender resilience. In particular, the child is supported in transitioning to the desired/experienced gender role. The rationale for supporting social transition before puberty is that children can revert to their originally assigned gender if necessary since the transition is solely at a social level and without medical intervention (e.g. Byne et al., 2012; Drescher, 2013; Hill, Menvielle, Sica, & Johnson, 2010). Critics of this approach believe that supporting gender transition in childhood may indeed be relieving for children with GD but question the effect on future development. The debate thereby focuses on whether a transition may increase the likelihood of persistence because, for example, a child may 'forget' how to live in the original gender role and therefore will no longer be able to feel the desire to change back; or that transitioned children may repress doubts about the transition out of fear that they have to go through the process of making their desire to socially (re)transition public for a second time (Steensma, 2013). The fact that transitioning for a second time can be difficult was indeed shown in the qualitative study by Steensma et al. (2011) where children who transitioned early in childhood reported a struggle with changing back to their original gender role when their feelings desisted, with the fear of being teased or excluded by their peers reported as the main reason for this.

Unfortunately, empirical answers about the best way to counsel children with GD and their caregivers are currently not available. The WPATH have therefore formulated a balanced position in their Standards of Care (Coleman et al., 2011), where clinicians are encouraged to help families by providing information about what is known about the development of children with GD and to help them to make decisions where the potential benefits and challenges of particular choices are weighted.

Conclusion

According to the DSM-5 diagnostic criteria for gender dysphoria, children with GD experience clinically significant distress because of the incongruence between their assigned gender at birth and experienced gender (APA, 2013). The clinical presentation of children who

present with gender identity issues is characterized by gender-nonconformity and a vulnerability to having psychological problems – primarily of an internalized nature (e.g. Cohen-Kettenis et al., 2003; Steensma et al., 2014), and an increased likelihood of ASD symptomatology (de Vries et al., 2010; VanderLaan et al., 2015). The extent and intensity of all three characteristics can be variable.

When considering the development of children with GD; studies show that gender dysphoric feelings eventually desist for the majority of children with GD, and that their psychosexual outcome is strongly associated with a lesbian, gay, or bisexual sexuality which does not require any medical intervention, instead of an outcome where medical intervention is required (e.g. Drummond et al., 2008; Wallien & Cohen-Kettenis, 2008; Singh, 2012). Factors predictive for the persistence of GD have been identified on a group level, with higher intensity of GD in childhood identified as the strongest predictor for a future gender dysphoric outcome (Steensma et al., 2013). The predictive value of the identified factors for persistence are, however, on an individual level less clear cut, and the clinical utility of currently identified factors is low.

Taken together this shows that there can be a great variability with regard to presentation of children with GD and their psychosexual outcome. The counselling of children with GD can therefore be complex and clinically challenging. To date, there is general agreement that the care for children with GD should not be aimed at avoiding adult same sex attraction or transsexualism; that no medical intervention should be provided in childhood (before puberty); that counselling should therefore be focused on reducing the child's distress related to the GD, on help with other psychological difficulties, and on optimizing psychological adjustment and wellbeing (e.g. Byne et al., 2012; Coleman et al., 2011).

However, besides these basic clinical values, there is currently no general consensus about the best approach to dealing with the (uncertain) future development of children with GD, and making decisions that may influence the functioning and/or development of the child – such as a social transition. Different clinical approaches are presented in the literature, and indeed taking the variability in presentation of children with GD into account, it seems important to underline that a 'one size fits all' approach is not best practice for children with GD. Therefore, different kinds of treatment options should be available which respect the unique needs of every child. In particular, the child's clinical psychological profile and gender development, as well as the contextual psychosocial characteristics of the child's family (e.g. belief system, supportive behaviours, access to health care) should always be taken into account in order to make balanced decisions. Currently, the limited empirical evidence in favour of a particular treatment makes treatment of teenagers with GD a controversial issue that raises intense, and often polarized, debate. Therefore, studies comparing different psychological treatment options are needed as well as research which aims to identify the factors involved in the persistence process of GD on an individual level. The primary goal is therefore to determine the safest and most efficacious mental and medical approach for the individual child with GD.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Gender Identity 5 Years After Social Transition

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abstract

BACKGROUND AND OBJECTIVES: Concerns about early childhood social transitions among transgender youth include that these youth may later change their gender identification (ie, retransition), a process that could be distressing. The current study aimed to provide the first estimate of retransitioning and to report the current gender identities of youth an average of 5 years after their initial social transitions.

METHODS: The current study examined the rate of retransition and current gender identities of 317 initially transgender youth (208 transgender girls, 109 transgender boys; $M = 8.1$ years at start of study) participating in a longitudinal study, the Trans Youth Project. Data were reported by youth and their parents through in-person or online visits or via e-mail or phone correspondence.

RESULTS: We found that an average of 5 years after their initial social transition, 7.3% of youth had retransitioned at least once. At the end of this period, most youth identified as binary transgender youth (94%), including 1.3% who retransitioned to another identity before returning to their binary transgender identity. A total of 2.5% of youth identified as cisgender and 3.5% as nonbinary. Later cisgender identities were more common among youth whose initial social transition occurred before age 6 years; their retransitions often occurred before age 10 years.

CONCLUSIONS: These results suggest that retransitions are infrequent. More commonly, transgender youth who socially transitioned at early ages continued to identify that way. Nonetheless, understanding retransitions is crucial for clinicians and families to help make retransitions as smooth as possible for youth.

Increasing numbers of children are socially transitioning to live in line with their gender identity, rather than the gender assumed by their sex at birth, a process that typically involves changing a child's pronouns, first name, hairstyle, and clothing.

identity may be more stable after this period for youth who show early gender nonconformity.[3]

Other clinicians argue that early social transitions can be beneficial for some gender-diverse youth.[4–6]

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Dr Olson conceptualized the current study, supervised data collection, carried out the initial analyses, and drafted the initial manuscript. Dr Durwood and Dr Devor conceptualized the current study and provided extensive revisions on the manuscript. Ms Horton acquired and compiled the data and tables and provided feedback on the manuscript. Dr Gallagher acquired, compiled, and analyzed the data and provided feedback on the manuscript. All authors approved the manuscript as submitted and agree to be accountable for all aspects of the work.

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who socially transition in childhood and then go on to retransition afterward. One paper included 4 youth who socially transitioned; none of them had retransitioned 7 years later.[10] We know of 3 mentions of early-transitioning youth who retransition.[8,9] However, these papers include no mention of how many other youth the same clinical team saw who did not retransition, making it impossible to guess a retransition rate.

In the present paper, we aimed to compute an estimate of retransition among a cohort of more than 300 early-transitioning children. Here, we report the retransition rate an average of 5 years after initial (binary) social transition, as well as how many of these participants are living as binary transgender youth, nonbinary youth, and cisgender youth at the same timepoint.

METHODS

A total of 317 binary socially transitioned transgender children (M_{age} = 8.07; SD = 2.36; 208 initially transgender girls, 109 initially transgender boys; see Table 1 for additional demographics) joined this longitudinal study (The Trans Youth Project) between July 2013 and December 2017. For inclusion in The Trans Youth Project, children had to be between 3 and 12 years of age and had to have made a "complete" binary social transition,[10] including changing their pronouns to the binary gender pronouns that differed from those used at their births.

As part of the larger longitudinal study, parents and youth were regularly asked about whether they had begun using puberty blockers and/or gender-affirming hormones. At most visits, they were not asked about whether puberty had begun, though our available data suggests that because these youth had socially transitioned at such early ages, most participants were followed by an endocrinologist well before puberty began. The endocrinologists helped families identify the onset of Tanner 2 (the first stage of puberty) and prescribed puberty blockers within a few months of this time; therefore, the onset of puberty blockers is used as our proxy for the onset of puberty in youth who received blockers. Of the youth in this sample, 37 (11.7%) had begun puberty blockers before beginning this study.

This study did not assess whether participants met criteria for the Diagnostic and Statistical Manual of Mental Disorders, Fifth edition, diagnosis of gender dysphoria in children. Many parents in this study did not believe that such diagnoses were either ethical or useful, even if they had been diagnosed, and some children did not experience the required distress criterion after transitioning. Based on data collected at their initial visit, these participants showed signs of gender identification and gender-typed preferences commonly associated with their gender, not their sex assigned at birth.[11] Further, parent report using the Gender Identity Questionnaire for Children[12] indicated that youth showed significant "cross-sex" identification and preferences (when scored based on sex at birth).[12]

Final identity classification for these analyses was based on our most recent interaction with the child and/or their parent before January 1, 2021. Because some families have not participated recently, we also separately report (Table 2) the results of the n = 291 youth with whom the research team had an interaction within the 2 years before that deadline. This additional analysis allows us to assess whether those who retransitioned were more likely to have missed their more recent appointments with our team. Importantly, only 1 of the 26 families with whom we did not meet in the past 2 years has formally dropped out of the study; the others often did not complete participation during these 2 years because of personal circumstances at the time we attempted re-recruitment. We anticipate that many in this group will participate again in the future.

TABLE 1 Participant Demographics (N = 317)

Demographics	%
Race	
White, non-Hispanic	69
White, Hispanic	9
Black	2
Asian	3
Native American	<1
Multiracial	17
Annual household income, $	
<25 000	3
25 001–50 000	10
50 001–75 000	21
75 001–125 000	31
>125 000	35
Location	
Northeast	15
Midwest/Upper Plains	21
Southeast	15
Mountain West	13
Pacific Northwest	20
Pacific South	16

Based on pronouns at follow-up, participants were classified as binary transgender (pronouns associated with the other binary assigned sex), nonbinary (they/them pronouns or, n = 3, a mix of they/them and binary pronouns), or cisgender (pronouns associated with their assigned sex). We confirmed this classification by reviewing other information available to the research team (eg, child's self-categorization in an interview or survey, e-mail communications with the parents). Only 1 classification was debatable; this participant was classified by pronouns (and in this paper) as nonbinary but could have been

TABLE 2 Participant Information and Current Identity at Last Visit Before January 1, 2021, Overall, for Those With Recent Visits Only, and by Initial Social Transition and Gender

	Total Sample	Recent Sample (With Visits in 2019 or 2020)	Sample Who Initially Socially Transitioned Before Age 6	Sample Who Initially Socially Transitioned at Age 6 or Later	Transgender Girls (At Recruitment)	Transgender Boys (At Recruitment)
Sample size	317	291	124	193	208	109
Assigned male at birth, %	65.6	65.3	73.4	60.6	100	0
Mean age at first transition, y	6.5	6.4	4.3	7.9	6.2	7.1
Mean age at start of study, y	8.1	8.0	5.9	9.5	7.7	8.7
Average time since start of study, y	3.8	4.1	3.8	3.8	3.9	3.7
Average time since first transition, y	5.4	5.7	5.4	5.4	5.5	5.3
Current identity, *n* (%)						
Binary transgender	298 (94.0)	276 (94.8)	112 (90.3)	186 (96.4)	194 (93.3)	104 (95.4)
Cisgender	8 (2.5)	6 (2.1)	7 (5.6)	1 (0.5)	7 (3.40)	1 (0.9)
Nonbinary	11 (3.5)	9 (3.1)	5 (4.0)	6 (3.1)	7 (3.40)	4 (3.7)

classified as binary transgender (and not retransitioned).

This study has been approved by the University of Washington and Princeton University institutional review boards.

RESULTS

The overall rate of retransition was 7.3%. An average of 5.37 years (SD = 1.74 years) after their initial binary social transition, most participants were living as binary transgender youth (94.0%; Table 2). Included in this group were 4 individuals (1.3% of the total sample) who retransitioned twice (to nonbinary then back to binary transgender). Some youth (3.5%) were currently living as nonbinary, including one who had retransitioned first to cisgender then to nonbinary. Finally, 2.5% were using pronouns associated with their sex at birth and could be categorized as cisgender at the time of data collection, including one who first retransitioned to live as nonbinary. Similar percentages were observed when examining the 291 youth who were in touch with the research team in the past 2 years (Table 2), when examining only those 280 youth who had not begun puberty blockers at the start of the study (Table 3), or if we examine only the 200 youth who had gone at least 5 years since their initial transition (Table 3).

We observed 1 potential (post hoc) age effect. Youth who initially socially transitioned before age 6 (n = 124), were more likely to be living as cisgender (n = 7; 5.6%) than youth who transitioned at age 6 or later (n = 1 of 193; 0.5%), Fisher exact test (comparing binary, cisgender, nonbinary; before vs. age 6 years or later), P = .02, although low rates of retransition were seen in both groups. In Table 2, we also report the results separately for children assigned male versus female at birth; this distinction was not significantly associated with later identity, P = .47, Fisher exact test. Finally, for exploratory purposes, in Table 3, we report outcomes separately for several subsets of our participants, including youth who had started puberty blockers, youth who had used puberty blockers and gender-affirming hormones, and youth who are at least 14 years old (the age at which past work[3] has suggested retransitions will be less likely).

DISCUSSION

Five years after an initial binary social transition, 7% of youth had retransitioned at least once. Most youth (94%) were living as binary transgender youth at the time of data analysis, including 1.3% who retransitioned initially to cisgender or nonbinary and then retransitioned back to binary trans identities. A small number of youth were living as cisgender youth (2.5%) or nonbinary youth (3.5%). We observed comparable rates when examining all participants who began the study (n = 317), those who had been in touch with the research team in the last two years (n = 291), those who had gone at least 5 years since initial social transition (n = 200), and

TABLE 3 Participant Information and Current Identity at Last Visit Before January 1, 2021, as a Function of Stages of Medical Transition and/or Age

	Total Sample	Sample of Youth Who Had Not Begun Blockers at Start of the Study	Sample of Youth Who Have Begun Blockers (and Not Gender-Affirming Hormones) at the End of the Study	Sample of Youth Who Have Begun Gender-Affirming Hormones at the End of the study	Sample of Youth 5+ y of Age Since Initial Binary Social Transition	Sample of Youth Who Are Currently 14+ y of Age
Sample size	317	280	92	98	200	70
Assigned male at birth, %	65.6	69.6	57.6	58.2	69.0	52.9
Mean age at first transition, y	6.5	6.1	6.6	8.4	6.2	8.9
Mean age at start of study, y	8.1	7.6	8.3	10.2	8.0	10.8
Average time since start of study, y	3.8	3.9	4	4.3	4.5	4.4
Average time since first transition	5.4	5.5	5.8	6.1	6.4	6.3
Current identity						
Binary transgender	$n = 298$; 94.0%	$n = 263$; 93.9%	$n = 88$; 95.7%	$n = 97$; 99.0%	$n = 190$; 95.0%	$n = 69$; 98.6%
Cisgender	$n = 8$; 2.5%	$n = 8$; 2.9%	$n = 1$; 1.1%	$n = 0$	$n = 4$; 2.0%	$n = 1$; 1.4%
Nonbinary	$n = 11$; 3.5%	$n = 9$; 3.2%	$n = 3$; 3.3%	$n = 1$, 1.0%	$n = 6$; 3.0%	$n = 0$

those who started the study before beginning puberty blockers ($n = 280$). We found no differences as a function of participant sex at birth. We observed slightly higher rates of retransition, and particularly later cisgender identity, among youth who initially socially transitioned before age 6 years. However, even in these youth, retransition rates were very low.

Among those who had begun puberty blockers and/or gender-affirming hormones, only 1 had retransitioned to live as cisgender (and this youth had begun blockers, but not gender-affirming hormones). One likely reason so few retransitions to cisgender occurred among those accessing medical transition is that most retransitioning in this cohort happened at early ages. All but 1 of the 8 cisgender youth had retransitioned by age 9 years (the last retransition was at age 11 years). Some of these youth are still not eligible for blockers because they are still prepubertal; we anticipate that those who identify as cisgender are unlikely to seek blockers or hormones, but that the participants who have not begun puberty and who identify as binary transgender or nonbinary likely will.

Past work has suggested that the ages 10 to 13 years are an especially critical time for retransition.[3] In our sample, many of the youth who retransitioned did so before that time frame, particularly the cisgender youth. In the nonbinary group, however, 6 of 11 retransitioned between ages 10 and 13 years, with the remainder retransitioning before age 10. Importantly, our sample differed from the past work on which this age range was determined in several key ways, including that our participants socially transitioned at earlier ages (perhaps pushing retransitions earlier, too), had undergone complete social transitions including pronouns and names (not just hairstyle and clothing changes as in most cases in previous studies[3]), and are living at a different historic time in a different country. Any, or all, of these may turn out to be key differences related to age of retransition.

Our observed low retransition rate is consistent with a study in which 4 youth who had completely socially transitioned had not retransitioned 7 years later.[10] That finding is in the same ballpark as our study's estimate of ~2.5% if we examine the percentage living as cisgender at the end of the study (ie, those "desisting" from gender-diverse outcomes). Together, these papers suggest this outcome is relatively rare in this group.

Our observation that few youth who have begun medical intervention have retransitioned to live as cisgender is consistent with findings in the literature. Several studies reporting on outcomes among transgender youth receiving blockers and gender-affirming hormones have reported relatively low rates of regret or stopping treatment,[13] which are potential indicators of retransition, though stopping treatment can occur for other reasons as well (eg, side

effects), as can regret (eg, experiences of transphobia).

Our key finding, that there was a relatively low rate of retransition about 5 years after initial social transition, may, on the surface, appear contradictory with past clinic-based research on what is sometimes called persistence and desistence[3] of childhood gender dysphoria. Several large studies attempted to recontact adolescents and adults who had previously been evaluated for gender dysphoria in childhood.[14–17] Many of those were formally diagnosed with what was, at the time, called gender identity disorder. Those studies reported that a minority of youth later identified in a way that might indicate a transgender identity by today's definition.

Interpretation of those results, and especially comparison with the present work, is difficult for several reasons. First, in past studies, when asked "are you a boy or a girl?" about 90% of the children supplied answers that aligned with their sex at birth,[18] leading some to question whether the majority of those children were the equivalent of transgender children today or not.[19–21] Second, participants in those studies were children between the 1960s and the 1990s, and many features of society have changed since then, including greater rates of acceptance and acknowledgment of transgender identities. Third, the parents of the youth in the current study support their children's identities, as indicated by their approval of their social transitions, whereas many of the parents of youth in past studies explicitly discouraged gender nonconformity or "cross-gender" identification.[15,22] In addition, it would have been exceedingly rare for youth in those studies to socially transition, especially completely.[1,10] Finally, there were substantial drop-out rates in all of the previous studies,[14,15,17] making the true estimates of persistence or desistence difficult to obtain.[19,21] Because there are so many possible contributors to differences in rates of persistence (in past work) and retransition in the current work, we urge caution about overinterpreting differences, or overconfidence about which contributing factors explain the differences.

There are also some reasons why we might have had such a low retransition rate. First, on average, participants had socially transitioned 1.6 years before joining our study. It is possible that some youth initially try socially transitioning and then change their minds quickly. Such youth would be unlikely to be enrolled in this study because their eligibility period would have been quite short and therefore the odds of finding the study and completing it would have been low. This means the children in our study may have been especially unlikely, compared with all children who transition, to retransition because they had already lived and presumably been fairly content with that initial transition for more than a year. Second, it is possible that families who failed to participate in the past 2 years of our study ($n = 26$) were disproportionately those whose children retransitioned and who were therefore hesitant to participate again. If true, their exclusion could have reduced our retransition rate. We are skeptical of this possibility for a few reasons. First, 4 of these participants did retransition and had told us about that outcome, so it does not appear that hesitancy in telling us was widespread in this group. Second, many of these families continue to be in touch with our research team and only missed participation because of ongoing personal issues (eg, COVID-19, emergency family circumstances). We anticipate that most of these families will be able to participate as we continue to follow these youth. Finally, from the beginning of the study, the research team has been clear in discussing with the families that we are open to any outcome in their youth.

As with past work, the present work has several key limitations. First, this is a volunteer community sample, meaning there could be biases in the kinds of families who sign up to participate. We know, for example, that unlike many samples of transgender youth, this sample of youth have normative levels of depression and only slight elevations in anxiety.[23] The parents of the participants in this study are disproportionately higher income and went to college at higher rates than the general population. We do not know whether these potential biases in the sample reflect biases in the cohort of children who socially transitioned in the mid-2010s in the United States and Canada. Therefore, whether the results generalize to youth without these characteristics is unknown.

Another potential limitation is that we used pronouns as the criterion for retransitions. Not everyone who, for example, uses they/them pronouns identifies as nonbinary and someone might identify as transgender even if they are currently using pronouns associated with their sex at birth. However, examination of other data provided by families suggests that our pronoun-based criteria were largely consistent with classification that would have arisen from other types of information provided to the research team (eg, labels used in an interview). Only 1 of the youth categorized as "retransitioned" might, by some other criteria, not meet that definition. However, because pronouns were the initial

inclusion criterion (that is, to be in the study children had to be using pronouns not associated with their sex at birth), they were the most consistent route of classification.

A related potential concern with these analyses is that we classified a change from using, for example, binary transgender to nonbinary as a retransition. Not everyone would categorize this change as a retransition. Many nonbinary people consider themselves to be transgender.[24] If we had used a stricter criterion of retransition, more similar to the common use of terms like detransition or desistence, referring only to youth who are living as cisgender, then our retransition rate would have been lower (2.5%).

One additional limitation in the present work is that the initial sample was disproportionately made up of trans girls. This is counter to recent reports that more peri- and postpubertal transgender youth seeking clinical services recently are transmasculine.[25–27] Historically, and consistent with our data, samples of parent-identified prepubertal gender nonconforming youth have included more assigned males at birth.[15,16,22] Importantly, we did not observe a significant gender effect in terms of rates of retransition, so we do not predict any change in pattern of results if we had a different ratio of participants by sex at birth.

We anticipate continuing to follow this cohort into adolescence and adulthood. This continued follow-up is necessary because it is possible that as more youth move into adolescence and adulthood, their identities could change. As we already saw, some youth will retransition more than once, so the present identities should not be interpreted as final.

As more youth are coming out and being supported in their transitions early in development, it is increasingly critical that clinicians understand the experiences of this cohort and not make assumptions about them as a function of older data from youth who lived under different circumstances. Though we can never predict the exact gender trajectory of any child, these data suggest that many youth who identify as transgender early, and are supported through a social transition, will continue to identify as transgender 5 years after initial social transition. These results also suggest that retransitions to one's gender assumed at birth (cisgender) might be likely to occur before age 10 years among those who socially transition at the earliest ages (before age 6 years), though retransitions are still unlikely in this group. These data suggest that parents and clinicians should be informed that not all youth will continue the same trajectory over time. Further understanding of how to support youth's initial and later transitions is needed.

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ORIGINAL RESEARCH—INTERSEX AND GENDER IDENTITY DISORDERS

Puberty Suppression in Adolescents With Gender Identity Disorder: A Prospective Follow-Up Study

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ABSTRACT

Introduction. Puberty suppression by means of gonadotropin-releasing hormone analogues (GnRHa) is used for young transsexuals between 12 and 16 years of age. The purpose of this intervention is to relieve the suffering caused by the development of secondary sex characteristics and to provide time to make a balanced decision regarding actual gender reassignment.

Aim. To compare psychological functioning and gender dysphoria before and after puberty suppression in gender dysphoric adolescents.

Methods. Of the first 70 eligible candidates who received puberty suppression between 2000 and 2008, psychological functioning and gender dysphoria were assessed twice: at T0, when attending the gender identity clinic, before the start of GnRHa; and at T1, shortly before the start of cross-sex hormone treatment.

Main Outcome Measures. Behavioral and emotional problems (Child Behavior Checklist and the Youth-Self Report), depressive symptoms (Beck Depression Inventory), anxiety and anger (the Spielberger Trait Anxiety and Anger Scales), general functioning (the clinician's rated Children's Global Assessment Scale), gender dysphoria (the Utrecht Gender Dysphoria Scale), and body satisfaction (the Body Image Scale) were assessed.

Results. Behavioral and emotional problems and depressive symptoms decreased, while general functioning improved significantly during puberty suppression. Feelings of anxiety and anger did not change between T0 and T1. While changes over time were equal for both sexes, compared with natal males, natal females were older when they started puberty suppression and showed more problem behavior at both T0 and T1. Gender dysphoria and body satisfaction did not change between T0 and T1. No adolescent withdrew from puberty suppression, and all started cross-sex hormone treatment, the first step of actual gender reassignment.

Conclusion. Puberty suppression may be considered a valuable contribution in the clinical management of gender dysphoria in adolescents. **de Vries ALC, Steensma TD, Doreleijers TAH, and Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. J Sex Med 2011;8:2276–2283.**

Key Words. Gender Identity Disorder; Transsexualism; Puberty Suppression; Gonadotropin-Releasing Hormone Analogues; Adolescents

Introduction

In recent years, the possibility of puberty suppression has generated a new dimension to clinical management of adolescents with a gender identity disorder (GID), the official diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) [1]. GID is characterized by feelings of gender dysphoria associated with strong

cross-gender identification as well as a persistent discomfort with one's natal sex. The most extreme form of GID, for which the term *transsexualism* is used in the International Classification of Diseases, Tenth Edition (ICD-10) [2], is accompanied by a strong wish for gender reassignment (GR). Gender dysphoria will remit in most prepubertal children with GID (e.g., references [3–6]), but not in most gender dysphoric adolescents [7,8]. Previous studies on the effectiveness of GR, starting with cross-sex hormone (CSH) treatment between the ages of 16 and 18, showed that the gender dysphoria had dissipated, 1 year or more after GR surgery and that psychological and social functioning of these young transsexuals was favorable [7,8]. Age 16 was chosen because some cognitive and emotional maturation is desirable when starting partially irreversible interventions and Dutch adolescents are legally competent to make a medical decision without parents' consent. However, as secondary sex characteristics develop before the age of 16, waiting for medical interventions is highly upsetting for most younger adolescents.

By prescribing gonadotropin-releasing hormone analogues (GnRHa), we enable gender dysphoric adolescents under the age of 16 to explore their gender dysphoria and the wish for GR without the distress of physical puberty development [9]. If an adolescent continues to pursue GR, arresting the development of secondary sex characteristics results in a lifelong advantage of a convincing physical appearance congruent with the desired gender role. Puberty suppression is fully reversible and can be discontinued should the adolescent decide not to pursue GR [10]. It is meant to prevent the emotional problems many young transsexuals experience when puberty has started [11,12]. While on GnRHa, a gender role change is not required, as no physical cross-gender characteristics develop yet. At the Amsterdam gender identity clinic, adolescents are eligible for puberty suppression when they are diagnosed with GID, have shown persistent gender dysphoria since childhood, live in a supportive environment, and have no serious comorbid psychiatric disorders that may interfere with the diagnostic assessment. For example, it can be complicated to disentangle whether the gender dysphoria evolves from a general feeling of being just "different" or a whether a true "core" cross-gender identity exists in adolescents who suffer from an autistic spectrum disorder [13]. In addition, adolescents should have physical changes of puberty to at least Tanner stage 2–3, confirmed by pubertal hormonal levels, so that they have experienced some of their biological puberty [14–16].

GR commences with the partially irreversible CSH treatment. CSH may be prescribed when adolescents reach the age of 16 and fulfill the same eligibility criteria as for puberty suppression, with the exception of the Tanner stage criterion. The irreversible step of GR surgery is not performed prior to legal adulthood, at the age of 18.

Although some gender identity clinics have adopted this strategy of puberty suppression for adolescents with GID, other professionals working with gender dysphoric youth remain critical (e.g., Viner et al. [17]). They are concerned that GnRHa may be physically hazardous for adolescents and that psychological functioning may be negatively affected by suppressing puberty. Furthermore, they state that one's gender identity is still subject to change during adolescence and that adolescents are therefore unable to make decisions regarding GR.

Aims

Thus far, no studies have been performed that compare psychological functioning and gender dysphoria before and after the start of GnRHa. This prospective follow-up study assessed psychological functioning and gender dysphoria of the first 70 puberty suppressed young transsexuals before and after the start of puberty suppression.

Methods

Participants

Between 2000 and 2008, 140 of 196 consecutively referred adolescents were considered eligible for medical intervention at the Amsterdam gender identity clinic of the VU university medical center (VUmc) (for a description of the protocol, see Delemarre-van de Waal and Cohen-Kettenis [15]). The 29 adolescents who were age 16 years or older were prescribed CSH. The other 111 adolescents were prescribed GnRHa to suppress puberty. Participants of this study were the first 70 adolescents (mean age at assessment 13.6 [standard deviation {*SD*} = 1.8] years, 33 natal males and 37 natal females), who had subsequently started CSH treatment between the years 2003 and 2009.

Mean ages of the participants at first assessment, at the start of GnRHa treatment and at the start of CSH are presented in Table 1. Table 1 further shows participants' intelligence, as measured by either the Wechsler Intelligence Scale for Children, revised or

Table 1 General characteristics

Variable	All participants (N = 70)	Natal males (N = 33)	Natal females (N = 37)	t or χ^2	df	P
Age (in years)						
At assessment						
M (SD)	13.65 (1.85)	13.14 (1.55)	14.10 (1.99)	−2.24	66.82	0.028*
Range	11.1–17.0	11.1–16.8	11.2–17.0			
At start GnRHa†						
M (SD)	14.75 (1.92)	14.25 (1.79)	15.21 (1.95)	−2.14	67.93	0.036*
Range	11.3–18.6	11.6–17.9	11.5–18.6			
At start CSH‡						
M (SD)	16.64 (1.90)	16.24 (1.21)	16.99 (1.07)	−2.73	64.22	0.008*
Range	13.9–19.2	13.9–18.9	15.9–19.3			
Time between start GnRHa and CSH						
M (SD)	1.88 (1.05)	1.99 (0.94)	1.78 (1.16)	0.838	67.41	0.405
Range	0.42–5.06					
Full-Scale IQ						
M (SD)	98.2 (15.0)	97.1 (13.3)	99.2 (15.2)	−0.60	63.81	0.55
Range	70–131	70–123	72–131			
Parents' marital status N, (%)						
Both parents§	44 (62.9)	23 (69.7)	21 (56.8)	1.25	1	0.26
Other	26 (37.1)	10 (30.3)	16 (43.2)			
Parents' educational level¶, N (%)						
High	7 (10.6)	1 (3.3)	6 (16.7)	3.75	2	0.15
Middle	44 (66.7)	23 (76.7)	21 (58.3)			
Low	15 (22.7)	6 (20.0)	9 (25.0)			
Sexually attracted to, N (%)						
Own natal sex**	62 (88.6)	29 (87.9)	33 (89.2)	2.70	3	0.44
Both sexes	6 (8.6)	2 (6.1)	4 (10.8)			
Other††	2 (2.8)	2 (6.0)	0			

*Significant difference in mean age between natal males and natal females, $P < 0.05$.
†Gonadotropin-releasing hormone analogues.
‡Cross sex hormones.
§For marital status, the category "Both parents" included "adopted" (n = 2, 2.9%).
¶Parents' educational level was measured by a 5-point scale where 1 = *university degree* and 5 = *grade 6 or less.* Education level was divided in three groups; 1 = high, 2 and 3 = middle, and 4 and 5 = low.
**Sexual attraction was coded as "attracted to own natal sex" when adolescents responded that they fell in love "only with boys or only with girls" or "mainly with boys or mainly with girls" (according to their natal sex) and as "attracted to both sexes" when their response was "somewhat more with boys or somewhat more girls" or "both with boys and girls."
††The category "Other" consisted of one natal male who responded "only with girls" and one adolescent who responded "don't know yet." [Correction added after online publication 14-Jul-2010: "only with boys" has been changed to "only with girls".]
M = mean; *SD* = standard deviation.

third edition, or the Wechsler Adult Intelligence Scale, third edition, depending on age and year of assessment [18–20], marital status and educational level of the parents. Compared with natal males, the age of natal females was significantly higher at the time of first assessment, at the start of treatment with GnRHa, and at the start of treatment with CSH. Significant differences between natal males and natal females regarding IQ, marital status, and educational level of the parents were not observed.

Participants' sexual orientation at T1 is also presented in Table 1. Understandably, at T0, quite a few could not report on their sexual orientation because they sometimes were not older than 11 or 12 years. At T1, adolescents answered to the question, "Do you know if you fall in love with girls or boys?" Response categories were "only with boys, mainly with boys, somewhat more with boys, both with boys and girls, somewhat more with girls, mainly with girls, only with girls, or don't know yet". Participants were coded as "attracted to own natal sex" when their answer was "only with boys or only with girls" or "mainly with boys or mainly with girls" (according to their natal sex) and as "attracted to both sexes" when their answer was "somewhat more with boys or girls" or "both with boys and girls." One natal male responded to the question with "only with boys" and one adolescent with "don't know yet." Separate results for both sexes are presented in Table 1.

When attending the clinic for the first time, the participants were not yet consistently and officially living in the cross-gender role (e.g., using a new first name). However, many were already seen and treated by their families and friends as a member of the other gender. During the diagnostic phase, which usually takes between half a year and a year, all but one made a more official transition. They adopted a new first name and asked their social environment (family, friends, school) to use the appropriate personal pronouns. A legal gender change could, of course, only be made after surgery at age 18.

Procedure

Participants were assessed twice: first, shortly after their attendance at the gender identity clinic (T0); and second, shortly before starting CSH treatment (T1). Both assessments were part of the diagnostic procedure during which eligibility is assessed for puberty suppression and CSH treatment.

The VUmc medical ethics committee approved the study, and all participants and their parents gave informed consent.

Main Outcome Measures

Psychological Functioning

Behavioral and emotional problems were measured by the Child Behavior Checklist (CBCL) and the Youth Self-Report (YSR) administered to the parents and the adolescents, respectively [21,22]. These are widely used questionnaires, assessing a broad range of behavioral and emotional problems, with good psychometric properties. In this study, *T*-scores and percentages in the clinical range were used for total problem behavior, internalizing and externalizing behavior. A *T*-score above 63 is considered to be in the clinical range. Of the Dutch adolescent norm group, the percentage scoring in the clinical range on the total problem score is 8–9% on both the CBCL and YSR [21,22]. Because the CBCL and YSR were intended to measure general behavior disturbance and not gender dysphoria (which was measured by other means), items referring to gender atypical behavior were scored as 0 for all the analyses in this study to avoid any artificial inflation (for a full description of the items that may refer to gender dysphoric behavior, see Cohen-Kettenis et al. [23]).

In addition, the adolescents completed the Beck Depression Inventory (BDI). This is a 21-item inventory in multiple-choice format measuring presence and degree of depression in adolescents and adults, with good psychometric properties [24]. The BDI-II has been developed to assess a depression. A score between 14 and 19 is suggestive of a mild depression, a score between 20 and 28 of a moderate depression, and a score of more than 29 of a severe depression. Furthermore, the Trait Anger and Anxiety (TPI and STAI, respectively) Scales of the State-Trait Personality Inventory were administered [25,26]. Only the "trait" versions were used, assessing the tendency to respond with anxiety or anger to a threatening or annoying situation, respectively. They each contain 20 statements concerning the frequency with which the emotions of anger and anxiety are experienced. Each response can range from 1 (*almost* never) to 4 (*almost* always). Total scores are often used to assess and evaluate feelings of anxiety and anger over time. Finally, the attending clinician rated the Children's Global Assessment Scale (CGAS), one of the most widely used measures of the overall severity of disturbance in children [27].

An official Dutch version of each of these instruments was available and used in this study.

Gender Dysphoria

The Utrecht Gender Dysphoria Scale (UGS) was used to measure adolescents' gender dysphoria. This is a 12 item questionnaire on which the subject rates his or her agreement on a 5-point scale. An example of an item is "I feel a continuous desire to be treated as a man/woman." The higher the score, the more gender dysphoria is indicated (for psychometric data, see Cohen-Kettenis and van Goozen [7]). In addition, the Body Image Scale (BIS) was administered to measure body satisfaction [28]. The scale consists of 30 body features, which the subject is asked to rate on a 5-point scale. Each of the 30 items falls into one of three basic groups based on its relative importance as a gender-defining body feature: primary sex characteristics, secondary sex characteristics, and neutral body characteristics. A higher score indicates more dissatisfaction. For this study, an adaptation for the Dutch population was used [29].

Statistical Analyses

Independent *t*-tests and Chi-square tests were used to ascertain differences between natal males and females.

Repeated-measures analysis of variance (ANOVA) was used to ascertain within-subject differences between baseline functioning (T0, before the start of GnRHa) and the start of CSH (T1), with sex entered as a between-subject variable.

Not all 70 adolescents completed both assessments, for example, because some lists were added to the test battery after the first eligible adolescents had started GnRHa. Only data of adolescents who administered questionnaires on both assessments could be used (CBCL, YSR: 54; BDI, TPI, STAI, CGAS, and UGS: 41; BIS: 57). Independent *t*-tests between mean scores on the CBCL, YSR, BDI, TPI, STAI, CGAS, UGS, and BIS of adolescents who completed both assess-

ments and mean scores of adolescents who completed only one of the assessments revealed no significant differences on all used measures, neither at T0 nor at T1.

Results

Psychological Functioning

Adolescents showed a significant decrease in behavioral and emotional problems over time on mean *T*-scores of the total problem scale, the internalizing and externalizing scale of both CBCL and YSR (see Table 2). In addition, the percentage of adolescents scoring in the clinical range significantly decreased between T0 and T1, on the CBCL total problem scale (44.4% vs. 22.2%, $\chi^2[1] = 6.00$, $P = 0.001$), and the internalizing scale (29.6% vs. 11.1%, $\chi^2[1] = 5.71$, $P = 0.017$) of the YSR. Depressive symptom scores on the BDI-II significantly decreased and global functioning ratings on the CGAS significantly increased between T0 and T1 (see Table 2). No significant change was observed in mean TPI or STAI scores over time, representing feelings of anger and anxiety, respectively (see Table 2).

With regard to sex differences, natal females showed significantly more problem behavior at T0 and T1 than natal males in mean externalizing *T*-scores of the CBCL and the YSR (see Table 2). In addition, compared with natal males, natal females reported significantly more feelings of anger and anxiety and had a significantly lower score on the global assessment of functioning scale at T0 and T1 (see Table 2).

There was no significant interaction effect between natal sex and time for any of the used measures.

Gender Dysphoria

No significant changes in gender dysphoria or body image scores between T0 and T1 emerged (see Table 3). Compared with natal males, natal females reported significantly more gender dysphoria and were more dissatisfied with their primary and secondary sex characteristics both at T0 and T1 (see Table 3). There was a significant interaction effect between natal sex and the changes of gender dysphoria between T0 and T1; natal females became more dissatisfied with their secondary ($F[1,55] = 14.59$, $P < 0.001$) and neutral ($F[1,55] = 15.26$, $P < 0.001$) sex characteristics compared with natal males.

Table 2 Psychological functioning of adolescents with gender dysphoria before (T0) and while on puberty suppression (T1)

	T0			T1			T0-T1 significance		Between-sex significance	
	All *M (SD)*	Natal males *M (SD)*	Natal females *M (SD)*	All *M (SD)*	Natal males *M (SD)*	Natal females *M (SD)*	*F (df, errdf)*	*P*	*F (df, errdf)*	*P*
CBCL (N = 54)										
Total *T* score	60.70 (12.76)	59.42 (11.78)	61.73 (13.60)	54.46 (11.23)	50.38 (10.57)	57.73 (10.82)	26.17 (1,52)	<0.001	2.64 (1,52)	0.110
Internalizing *T*-score	61.00 (12.21)	60.00 (9.51)	61.80 (14.12)	54.46 (10.22)	52.17 (9.81)	56.30 (10.33)	22.93 (1,52)	<0.001	1.16 (1,52)	0.286
Externalizing *T*-score	58.04 (12.99)	54.71 (12.91)	60.70 (12.64)	53.81 (11.86)	48.75 (10.22)	57.87 (11.66)	12.04 (1,52)	0.001	6.29 (1,52)	0.015
YSR (N = 54)										
Total *T*-score	55.46 (11.56)	53.56 (12.26)	57.10 (10.87)	50.00 (10.56)	47.84 (10.86)	51.86 (10.11)	16.24 (1,52)	<0.001	1.99 (1,52)	0.164
Internalizing *T*-score	56.04 (12.49)	55.88 (11.81)	56.17 (13.25)	49.78 (11.63)	49.24 (12.24)	50.24 (11.28)	15.05 (1,52)	<0.001	0.049 (1,52)	0.825
Externalizing *T*-score	53.30 (11.87)	48.72 (11.83)	57.24 (10.59)	49.98 (9.35)	46.52 (9.23)	52.97 (8.51)	7.26 (1,52)	0.009	9.14 (1,52)	0.004
Depression (BDI) (N = 41)	8.31 (7.12)	5.71 (4.31)	10.34 (8.24)	4.95 (6.72)	3.50 (4.58)	6.09 (7.93)	9.28 (1,39)	0.004	3.85 (1,39)	0.057
Trait anger (TPI) (N = 41)	18.29 (5.54)	5.22 (2.76)	6.43 (2.78)	17.88 (5.24)	5.00 (3.07)	6.39 (2.59)	0.46 (1,39)	0.503	5.70 (1,39)	0.022
Trait anxiety (STAI) (N = 41)	39.43 (10.07)	4.33 (2.68)	7.00 (2.36)	37.95 (9.38)	4.39 (2.64)	6.17 (2.62)	1.21 (1,39)	0.276	16.07 (1,39)	<0.001
Global functioning (CGAS) (N = 41)	70.24 (10.12)	73.10 (8.44)	67.25 (11.06)	73.90 (9.63)	77.33 (8.69)	70.30 (9.44)	8.76 (1,39)	0.005	5.77 (1,39)	0.021

M = mean; *SD* = standard deviation; CBCL = Child Behavior Checklist; YSR = Youth Self Report; BDI = Beck Depression Inventory; TPI = Spielberger's Trait Anger Scale; STAI = Spielberger's Trait Anxiety Scale; CGAS = Children's Global Assessment Scale; df = degrees of freedom.

Table 3 Gender dysphoria of adolescents with gender dysphoria before (T0) and while on puberty suppression (T1)

	T0			T1			T0-T1 significance		Between-sex significance	
	All *M (SD)*	Natal males *M (SD)*	Natal females *M (SD)*	All *M (SD)*	Natal males *M (SD)*	Natal females *M (SD)*	*F (df, errdf)*	*p*	*F (df, errdf)*	*P*
Gender dysphoria scale (UGDS) (N = 41)	53.20 (7.91)	47.95 (9.70)	56.57 (3.89)	53.9 (17.42)	49.67 (9.47)	56.62 (4.00)	0.959 (1,39)	0.333	15.98 (1,39)	<0.001
Body image (BIS) (N = 57)										
Primary sex characteristics	4.10 (0.56)	4.02 (0.61)	4.16 (0.52)	3.98 (0.71)	3.74 (0.78)	4.17 (0.58)	2.18 (1,55)	0.145	4.11 (1,55)	0.047
Secondary sex characteristics	2.74 (0.65)	2.66 (0.50)	2.81 (0.76)	2.82 (0.68)	2.39 (0.69)	3.18 (0.42)	0.327 (1,55)	0.569	11.57 (1,55)	0.001
Neutral characteristics	2.41 (0.63)	2.60 (0.58)	2.24 (0.62)	2.47 (0.56)	2.32 (0.59)	2.61 (0.50)	0.248 (1,55)	0.620	0.081 (1,55)	0.777

M = mean; *SD* = standard deviation; UGDS = Utrecht Gender Dysphoria Scale; BIS: Body Image Scale; df = degrees of freedom.

Discussion

This is the first prospective study showing that psychological functioning of adolescents diagnosed with GID had improved in many respects after an average of nearly 2 years of GnRHa use. Adolescents showed fewer behavioral and emotional problems, reported fewer depressive symptoms, feelings of anxiety and anger remained stable, and their general functioning improved.

There may be various explanations for these results. Foremost, suppression of the development of secondary sex characteristics resulted in a physical appearance allowing for a smooth transition into the desired gender role. In adult transsexuals, postoperative psychopathology is associated with difficulties in passing in their new gender [30]. Furthermore, by receiving puberty suppression, gender dysphoric adolescents may trust that GR will be offered if needed. In addition, stigmatization and discrimination (e.g., references [11,31].) may have been limited because the adolescents in this study received extensive family or other social support. Finally, the adolescents were all regularly seen by one of the clinic's psychologists or psychiatrists. Psychological or social problems could thus be timely addressed. All these factors may have contributed to the psychological well-being of these gender dysphoric adolescents.

As expected, puberty suppression did not result in an amelioration of gender dysphoria. Previous studies have shown that only GR consisting of CSH treatment and surgery may end the actual gender dysphoria [7,8,32]. None of the gender dysphoric adolescents in this study renounced their wish for GR during puberty suppression. This finding supports earlier studies showing that young adolescents who had been carefully diagnosed show persisting gender dysphoria into late adolescence or young adulthood [7,8].

Although both adolescent natal boys and girls had profited from GnRHa treatment, there were some sex differences. At baseline, gender dysphoric natal males were younger and showed less problem behavior than natal females. With a mean age of 14, most natal females had developed breasts and had their menarche. Why natal female gender dysphoric adolescents do not come to the gender identity clinic at an earlier age should be investigated further. One hypothesis is that parents of gender dysphoric natal female adolescents may consider some puberty development (e.g., menstruation) not as dramatic as beard growth or breaking of the voice in gender dyspho-

ric boys because it is less visible for the environment. The higher problem scores of natal females in this study may indicate that this assumption would be erroneous. Another explanation is that, in the period that this very first cohort received GnRHa treatment, the public as well as referring clinicians may not have been aware yet that girls might also profit from puberty suppression. In further studies, this explanation could be tested. Finally, a reason for a later referral of natal females may be that the threshold for seeking clinical help in girls is higher than in boys. Indeed, prepubertal girls with GID seen at two large gender identity clinics appeared to show more extreme gender dysphoria than boys and came to the clinics at a later age [23].

Some limitations of this study warrant comment. This study of psychological functioning and gender dysphoria did not focus on social and sexual relationships. Although it is not likely that the gender dysphoric adolescents would report favorable psychological functioning in the absence of satisfactory relationships with their peers and family, the topic deserves more attention. This is also applicable to sexuality, which is a complicated issue for young people having primary sex characteristics that do not match their gender identity.

Furthermore, this study only focused on the functioning of gender dysphoric adolescents before the actual GR. It showed that their situation improved, as compared with the pre-GnRHa phase. Long-term follow-up studies, however, should be performed to examine whether these adolescents will be able to maintain their relatively good functioning into their adult years after GR. In addition, effects of GnRHa on physical parameters are needed before broad conclusions can be drawn regarding the safety of puberty suppression [15].

Finally, this study was a longitudinal observational descriptive cohort study. Ideally, a blinded randomized controlled trial design should have been performed. However, it is highly unlikely that adolescents would be motivated to participate. Also, disallowing puberty suppression, resulting in irreversible development of secondary sex characteristics, may be considered unethical [33].

Conclusions

Gender dysphoria did not resolve as a result of puberty suppression. Psychological functioning, however, improved in various respects. We cautiously conclude that puberty suppression may be a valuable element in clinical management of adolescent gender dysphoria. It relieves the acute distress accompanying gender dysphoria. Hence, by offering youths the possibility of healthy psychological development, puberty suppression helps in the exploration of suitable treatment options and making a balanced decision regarding GR.

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Understanding the Well-Being of LGBTQI+ Populations

Committee on Understanding the Well-Being of Sexual and Gender Diverse Populations

Charlotte J. Patterson, Martín-José Sepúlveda, and Jordyn White, *Editors*

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12

Coverage, Access, and Utilization of Evidence-Based Health Care

Research indicates that access to adequate insurance coverage, culturally responsive providers, and high-quality, evidence-based health care services has the potential to significantly reduce the effects of health disparities on sexual and gender diverse (SGD) populations. This chapter first reviews the literature on access to care, insurance coverage, and health services utilization in SGD populations. It then discusses in detail three topics that are particularly critical to ensure that clinical and policy approaches to health care for SGD populations are evidence based: gender-affirming care for transgender people, conversion therapy targeting sexual orientation or gender identity, and early genital surgeries for infants with intersex traits.

The importance of grounding clinical protocols and health-related policies on a firm evidence base is a central component of providing high-quality care to SGD people and developing effective strategies to improve SGD population health. Evidence indicates that gender-affirming medical care can significantly improve the health and well-being of transgender people. Conversely, virtually all major medical authorities agree that both "conversion therapy" to change the sexual orientation or gender identity of LGBTQ people and procedures to "normalize" the sex characteristics of children with intersex traits who are too young to participate in consent lack evidence of benefit and show evidence of physical and mental health harms.

Over the past decade, the evidence regarding the importance of gender-affirming care for transgender people has grown exponentially, with increasingly robust data on improvements in mental health outcomes and overall

well-being in particular. With regard to conversion therapy and early genital surgeries on infants with intersex traits, however, the evidence base has evolved in the opposite direction, indicating that these procedures have harmful consequences for the health of SGD people.

COVERAGE, ACCESS, AND UTILIZATION

SGD people often encounter barriers to health care services. These barriers include individual factors, such as health literacy; interpersonal factors, such as individual experiences of discrimination by health care providers and insurers; and broader structural factors, such as lower rates of health insurance coverage and higher rates of poverty among lesbian, gay, bisexual, and transgender (LGBT) communities and households headed by same-sex couples, which puts health care financially out of reach for many. Another common barrier is a widespread lack of training for providers in SGD population health, which means that many individuals, particularly transgender and people with intersex traits, struggle to find culturally and clinically competent health care providers.

This section discusses insurance coverage, access to care, and utilization of health care services by SGD people. It focuses first on discrimination in access to health care and health insurance, which is an important influence on the well-being of SGD populations. It then discusses other insurance coverage issues for SGD people, followed by what is known about health services utilization in SGD populations, including considerations of care quality and health professions training.

Discrimination in Health Care and Health Insurance Coverage

Despite cultural and legal shifts such as the nationwide expansion of marriage equality for same-sex couples, discrimination against LGBT people in health care and coverage remains pervasive in the United States. A 2017 survey conducted by National Public Radio (NPR), the Harvard School of Public Health, and the Robert Wood Johnson Foundation found that 16 percent of LGBT people reported encountering discrimination on the basis of their sexual orientation or gender identity when seeking medical care (NPR, Robert Wood Johnson Foundation, and Harvard T.H. Chan School of Public Health, 2017). Transgender people are particularly likely to encounter discrimination in health care settings. According to the 2015 U.S. Transgender Survey (USTS), 33 percent of transgender people who had seen a health care provider in the previous year had at least one negative experience related to being transgender, such as being verbally harassed, physically assaulted, or refused treatment (James et al., 2016). A 2019 review found that, across eight studies, 27 percent (range: 19–40%)

of transgender people reported having been denied health care outright (Kcomt, 2019).

In health insurance, discrimination against SGD people has historically taken many forms. Some types of insurance discrimination prevent people from being able to obtain or afford a health insurance plan at all. These include denials of family coverage to same-sex couples, including legally married spouses (CCIIO, 2014), and preexisting condition exclusions targeting conditions such as cancer and HIV (CCIIO, n.d.). Those who do obtain a plan may then encounter barriers to using their coverage. For SGD people living with HIV, these barriers include adverse tiering (when insurers place certain drugs, such as HIV antiretrovirals, in high cost-sharing levels) and coverage exclusions for pre- and post-exposure prophylaxis (Jacobs and Sommers, 2015; Underhill, 2012). For other SGD people, frequent coverage barriers include difficulty accessing preventive screenings (Agénor et al., 2014; CMS, 2015; Tabaac et al., 2018) and exclusion of coverage for such services as mental and behavioral health care, infertility treatments for same-sex couples, and gender-affirming care for transgender people (American Society for Reproductive Medicine, 2013; Baker, 2017; Coursolle, 2019). Among USTS respondents with insurance, 25 percent reported insurance discrimination on the basis of their gender identity (James et al., 2016). Their experiences included being denied coverage for what are often construed as "gender-specific" services, such as mammograms, cervical cancer screenings, and prostate exams (13%); being denied coverage for care not related to gender affirmation (7%); and being denied coverage for gender-affirming surgery (55%) or hormone therapy (25%). Gender-affirming medical care for transgender people is discussed in detail below.

As described in Chapter 11, discrimination has direct negative consequences for health and well-being and exacerbates the significant health disparities that affect LGBT, intersex, and other SGD populations. Encounters with discrimination in health care settings also jeopardize health by engendering avoidance. In the NPR et al. study, 18 percent of LGBT people reported not seeking health care when they needed it for fear of discrimination; in the 2015 USTS, 23 percent of transgender respondents had not sought care they needed in the last year for fear of mistreatment (James et al., 2016; NPR, Robert Wood Johnson Foundation, and Harvard T.H. Chan School of Public Health, 2017). Similarly, people with intersex traits may avoid routine health care due to previous negative experiences with medical providers (Lambda Legal, 2018).

Given the health consequences of discrimination, laws and policies that prohibit discrimination are a critical intervention for protecting and improving the health and well-being of LGBT, intersex, and other SGD people. Both public and private entities have increasingly established

nondiscrimination protections that include these populations. Beginning in 2006, the U.S. Department of Health and Human Services (HHS) promulgated a number of regulations that sought to ensure that discrimination on the basis of sexual orientation or gender identity did not hinder beneficiaries' access to a wide range of programs, including Medicare's Program of All-Inclusive Care for the Elderly,[1] HHS grants and services,[2] HealthCare.gov and the state-based health insurance marketplaces,[3] Medicaid managed care plans,[4] plans covering the essential health benefits outlined in the Affordable Care Act (ACA),[5] qualified health plans,[6] and ACA-regulated health insurance plans more broadly.[7] In 2011, the Joint Commission, which accredits approximately 80 percent of U.S. hospitals, began requiring accredited entities to establish nondiscrimination policies inclusive of sexual orientation and gender identity (Joint Commission, 2011).

In 2016, HHS released a regulation outlining its enforcement of Section 1557 of the ACA.[8] This ACA provision, sometimes known as the [illegible] discrimination on the basis of race, [illegible]y (including HIV status), or sex in [illegible]gram or activity.[9] The 2016 regula[illegible]ination protections in Section 1557 [illegible] status (as well as pregnancy status) [illegible]invited complaints of sexual orienta[illegible]stereotyping prohibited under Section 1557. In addition to requiring equal access to health care services and health insurance coverage, the regulation clarified that such actions as refusing to use a transgender person's correct name and pronoun, assigning a transgender person to a hospital room or other facility on the basis of their sex assigned at birth, or excluding coverage for all care related to gender affirmation constitute discrimination (insurance coverage for gender-affirming care is covered in more detail below). Evidence indicates that this regulation was effective in addressing numerous forms of discrimination against LGBT people in health care settings (Gruberg and Bewkes, 2018).

As this report goes to press, the Section 1557 regulation is being contested through lawsuits in federal court regarding the scope of its protec-

[1] 42 C.F.R. § 460.98(b)(3) and § 460.112(a).
[2] 45 C.F.R. § 75.300.
[3] 45 C.F.R. § 155.120(c)(ii) and § 155.220(j)(2).
[4] 42 C.F.R. § 438.3(d)(4), § 438.206(c)(2), and § 440.262.
[5] 45 C.F.R. § 156.125(a) and (b).
[6] 45 C.F.R. § 156.200(e) and § 156.1230(b)(3).
[7] 45 C.F.R. § 147.104(e).
[8] 45 C.F.R. Part 92.
[9] 42 U.S.C. 18116.

tions for sex nondiscrimination. It is expected, however, that the Supreme Court's decision in the case of *Bostock v. Clayton County*, in which the Court ruled that the sex nondiscrimination protections in Title VII of the Civil Rights Act include gender identity and sexual orientation (see Chapter 5), will supersede contradicting interpretations of the ACA's sex nondiscrimination provision and lead to SGD populations being protected under Section 1557 (Keith, 2020). Still unresolved, however, are such issues as access to abortion and other health care services that are increasingly targeted by laws allowing health care providers to opt out of nondiscrimination requirements that they claim conflict with their religious beliefs (Keith, 2019). The impact of religious refusal laws on the health and well-being of SGD populations is a critical and understudied issue.

Health Insurance Coverage

Several factors have changed the landscape of health insurance coverage for LGBT people over the past decade. In addition to the nondiscrimination protections described above, these factors include marriage equality for same-sex couples and the implementation of coverage expansions under the ACA.

Legal relationship recognition expands the availability of health insurance coverage for same-sex couples. Prior to the 2015 Supreme Court decision legalizing marriage equality nationwide, state recognition of same-sex domestic partnerships, civil unions, or marriage was associated with narrower coverage gaps for same-sex couples and their children relative to families headed by different-sex couples (Gonzales, 2015; Gonzales and Blewett, 2013, 2014). The effects of the Supreme Court decision itself are difficult to discern given their overlap with the major expansion of coverage driven by the ACA. The ACA, which was enacted in 2010 and went into full effect in 2014, expanded the availability of coverage in two main ways. First, the law created sliding-scale tax credits intended to facilitate the purchase of health insurance coverage through new health insurance marketplaces, such as HealthCare.gov. Second, under the Supreme Court's 2012 interpretation of the ACA, states were given the choice to expand the eligible income ranges for their Medicaid programs.

Both of these mechanisms are important pathways to coverage for LGBT people, who tend to have lower incomes and higher rates of uninsurance than non-LGBT people. In the first half of 2013, prior to the full implementation of the ACA, 34 percent of a nationally representative sample of LGBT people making less than $45,000 per year (the income range eligible for health insurance marketplace subsidies) were uninsured (Baker, Durso, and Cray, 2014). Following the opening of the marketplaces in fall 2013, uninsurance among LGBT people in this income bracket dropped to

26 percent in 2014 and to 22 percent in 2017 (Baker and Durso, 2017). Data from the Urban Institute's Health Reform Monitoring Survey similarly indicate that the share of LGB adults without health insurance across all income ranges decreased from 21.7 percent in 2013 to 11.1 percent in 2015 (Karpman, Skopec, and Long, 2015). In 2015, uninsurance among transgender USTS respondents stood at 14 percent (James et al., 2016). A 2017 study based on Gallup data, however, found that the adult LGBT population as a whole remained more likely to be uninsured than the non-LGBT population—15 percent and 12 percent, respectively—though this analysis did not account for a greater proportion of young people in the LGBT group.[10]

One risk factor for uninsurance among LGB adults in the post-ACA era is being just older than 26, when coverage for young people through their parents' plans often ends (Gonzales, Driscoll, and Quinones, 2019). Living in the South or Midwest is also a risk factor for uninsurance. These regions comprise the bulk of the states that have not expanded their Medicaid programs and are home to substantial numbers of LGBT people living in poverty. Williams Institute estimates that 24 and 23 percent of LGBT people living in the South and the Midwest, respectively, have incomes below the federal poverty level (Choi, Badgett, and Wilson, 2019). An analysis of data from the 2014 Behavioral Risk Factor Surveillance System (BRFSS) indicated that a lack of Medicaid expansion is associated with higher prevalence of uninsurance among lower-income LGB adults: LGB adults with annual household incomes under $25,000 in states that did not expand Medicaid in 2014 had higher rates of uninsurance than LGB adults in states that did expand Medicaid—37.5 and 23.3 percent, respectively—though this analysis could not confirm that all of the uninsured would have been eligible for expanded Medicaid (Gonzales and Henning-Smith, 2017a).

Beyond providing coverage to low-income people, Medicaid is also particularly important for LGBT people with specific health care needs, such as people with disabilities and people living with HIV. Both population-based and purposive sampling studies indicate that the prevalence of disability is higher among LGBT people than in the general population. An analysis of Washington state BRFSS data, for instance, found that 35.5 percent of lesbians and 36.2 percent of bisexual women had a disability, compared with 25.9 percent of heterosexual women; 26.2 percent of gay men and 40.1 percent of bisexual men had a disability, compared with 22.5 percent of heterosexual men (Fredriksen-Goldsen, Kim, and Barkan, 2012). Among transgender people, 39 percent of 2015 USTS respondents reported having a disability, compared with 15 percent of the general population (James et

[10] See: https://williamsinstitute.law.ucla.edu/visualization/lgbt-stats/?topic=LGBT#economic.

al., 2016). In comparison with binary-identified transgender people, nonbinary transgender adults in a pooled BRFSS sample from 30 states and Guam between 2014 and 2016 were more likely to report activity limitations due to physical, mental, or emotional problems (adjusted odds ratio [aOR]: 2.44; 95% confidence interval [CI]: 1.36, 4.34) (Streed, McCarthy, and Haas, 2018).

Though precise statistics are not available, disability for some LGBT people is related to living with HIV. To qualify for Medicaid coverage under pre-ACA eligibility rules, people living with HIV had to have both low incomes and a disability (or otherwise be categorically eligible by, for example, being a parent) (Kaiser Family Foundation, 2019). This led to situations in which people living with HIV could not afford treatment and had to allow their health to deteriorate to a disabling AIDS diagnosis before being able to access Medicaid coverage that could have kept them healthy (IOM, 2011a). The ACA resolved this problem in states that expanded their Medicaid programs. Access to care for people living with HIV is one of the many reasons that Medicaid expansion or broader health system reform, such as "Medicare for All" or another form of universal coverage, is a critical health issue for SGD populations.

Medicaid is also an important source of health insurance coverage for transgender people for both income and medical reasons. In the 2015 USTS, 29 percent of transgender respondents were living below 124 percent of the federal poverty line, which is nearly twice the rate of poverty among the general population (14%). Rates of poverty were higher among transgender respondents who were living with HIV (51%), had a disability (45%), or belonged to communities of color (43, 41, 40, and 38% among Latinx, Native American, multiracial, and Black respondents, respectively). The proportion of USTS respondents insured by Medicaid, however, was slightly smaller (13%) than the general population (15%). Barriers to Medicaid coverage for transgender people include restrictive income eligibility requirements in states that have not expanded Medicaid and the checkered history of Medicaid coverage for gender-affirming services, which is discussed in more detail in a later section of this chapter.

Health Services Utilization

Factors that can encourage or discourage care seeking include insurance coverage and benefit design; income and education; health status, including chronic conditions and acute care needs; health literacy; clinical and cultural competency among medical providers; geographic availability and physical accessibility of providers; and previous positive or negative experiences in health care settings (Committee on Health Care Utilization and Adults with Disabilities, 2018). Given the complexity of this constel-

lation of factors, it is difficult to characterize or predict broad trends in care utilization among SGD populations. For instance, the establishment of new legal protections may improve SGD population health and thus lead to fewer care visits; at the same time, however, the existence of new protections may encourage SGD people to seek care instead of avoiding it for fear of discrimination, which might lead to more care visits.

Some evidence suggests that sexual minority populations have high baseline care utilization. An analysis of data from the 2003–2011 nationwide Medical Expenditure Panel Survey, adjusted for sociodemographic factors, health risk behaviors, and health conditions, found that both men and women in same-sex partnerships had 67 percent (aOR: 1.67; 95% CI: 1.04, 2.67) increased odds of past-year emergency department visits and 51 percent (aOR: 1.51; 95% CI: 1.11, 2.07) increased odds of more than three physician visits in the previous year in comparison with people in different-sex partnerships (Blosnich et al., 2016). This finding is in keeping with the minority stress model, which suggests that sexual and gender minorities have worse health related to their lower social status and thus may require more medical care than their heterosexual and cisgender peers. Also in keeping with this model, Hatzenbuehler and colleagues (2012) observed a decline in medical care visits and mental health care visits among both partnered and single sexual minority men in the 12 months following the establishment of marriage equality for same-sex couples in Massachusetts.

Among transgender people, an analysis of data from the California Health Interview Survey found that transgender respondents had lower utilization rates of both primary and specialty care than non-transgender respondents (Ehrenfeld, Zimmerman, and Gonzales, 2018). Similarly, a study of transgender Medicare beneficiaries found a decreasing trend in mental health care use between 2009 and 2014 (Progovac et al., 2019). Use of gender-affirming health care services, however, has been rising since 2000 (Canner et al., 2018). This trend is likely related to a combination of a growing transgender population in the United States, improved coding practices that make it easier to identify transgender people and gender-affirming medical services in data sources such as insurance claims, and removal of barriers to insurance coverage for these services.

Further complicating assessments of care utilization is evidence that barriers to care can persist even after coverage becomes more available. Using data from the 2013–2015 National Health Interview Survey, for instance, Hsieh and Ruther (2017) documented numerous issues facing sexual minority people seeking health care, including ongoing use of emergency departments for primary care; delayed or unmet care needs due to cost; and delayed or unmet care needs for nonfinancial reasons, such as

not being able to get an appointment with a medical provider or lacking transportation to a provider's office. Gonzales and Henning-Smith (2017b) similarly found that gender-nonconforming people in a 2014–2015 BRFSS sample from 27 states and Guam were almost twice as likely as a reference group of cisgender women to have unmet care needs due to financial issues (aOR: 1.93; 95% CI: 1.02, 3.67), and they were more than twice as likely not to have received a routine check-up in the previous year (aOR: 2.41; 95% CI: 1.41, 4.12). There is a lack of data on utilization among people with intersex traits.

Quality of Care and Health Professions Training

Common frameworks for quality improvement in health care include the six aims of safety, timeliness, effectiveness, efficiency, patient-centeredness, and equity set forth by the Institute of Medicine (2001) and the "triple aim" of improved patient experiences of care, improved population health outcomes, and reduced costs developed by the Institute for Healthcare Improvement (Berwick, Nolan, and Whittington, 2008). Scant research has explored quality of care issues, including definitions, priority outcomes, and measurement, among SGD populations. Another aspect of care quality is attention to the social determinants of health at the population level and to the social needs of individuals in health care contexts. Major negative social influences on the health of SGD populations include but are not limited to discrimination and a lack of access to culturally responsive providers; family and peer rejection and bullying; unemployment and poverty; and a dearth of feelings of community cohesion, safety, and participation (IOM, 2011b). These generate social needs such as trauma, housing insecurity, financial strain, and social isolation, particularly among groups such as SGD youth and older adults. It is important for researchers, care providers, and policy makers to develop and evaluate targeted efforts to address social determinants of health and meet social needs for SGD people. The experiences of SGD patients have also not been fully explored in the context of new care delivery models intended to improve quality, coordinate care, and restrain costs, such as accountable care organizations and patient-centered medical homes (National LGBT Health Education Center, 2016).

Regardless of how care delivery is organized, providing cultural and clinical competency training about SGD populations for the entire health workforce is critical to ensuring that SGD people can access high-quality care. Training in providing culturally responsive and clinically appropriate care for SGD people needs to begin early for medical students and other health professions trainees, including but not limited to nurses, physician assistants, and nurse practitioners (AMA, 2019; Obedin-Maliver et al., 2011; Streed et al., 2019b). The American Association of Medical Colleges

has published curriculum resources to support early clinician training in SGD health topics (Hollenbach, Eckstrand, and Dreger, 2014).[11]

Another strategy for promoting cultural responsiveness to SGD concerns in health care settings is encouraging the career development of SGD-identified health professionals. Sexual and gender diversity, alongside other forms of representation such as racial diversity, strengthens the health care workforce by bringing in new perspectives to inform the delivery of care and helping patients build trust with providers whose backgrounds mirror theirs (Tanner, 2020). Unfortunately, research indicates that SGD people remain significantly underrepresented in the scientific workforce, and many workforce diversity initiatives—such as those supported by the National Institutes of Health (NIH)—do not include SGD populations despite the designation of sexual and gender minorities as an NIH health disparity population in 2016 (Freeman, 2018).

In terms of SGD cultural responsiveness among practicing providers, a 2016 systematic review by the Agency for Healthcare Research and Quality called for clearer definitions of cultural competency for LGBT populations, clarification on the relationship between cultural competence and patient-centered care, and greater availability and assessment of training curricula (Butler et al., 2016). In 2020, the Human Rights Campaign's Healthcare Equality Index, which provides training and assesses LGBT cultural competency at hospitals and other health care organizations across the country, reported that the 765 health care facilities evaluated nationwide in the previous year had accumulated more than 150,000 hours of LGBT-specific cultural competency training (Human Rights Campaign Foundation, 2020).

Another resource related to cultural responsiveness in working with SGD patients are the federal Culturally and Linguistically Appropriate Services Standards, which include sexual orientation and gender identity among aspects of patient identity that require attention and respect from care providers (Office of Minority Health, 2013). The federal Substance Abuse and Mental Health Services Administration (SAMHSA) also promotes cultural competency training around sexual and gender diversity (SAMHSA, 2020), and the Health Resources and Services Administration (HRSA), which oversees the community health centers program and the Ryan White program, funds the National LGBT Health Education Center at Fenway Health, a federally qualified community health center located in Boston that specializes in serving LGBTQ people and people living with HIV.[12] The National LGBT Health Education Center provides a variety of downloadable resources and continuing medical education modules on

[11] See https://www.aamc.org/what-we-do/mission-areas/diversity-inclusion/lgbt-health-resources.
[12] See https://www.lgbthealtheducation.org.

culturally responsive and clinically appropriate care for LGBTQ people and people with intersex traits.

In addition to the National LGBT Health Education Center, HRSA supports the Center of Excellence for Transgender Health at the University of California at San Francisco, which conducts research and publishes care guidelines and other resources about various aspects of transgender health, particularly in relation to HIV.[13] Between 2012 and 2017, HRSA partnered with the Center of Excellence and several other community-based organizations on a Special Project of National Significance that investigated strategies for engaging and retaining HIV-positive transgender women of color in high-quality care. Important factors identified in this project included providing transgender-specific cultural and clinical competency training for the health care workforce; addressing social determinants of health, such as housing, as part of the provision of health care services; and recognizing the central role that gender-affirming services and personal empowerment can play in improving care and outcomes for transgender people living with HIV, particularly transgender women of color (Health Resources and Services Administration, n.d.; Rebchook et al., 2017). Resources on serving other specific SGD populations have also been created by both public and private entities: in 2010, the federal Administration on Aging (now the Administration for Community Living) funded the creation of the National Resource Center on LGBT Aging to provide information and resources for health care personnel working with LGBT elders,[14] and organizations such as Lambda Legal have published guidelines for hospitals on establishing affirming policies for transgender people (Lambda Legal, 2016) and people with intersex traits (Lambda Legal, 2018).

Alongside cultural and clinical competency training and a diverse health professions workforce, data collection about sexual orientation, gender identity, and intersex status in health care and public health activities is a critical component of understanding and effectively addressing health disparities among SGD populations. Both *Healthy People 2020*, released in 2010, and *Healthy People 2030*, released in 2020, call for an increase in the number of population health surveys that include sexual orientation and gender identity measures,[15] and federal regulations governing incentive programs for electronic medical records require that certified systems have the capacity to collect, store, and retrieve structured data on sexual orientation and gender identity (Cahill et al., 2016). The NIH Sexual and Gender Minority Research Office also promotes research into the health of

[13] See https://prevention.ucsf.edu/transhealth.
[14] See https://www.lgbtagingcenter.org.
[15] See https://www.healthypeople.gov.

SGD populations[16] (see Chapter 4 for a more detailed discussion of data collection).

GENDER-AFFIRMING CARE FOR TRANSGENDER PEOPLE

The first U.S. clinics providing gender-affirming care to transgender individuals opened in the 1960s and 1970s. Practice and research in the field of transgender health, however, was stymied in the 1980s and 1990s by the spread of public and private insurance exclusions for gender-affirming care. As these exclusions have begun to be removed, there has been exponential growth in evidence regarding the medical necessity of this care, and gender affirmation has emerged as a core intervention to improve the health and well-being of transgender people. This section reviews the components of and clinical and population evidence concerning gender affirmation.

Components of Gender Affirmation

Broadly speaking, gender affirmation is a process by which people who identify as transgender, non-binary, or gender diverse take steps to fully express their true gender. (An older but still common term for the process of gender affirmation is gender transition.) Gender affirmation may have social, legal, and medical components. Socially, people may use a name or pronoun different from those they were assigned at birth, or they may change aspects of their gender expression, such as hairstyle and clothing. Legal affirmation may include name or gender marker changes on identification documents—such as passports, driver's licenses, and birth certificates—which are affected by state and federal laws and policies. Gender-affirming clinical care may include psychosocial support, hormone therapy, and surgeries.

Psychosocial support for gender affirmation typically focuses on reducing emotional distress and supporting decision making regarding social, legal, and medical steps. Some young transgender people and their families opt for medication to delay the onset of puberty. Adults and some adolescents may take feminizing or masculinizing hormones to achieve gender-congruent secondary sex traits, often in conjunction with medications that suppress menses or block androgens. Many transgender adults and older adolescents undergo surgery to align the appearance of their face, chest or breasts, body shape, and genitals with their gender, and some may also pursue speech therapy or hair removal. Gender affirmation is different for every person: some people may take only social or legal steps, while others may need gender-affirming prescriptions or medical procedures. Regardless

[16] See https://dpcpsi.nih.gov/sgmro.

of an individual's path in relation to gender affirmation, social support and integrated, multidisciplinary care are essential for all transgender people, especially youth, and are consistently associated with improved mental health, social involvement, and self-esteem (Rafferty, Committee on Psychosocial Aspects of Child and Family Health, and Committee on Adolescence, 2018).

Guidelines and Policies Related to Gender Affirmation

Clinicians who provide gender-affirming psychosocial and medical services in the United States are informed by expert evidence-based guidelines. In 2012, the World Professional Association for Transgender Health (WPATH) published version 7 of the *Standards of Care for the Health of Transgender, Transsexual, and Gender-Nonconforming People*, which have been continuously maintained since 1979, and revisions for version 8 are currently under way (Coleman et al., 2012). Two newer guidelines have also been published by the Endocrine Society (Hembree et al., 2017) and the Center of Excellence for Transgender Health (UCSF Transgender Care, 2016). Each set of guidelines is informed by the best available data and is intended to be flexible and holistic in application to individual people. All of the guidelines recommend psychosocial support in tandem with physical interventions and suggest timing interventions to optimize an individual's ability to give informed consent. Mental and physical health problems need not be resolved before a person can begin a process of medical gender affirmation, but they should be managed sufficiently such that they do not interfere with treatment.

A major success of these guidelines has been identifying evidence and establishing expert consensus that gender-affirming care is medically necessary and, further, that withholding this care is not a neutral option (World Professional Association for Transgender Health, 2016). A number of professional medical organizations have joined WPATH in recognizing that gender-affirming care is medically necessary for transgender people because it reduces distress and promotes well-being, while withholding care increases distress and decreases well-being (American Academy of Family Physicians, 2012; American Academy of Pediatrics, 2018; American College of Nurse Midwives, 2012; American College of Obstetricians and Gynecologists, 2011; AMA, 2008; American Psychiatric Association, 2018; American Psychological Association (APA), 2008, 2015; Endocrine Society, 2017). Accordingly, public and private insurers have expanded access to gender-affirming care; some have done so proactively, while others have been required by state and federal nondiscrimination laws to remove coverage exclusions (Baker, 2017).

Coverage requirements for gender-affirming care typically rely on an overarching principle of parity between medically necessary services for transgender and cisgender people. Treatments that are gender affirming for transgender patients are covered by public and private insurers for

intersex and cisgender people for a variety of conditions, including genital difference, endocrine disorders, cancer prevention or treatment, and reconstructive surgeries following an injury. Examples of these services include testosterone or estrogen replacement therapy after surgery or menopause, vaginoplasty after pelvic surgery or for women with vaginal agenesis in the context of an intersex condition, and phalloplasty for cisgender male service members injured in war (Baker et al., 2012; Balzano and Hudak, 2018; Spade et al., 2009).

As this report goes to press, 24 states and the District of Columbia have enacted laws or made administrative changes prohibiting transgender-specific insurance exclusions in private coverage (Movement Advancement Project, 2020a). However, Medicaid programs in 10 states continue to explicitly exclude gender-affirming care for transgender individuals, and many states do not address the issue of this coverage in Medicaid (Mallory and Tentindo, 2019). At the federal level, the Medicare program removed its exclusion for "transsexual surgery" in 2014 (HHS, 2014), though coverage decisions related to gender-affirming surgeries are still made on a case-by-case basis (CMS, 2016). As discussed above, Section 1557 of the Affordable Care Act also has substantial ramifications for coverage of gender-affirming care: the 2016 HHS regulation embraced the principle of parity and prohibited categorical exclusions of gender-affirming care under the rubric of sex nondiscrimination. This aspect of the regulation remains contested in court, but it is expected that the original regulation's specific protections for transgender people will be found to be well within the scope of federal law and the agency's authority (Keith, 2020).

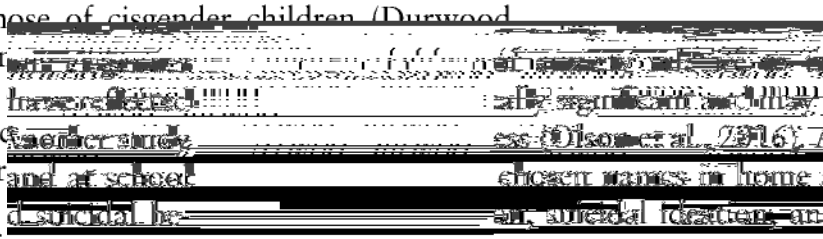
In order to justify coverage for gender-affirming care, insurance providers in the United States and most other countries require a supporting diagnosis. In 2013, the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), 5th edition (American Psychiatric Association, 2013) replaced the diagnosis of gender identity disorder with gender dysphoria. Whereas gender identity disorder was perceived as pathologizing a person's gender identity, gender dysphoria emphasizes the clinically significant distress and impairment that can accompany incongruence between assigned sex and gender identity (Robles et al., 2016). A person who experiences no distress or impairment due to this incongruence will not meet diagnostic criteria for gender dysphoria. More recently, the *International Classification of Diseases*, 11th revision (WHO, n.d.) has replaced transsexualism and gender identity disorder with gender incongruence and moved the diagnosis out of the mental and behavioral disorders chapter and into a new chapter on sexual health.

Many insurers and some health care providers require documentation that an individual meets guideline requirements, including diagnostic criteria for gender dysphoria, as a prerequisite for hormonal or surgical

treatment. Because of the power differential inherent in this construct, this practice has been described as "gatekeeping" and can function as a significant barrier to accessing care. In a survey of transgender adolescents, for instance, participants described distress at having to prove to a mental health provider that they were "trans enough," having to wait for approval for treatment, and perceiving that their therapist feared legal liability should a person later regret the treatment (Gridley et al., 2016). Even transgender people with insurance coverage and access to providers report difficulty in navigating diagnosis-based requirements imposed by providers and insurers (James et al., 2016). Over the past 10 years, some U.S. medical professional organizations have increasingly moved to reduce psychiatric gatekeeping by shifting toward an informed consent and shared decision-making model, especially for adults (Schulz, 2018). Some countries have further underscored that transgender identity is not a pathology by recognizing gender affirmation as fundamental to the human right to self-definition and removing requirements that transgender people seeking gender-affirming medical care present with a diagnosis such as gender dysphoria (Arístegui et al., 2017).

Outcomes of Gender-Affirming Interventions

The evidence base for gender affirmation across age groups has grown rapidly over the last decade. For transgender youth who have not yet reached puberty, social affirmation and support are primary interventions. Using data from electronic records from the Kaiser Permanente system, recent work has suggested that prepubescent transgender children experience increased rates of mental health problems, especially anxiety, depression, and attention deficit disorders, relative to cisgender children (Becerra-Culqui et al., 2018). However, research also shows that, when transgender children in this age group are socially affirmed and supported by their families, their rates of depression are much nearer to those of cisgender children (Durwood, McLaughlin, and Olson, 2017). In or[illegible] socially affirmed had elevated rates [illegible] peers, but this difference was not clini[illegible] ongoing social stigma and minority str[illegible] found that using transgender youths' [illegible] was associated with reduced depressi[illegible] havior (Russell et al., 2018).



Puberty blockers, typically gonadotropin-releasing hormone analogs, have been used since at least the late 1990s to prevent development of irreversible secondary sex traits and to give youth more time to explore their gender identity (Cohen-Kettenis and Van Goozen, 1998). In 2014, a landmark paper provided longitudinal data from a cohort of youth in the Netherlands: among this group, puberty suppression, followed several years

later by gender-affirming hormones and surgery, was effective in reducing gender dysphoria and restoring well-being equal to or better than same-age cisgender young adults (de Vries et al., 2014). Though most data on puberty suppression are limited and drawn from convenience samples in European clinics, this fully reversible gender-affirming intervention appears to confer improved psychological functioning and may reduce gender dysphoria (Mahfouda et al., 2017).

There is inconsistent and limited evidence regarding risks of irreversible low bone density and infertility (Chew et al., 2018; Mahfouda et al., 2017; Rafferty, Committee on Psychosocial Aspects of Child and Family Health, and Committee on Adolescence, 2018). In recognition of these risks, guidelines recommend monitoring bone density and counseling on fertility preservation prior to treatment (Hembree et al., 2017). Of note, while evidence indicates that social affirmation and puberty suppression are low risk and effective interventions for young transgender youth, there may be a significant delay between recognition and disclosure of gender incongruence: in one cohort, participants reported identification of gender incongruence on average at age 8 and disclosure to caregivers on average at age 17 (Olson et al., 2015). Support from parents and affirmation of gender diversity are critical to creating safe opportunities for young people to access the psychosocial and medical care that they need in a timely manner.

Hormone therapy with testosterone or estrogen is a common gender-affirming treatment for transgender adults and older adolescents. Though limited by heterogeneity of methodology, regimen, and outcomes measures, systematic reviews and meta-analyses consistently find that gender-affirming hormone treatment is associated with significant reductions in gender dysphoria, psychological symptoms, and psychiatric diagnoses and with improved markers of well-being, including quality of life, interpersonal functioning, psychological adjustment, sexual function, body satisfaction, and self-esteem (Costa and Colizzi, 2016; Dhejne et al., 2016; Keo-Meier et al., 2015; Murad et al., 2010; Nguyen et al., 2018; Rowniak, Bolt, and Sharifi, 2019; White Hughto and Reisner, 2016).

Both the WPATH and Endocrine Society guidelines identify age 16 as a general starting point for gender-affirming hormones, with the recognition that some adolescents benefit from earlier treatment (Coleman et al., 2012; Hembree et al., 2017). Evidence for hormone therapy in adolescents comes largely from outside of the United States and inconsistently tracks outcomes (Chew et al., 2018; Olson-Kennedy et al., 2016). The data available suggest that hormone therapy in adolescents likely yields reductions in dysphoria and distress and improvements in well-being similar to those in adults (Mahfouda et al., 2019). Gender-affirming hormone therapy can be managed for most patients by primary care providers,

as it typically involves long-term maintenance on doses similar to those used for cisgender patients with conditions such as hypogonadism (Wylie et al., 2016).

Surgeries involving the genitals or secondary sex characteristics can also improve health and well-being among transgender people and are an important and medically necessary aspect of gender-affirming care (Bailey, Ellis, and McNeil, 2014; Castellano et al., 2015; Murad et al., 2010; Passos et al., 2020; Wernick et al., 2019). Many factors affect an individual's need for and access to gender-affirming surgeries. In the 2015 USTS, only 25 percent of respondents had undergone some form of gender-affirming surgery, such as genital reconstruction or chest reconstruction, and having surgery was correlated with higher incomes (James et al., 2016). Respondents also reported varying degrees of experience with or need for specific procedures: 97 percent of transgender men had or needed chest reconstruction surgery, and 22 percent of transgender men had or needed phalloplasty. Similarly, 95 percent of transgender women had or needed hair removal procedures, and 76 percent had or needed vaginoplasty. Non-binary individuals generally had and needed fewer surgeries than their binary-identified counterparts: 48 percent of non-binary individuals assigned female at birth had or needed chest surgery, and 12 percent of non-binary individuals assigned male at birth had or needed vaginoplasty.

Surgeries for transgender men and other trans-masculine people may include bilateral chest reconstruction, salpingo-oophrectomy (removal of the ovaries and fallopian tubes), hysterectomy, genital reconstruction (metoidioplasty or phalloplasty with or without prosthesis), and, rarely, vocal surgery. Chest reconstruction, which involves removal of breast tissue and nipple preservation, is associated with significant improvements in mental health and well-being among trans-masculine adolescents and adults (Agarwal et al., 2018; Mahfouda et al., 2019; Van Boerum et al., 2019). A systematic review of studies of genital surgeries that included metoidioplasty indicated that 93 percent of patients were satisfied with the outcome, including preserved erogenous sensitivity, despite significant rates of postoperative complications (Morrison et al., 2016). A systematic review of penile prosthetic outcomes for 792 transgender men over a mean follow-up period of three years found inconsistent reporting of sensory, urinary, satisfaction, and sexual outcomes after surgery, with 36 percent reporting prosthesis complications (Rooker et al., 2019).

Surgeries for transgender women and other trans-feminine people may include breast augmentation, facial feminization, vocal surgery, orchiectomy, and vaginoplasty. Some studies have shown improvements in quality of life and high patient satisfaction following facial feminization procedures for trans-feminine individuals, including reshaping the contours of the face and larynx (Ainsworth and Spiegel, 2010; Van Boerum et al., 2019). A

systematic review of vaginoplasty for transfeminine individuals identified 26 studies with a total of 1,563 patients; although measures used to track outcomes varied between studies, and complications were frequent, with neovaginal stenosis the most common, patients tended to report high ratings in both sexual function and satisfaction after surgery (Horbach et al., 2015).

The research regarding outcomes for surgery in youth under 18 is sparse, in part because it is generally not clinically recommended for legal minors, though there is only a small amount of low-quality evidence that supports this limitation (Hembree et al., 2017). Chest masculinization is sometimes appropriate for youth 16 or older (Coleman et al., 2012), and some surgeons perform vaginoplasty on minors under specific circumstances (Milrod and Karasic, 2017). Several studies provide positive evidence regarding the benefits of chest reconstruction in minors, with reduced depressive and anxious symptoms and improved chest dysphoria; the most common complications were changes in sensation and scar cosmesis (Mahfouda et al., 2019). There are very few data regarding genitoplasty for minors.

As noted above, available evidence generally indicates that gender-affirming medical interventions, including surgeries, are associated with improvements in gender dysphoria, mental health, and quality of life for transgender people. Evidence also suggests, however, that mental health conditions can persist after treatment: for instance, a 2011 Swedish registry study of 324 patients who had undergone gender-affirming surgeries between 1973 and 2003 found increased rates of suicide attempts and psychiatric hospitalizations relative to population controls (Dhejne et al., 2011). The study notes that surgeries did alleviate gender dysphoria, and the study was unable to determine how patients might have fared without surgery. When a more recent Swedish registry study tracked mental health treatment utilization among people with a gender incongruence diagnosis relative to people without gender incongruence between 2005 and 2015 (N = 2,679), time since gender-affirming surgery was associated with reduced need for mental health services (aOR: 0.92; 95% CI: 0.87, 0.98) (Bränström and Pachankis, 2019). A reanalysis of these data compared individuals with gender incongruence who had gender-affirming surgery with those who did not and found comparable rates of reduced need for treatment for mood disorders between the groups, but higher rates of treatment for anxiety disorders among the group who did have surgery (aOR: 1.40; 95% CI: 1.00, 1.97) (Bränström and Pachankis, 2020). The authors note that the comparator nonsurgical group is heterogeneous, including a mixture of patients who both did and did not want surgery. Furthermore, as was discussed in detail in Chapter 11, transgender people have significantly elevated rates of mental health problems due not just to the experience of

gender dysphoria but also because of minority stress and stigma. While social and medical affirmation reduce gender dysphoria and can mitigate the impact of social factors, such as discrimination and family rejection, medical affirmation may not fully resolve or protect from experiences of stigma and stress. Future studies examining outcomes of gender affirmation should assess and control for these factors. Related research needs include exploration of factors that can promote resilience in different family and community settings and across the life course (Bockting et al., 2016).

Another major limitation in research on postsurgical outcomes is the absence of patient-reported outcome measures that have been validated in transgender and non-binary post-operative patient populations (Andréasson et al., 2018; Barone et al., 2017; Dy et al., 2019). Recent data overall suggest that satisfaction after gender-affirming surgeries is high and risk of regret is very low. For example, the Center of Expertise on Gender Dysphoria at the Free University Medical Center in Amsterdam published results from 43 years of clinical care in which regret was reported in only 14 patients (0.5%) of the more than 5,300 patients who underwent gonadectomy as part of gender affirmation (Wiepjes et al., 2018). A smaller study found that only 1 of 68 patients who received chest masculinization surgery experienced regret "sometimes" (Olson-Kennedy et al., 2018), consistent with findings from older research (Gijs and Brewaeys, 2007). Similarly, a 2018 systematic review and meta-analysis of 46 articles with 3,716 cases of vaginoplasty for transgender women reported a cumulative rate of regret of 1 percent, compared with an overall satisfaction rate of 92 percent across different surgical techniques (Manrique et al., 2018). While many studies do not qualitatively assess degree and reasons for regret, in one study patients who reported regret with surgeries reported mild regret and attributed this to cosmetic or functional outcomes rather than the decision to have surgery (van de Grift et al., 2017).

Substantial progress has been made over the past decade in research on outcomes of gender-affirming interventions, and there are ample opportunities for improvement. To address the scarcity of data and difficulties extrapolating findings from relatively homogeneous European samples, a United States-based comprehensive registry that tracks patient-centered outcomes for both youth and adults could lead to valuable insights on the benefits of medically supervised gender affirmation (Kimberly et al., 2018). Much remains to be learned regarding optimal timing and risk profiles for surgeries and other medical interventions, aided by standardized and validated tools for body satisfaction, gender-related quality of life, gender dysphoria, and mental health (Olson et al., 2016). Standardized assessment and reporting of outcomes are particularly essential for helping clinicians and patients understand surgical options. In this area, too, more attention is needed to populations that tend to be invisible or underrepresented in

clinical research, especially transgender people of color and non-binary individuals. Very little is known about the experiences and options for treatment for transgender individuals with intersex traits, especially those who had irreversible treatments as children. Overall, however, the evidence indicates that gender-affirming interventions, including social affirmation, hormonal treatment, and surgeries, are medically necessary for reducing distress and improving the health and well-being of transgender people.

CONVERSION THERAPY

Efforts to change sexual orientation or gender identity, which initially gained traction in the 1960s and which are often referred to as conversion or reparative therapies, assume that non-cisgender and non-heterosexual identities are abnormal. In 2009 the APA produced a landmark report that systematically reviewed the evidence of efficacy for sexual orientation change efforts (APA, 2009). Most of this research was conducted prior to 1981, and very few studies were experimental in design. The task force found that some people sought sexual orientation change efforts due to distress over their sexual orientation but that the treatments were unable to reduce same-sex attractions or increase other-sex attractions. Furthermore, there was evidence that individuals experienced harm from these treatments, including sexual dysfunction, depression, anxiety, and suicidality. With regard to gender identity, while interest in the so-called "desistence" of transgender identity has been informed by studies suggesting that as high as 80 percent of prepubertal youth presenting to pediatric gender clinics ultimately do not identify as transgender, many of the youth included in these studies did not meet full DSM criteria for a gender incongruence diagnosis (Olson, 2009). Recent evidence supports that early social affirmation of transgender identity is associated with good outcomes (Olson et al., 2016; Durwood, McLaughlin, and Olson, 2017) and that lack of social affirmation correlates with depression, anxiety, and suicidality (de Vries et al., 2016; James et al., 2016).

Consequently, sexual orientation and gender identity conversion efforts have fallen out of favor in mainstream psychological and psychiatric practice. By the time of the 2011 Institute of Medicine report, many medical organizations had issued statements condemning sexual orientation change efforts based on the lack of efficacy and evidence of harm. Many of these organizations have since updated their positions to decry conversion therapy for both sexual orientation and gender identity (AMA and GLMA: Medical Professionals Advancing LGBTQ Equality, 2018; American Academy of Child and Adolescent Psychiatry, 2018; Rafferty, Committee on Psychosocial Aspects of Child and Family Health, and Committee on Adolescence, 2018; SAMHSA, 2015; Streed et al., 2019a).

However, there is recent evidence that LGBTQ youth and adults continue to be exposed to conversion therapy. A 2019 report from Williams Institute estimated that 698,000 adults between ages 18 and 59 have undergone conversion therapy from a licensed professional or religious advisor, of whom 350,000 were adolescents when treated (Mallory, Brown, and Conron, 2019). The same study estimated that an additional 57,000 youth will receive conversion therapy from [illegible] before 18 years of age. Among 25,000 [illegible] national survey, 67 percent reported that someone attempted to convince them to change their gender identity or sexual orientation (Trevor Project, 2019). A survey of 762 marriage and family therapists and members of the American Academy of Marriage and Family Therapists, which has a position statement against conversion therapy, found that 19.4 percent of respondents believed it was ethical to practice sexual orientation change therapy, and 3.5 percent of respondents had done so. This belief was associated with higher levels of negative beliefs about LGB clients than those of other therapists (McGeorge, Carlson, and Toomey, 2015).

A recent survey was among the first to evaluate the link between sexual orientation change therapy and the health of young people: among 245 white and Latinx LGBT individuals between the ages of 21 and 25, exposure to conversion efforts within or outside of their families during adolescence was associated with higher family religiosity, lower family socioeconomic status, and higher individual gender nonconformity (Ryan et al., 2018). In addition, exposure to conversion efforts during adolescence was significantly associated with increased suicidal ideation, suicide attempts, and depression, as well as diminished life satisfaction, self-esteem, social support, educational attainment, and lower income in young adulthood.

A systematic narrative review of gender identity conversion efforts found few data and a notable absence of research about their effects on both adolescents and adults (Wright, Candy, and King, 2018). However, a recent study using data from the 2015 USTS found that 14 percent of respondents had been exposed to gender identity conversion therapy during their lifetimes; exposure was associated with significantly higher rates of past-month severe psychological distress and lifetime suicide attempts compared with respondents who had not been exposed to such therapy (Turban et al., 2019). Exposure to gender identity conversion therapy before age 10 was associated with nearly twice the rate of lifetime suicide attempts.

The available evidence suggests that sexual orientation and gender identity conversion efforts are ineffective and dangerously detrimental to the health of SGD populations, especially for minors who are unable to give informed consent. As of early 2020, 20 states, the District of Columbia, Puerto Rico, and a number of municipalities had outlawed sexual orientation and gender identity conversion therapy for minors (Move-

ment Advancement Project, 2020b). As growing numbers of professional organizations and governments call for or legislate an end to conversion therapy, particularly for minors, it is important for clinicians working with SGD populations to understand the effects that these experiences can have on individuals, even many years later. Research on strategies for helping individuals who have experienced conversion therapy to heal and recover is essential. In order to end the practice of conversion therapy, it is not sufficient for professional organizations to recommend against conversion therapy; rather, professionals may require dedicated and specific training on the inefficacy and danger of conversion treatments, and insurance providers should consider limiting coverage for these non-evidence-based practices.

INTERSEX GENITAL SURGERY

The most expansive estimations of the prevalence of intersex traits, including any variation in any marker of sex (chromosomes, internal reproductive anatomy, external genital shape, and secondary sex traits), concludes that up to 1.7 percent of the population has an intersex trait (Fausto-Sterling, 2000). Estimates based on the number of people with clinically identifiable sexual or reproductive anatomic variations are closer to 0.5 percent (Nordenvall et al., 2014). Estimates for prevalence of infants born with obvious genital diversity, sometimes known as ambiguous genitalia, range from 0.03 percent to 0.1 percent (Blackless et al., 2000; Hughes et al., 2007; Thyen et al., 2006). Such variations can include differences in the length of the genital tubercule or glans (as in a shorter penis or longer clitoris), a narrow or absent vaginal opening, or presence of partially fused labia or a partially separated scrotum. This section focuses primarily on early genital surgery for children born with obvious genital diversity, which remains the most contentious area of clinical care—and increasingly, health law and policy—for persons with intersex traits (Dalke et al., 2020).

Genital Diversity and Early Genital Surgeries

Although some infants with genital diversity require urgent surgery to address urinary obstruction or exposed pelvic organs (Woo, Thomas, and Brock, 2010), many have no immediate medical concerns and do not require urgent medical treatment (Romao and Pippi Salle, 2017). Because the appearance of the external genitals is typically the primary datum for the sex assigned to infants at birth, genital diversity can lead to uncertainty about which sex a child with intersex traits should be assigned. Similarly, eventual gender identity cannot be readily predicted for many people with intersex traits based on the appearance of their genitals at birth (see more

detailed discussion below). Currently, clinicians and advocates alike typically recommend a binary but flexible sex assignment, informed by the balance of sex markers and the specific intersex condition the child has, which will contribute to the person's gender identity later in life.

Early genital surgeries primarily seek to align genitalia with assigned sex. Feminizing surgeries reduce the size of a clitoris, shape a vulva, or create or lengthen the vagina of a child assigned female. Masculinizing surgeries may reposition a urethra that is not located at the tip of the penis or create a phallus for a child assigned male. Early removal of gonadal tissue may also be recommended to reduce risk of malignancy or the pubertal production of hormones (and therefore secondary sex traits) that are discordant with the child's assigned sex. In the United States, many of these surgeries are performed in infancy.

In 2016, an international consensus group offered an update on genital surgery for children with obvious genital difference and identified a broad set of benefits for surgeries (Mouriquand et al., 2016). Physically, surgeries seek to promote "functional genital anatomy to allow future penetrative intercourse (as a male or a female)" (p. 141), as well as fertility, urinary function, menstruation, and the avoidance of malignancy and secondary sex traits that are discordant with assigned sex. Psychosocially, surgeries also purportedly "foster development of 'individual' and 'social identities'," reduce genital-related stigma, and support "the parents' desire to bring up a child in the best possible conditions" (p. 142). Since the early 1990s, however, intersex advocates have called attention to the physical and emotional harms of surgery, especially when performed before a child is old enough to participate in the decision. Indeed, in the absence of cloacal exstrophy (exposure of pelvic organs), urinary obstruction, or current malignancy, there is no medical urgency for such surgeries; they can be safely deferred until a child is older. At the core of the debate is a question as to what to do and when: what, if any, surgeries should be performed on very young children? This question ultimately calls for the weighing of relative physical and emotional risks, benefits, and alternatives to such surgeries.

Synthesis of the evidence base is complicated by significant heterogeneity of anatomic and medical considerations, surgical procedures, and dynamic psychosocial aspects over the life course. The available research on outcomes also has significant methodological limitations, with many

ons or programs and inconsistency in
gns, sample sizes, reported outcomes,
have insufficient postsurgical follow-
od interventions on adult physical,
. Many studies also lack an effective
ndard nonsurgical pathways for chil-

A review of these surgeries follows, along with an assessment of what is known about the outcomes of these interventions. The risks and benefits of each group of surgeries are discussed together, as these tend to be specific to the physical intervention itself. Some psychosocial outcomes, however, are discussed in aggregate, to reflect more limited data and overlaps in psychosocial experiences among intersex variations.

Gonadectomy

Removal of the gonads yields two potential benefits in the form of risk reduction: avoiding gonadal malignancy and undesired secondary sex traits. The risk of malignancy tends to be higher for intra-abdominal testes or atypically developed gonads, but it has to be balanced against the potential benefits of hormone-producing tissue (Pyle and Nathanson, 2017). Individuals with complete androgen insensitivity syndrome (AIS) have very low risk of testicular malignancy in childhood or adolescence, do not develop masculine secondary sex traits in puberty, and derive a high bone health benefit from endogenous hormone production; in these cases, it is generally recommended to defer gonadectomy until after puberty. Individuals with gonadal dysgenesis (in which gonads do not fully develop into ovarian or testicular tissue) have a higher risk of malignancy with little hormone production, and childhood gonadectomy is consistently recommended (Mouriquand et al., 2016). Some assigned girls with a 46,XY karyotype, testicular tissue, and full or partial androgen response, as in partial AIS or 5-alpha reducta[redacted] risk of malignancy and less predicta[redacted] at puberty. Gonadectomy is sometim[redacted] reduce distress and uncertainty arou[redacted] et al., 2016).

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For such people, gonadectomy can
sex hormone-producing gonadal tiss
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may require a lifetime of hormone replacement therapy. If the surgery is performed prior to puberty, people may be prescribed hormones congruent with their assigned sex rather than identified gender. Importantly, recent evidence suggests that puberty blockers may be a viable nonsurgical alternative to support gender identity exploration and allow time for informed consent, and in most cases, surgery need not be done in early childhood (Canalichio et al., 2020).

Feminizing Surgeries

Feminizing surgeries include clitoral and vaginoplasty surgeries. Clitoral surgery is most often recommended for 46,XX children with congenital adrenal hyperplasia (CAH) who are assigned female, with concerns primarily about genital "ambiguity" (Mouriquand et al., 2016). In recognition of inadequacies of earlier techniques, like clitoral amputation and recession, microsurgical approaches aim to preserve clitoral nerve and vascular supply, and in some cases they "bury" rather than remove parts of the clitoris should an individual wish to reverse the surgery in the future (Mouriquand et al., 2016). Vaginoplasty may also be recommended for assigned girls whose vaginas do not connect to the perineum, thereby limiting penetrative sex and impairing fertility and outflow of menstrual blood (Mouriquand et al., 2016). For assigned girls with shorter or absent vaginas and without uteruses (as in AIS, gonadal dysgenesis, or Mullerian agenesis), vaginoplasty carries the sole benefit of allowing penetrative intercourse.

There is some evidence that 46,XX women with CAH were satisfied with feminizing genital surgeries (Mouriquand et al., 2016). Reviewers have concluded from surveys of women who had undergone feminizing genitoplasty as children that women prefer earlier timing of surgery (de Jesus, 2018). Indeed, in one survey of adult women with CAH or AIS who had genital surgeries at an average of 3.8 years, 17 out of 24 reported that surgery had been done at the proper age (Fagerholm et al., 2011). However, these surveys are small and limited. Importantly, a large systematic review and meta-analysis found that only two studies surveyed 46,XX female CAH patients' satisfaction with surgery, of which the majority were satisfied (Almasri et al., 2018).

Long-term data regarding the reversibility of and sensory and sexual outcomes from these procedures are lacking, especially for more novel microsurgical approaches. Data regarding preserved sexual function after clitoral surgery is challenged by studies revealing significant rates of long-term sexual dysfunction and anorgasmia (de Jesus, 2018). Because studies of sexual quality of life may be confounded by psychosocial issues, attempts have been made to study postsurgical sensitivity objectively with a device capable of analyzing thermal and vibratory sensation. Many patients, however, have refused to participate in such studies, which may reflect discomfort or even trauma associated with previous experiences of medical care (de Jesus, 2018). Limited data suggest unfavorable patient satisfaction with cosmesis after vaginoplasty, as well as a high incidence of postsurgical vaginal stenosis. If this occurs, patients may experience pain with intercourse and require self-dilation or repeat surgery. While there has been some evidence supporting benefit of surgery for women with CAH, multiple studies of adult women with CAH find less frequent sexual activ-

ity and lower frequency of orgasm, including among the small reported number of people with CAH who did not undergo surgery (de Jesus, 2018). Notably, there are no objective scales validated to assess sexual function in women with intersex traits. There are few data evaluating long-term urological complications after feminizing genitoplasty.

Masculinizing Surgeries

Masculinizing surgeries aim to facilitate standing urination, penetrative intercourse, and a "cosmetically pleasing appearance" (Winship, Rushton, and Pohl, 2017). These procedures include hypospadias repair and phalloplasty. Hypospadias is characterized along a spectrum from distal (urethra opening near, but not at, the tip of the penis) to proximal (urethra opening at the base of the penis). Most individuals with distal hypospadias do not have differences of sex development (DSD), so this variation is not reviewed here.

Proximal hypospadias is often associated with diversity of penile and scrotal appearance, and at least one of three children born with proximal hypospadias and an undescended gonad will have other features of a DSD, such as non-XY karyotype (Romao and Pippi Salle, 2017). Phalloplasty may be recommended for 46,XY assigned boys born with a smaller than usual, or absent, penis. Although many of these children were historically assigned female, longitudinal data have revealed higher rates of gender dysphoria for those assigned girls than those assigned boys (Meyer-Bahlburg, 2005), and there is some evidence that urologists increasingly favor male sex assignment (Diamond et al., 2011).

The primary cited benefit of proximal hypospadias repair is avoidance of distress due to difference and stigma (Bush and Snodgrass, 2017), which is accomplished through achieving decreased spraying with urination and capacity for penetrative intercourse. Although long-term outcome studies for proximal hypospadias do not consistently track lower urinary tract symptoms, some studies have reported rates of lower urinary tract symptoms as high as 100 percent after proximal hypospadias surgeries (Gong and Cheng, 2017). Multiple studies have found persistent penile curvature and dissatisfaction with cosmesis after masculinizing surgeries (Tourchi and Hoebeke, 2013), and there is no commonly used objective measure of penile appearance after surgery (Gong and Cheng, 2017). Very few outcome studies for masculinizing surgeries have evaluated erectile dysfunction, and "most pediatric urologists do not follow patients into adulthood and have little experience in sexual medicine" (Winship, Rushton, and Pohl, 2017, p. 287). One study found that more than two-thirds of adult men with proximal hypospadias reported some sexual dysfunction and decreased sexual quality of life after surgery (Chertin et

al., 2013). Reoperations and complications may contribute to urinary and sexual dysfunction, with complicatio
and reoperation rates ranging from
2017). Higher rates of reoperations a
longer durations of follow-up, sug
may be important elements of studi
outcomes (Gong and Cheng, 2017).

Psychosocial Outcomes after Genital Surgery

Patient Considerations

The absence of holistic and validated tools for assessment of sexual well-being and gender identity, patient satisfaction, and patient-centered surgical outcome measures present significant challenges in identifying robust conclusions regarding the psychosocial risks and benefits of early surgery. There are, however, some data regarding the outcomes of psychosocial distress and gender identity in the context of surgery.

Avoidance of distress due to social stigma and bodily difference has been offered as an indication for feminizing surgeries (de Jesus, 2018), masculinizing surgeries (Bush and Snodgrass, 2017), and gonadectomy for patients who may develop discordant secondary sex traits at puberty (Mouriquand et al., 2016). Of note, as discussed in Chapter 11, evidence indicates greater rates of psychological distress for individuals with intersex traits than the general population, but there is very little research exploring why. Rather, much of the research and clinical discourse reveals an implicit bias that genital or sexual difference is *de facto* abnormal and distressing and that "normalizing" surgery is a solution to this problem (Dalke, Baratz, and Greenberg, 2020). One series of qualitative studies suggested that 46,XX assigned and identified females with CAH experience stigma in medical, social, and sexual settings related to their genitalia and secondary sex traits; however, these studies included both women who did and did not have surgery, suggesting that surgery did not fully protect women from experiencing stigma (Meyer-Bahlburg et al., 2017a, 2017b, 2018). Of note, there are very few robust data exploring the benefits of surgery for patients with intersex traits, especially those who do not have CAH. Because standard practice has been to perform surgery early, however, there are few studies evaluating rates of psychosocial distress or satisfaction among individuals who did not undergo surgery, nor is there clear evidence that genital surgery itself reduces psychosocial stress (Roen, 2019). In a series of interviews, parents of children who did not undergo genital surgery reported that their children had attended school, had friends, and had not experienced bullying or harassment (Human Rights Watch, 2017).

There is some evidence that early genital surgery may unintentionally compound psychosocial distress. Multiple studies report that genital examinations in childhood can be experienced as intrusive, aversive, stigmatizing, and objectifying, particularly when children are not engaged in dialog with their providers (Roen, 2019). Qualitative research suggests that shame and a sense of "differentness" are correlated with both feminizing and masculinizing interventions: "going through surgery as a child might highlight bodily difference as stigmatising rather than facilitating the management of shame" (Roen, 2019, p. 517). This finding is consistent with information from intersex people themselves, who report experiences of anger, guilt, and trauma related to early surgery that was carried out without their consent, especially when they did not receive adequate information about their bodies or the procedures that were performed on them (Human Rights Watch, 2017).

Of particular interest in genital surgery is gender outcomes, particularly given the risk of developing a gender identity discordant with a sex that was assigned at birth and then surgically reinforced. Some intersex traits, such as complete AIS, complete gonadal dysgenesis, and proximal hypospadias without DSD, are associated with very low likelihood of gender dysphoria (Meyer-Bahlburg et al., 2016). Other intersex traits are associated with much higher rates, such as 46,XY individuals with cloacal exstrophy who are assigned female (Meyer-Bahlburg, 2005). A systematic review and meta-analysis found that 8 to 13 percent of 46,XX assigned female individuals with CAH did not identify as female (Almasri et al., 2018), which is much higher than the estimated 0.6 percent population prevalence of transgender identity among the general population (Flores et al., 2016). One very small, non-U.S. study found 46,XX assigned males with CAH can also experience gender dysphoria (de Jesus, Costa, and Dekermacher, 2019). Few data have been published on gender identity among individuals with partial AIS, 5-alpha reductase deficiency, or 17-beta hydroxysteroid dehydrogenase deficiency. Most studies evaluating gender identity among individuals with intersex traits have taken a binary view of gender, which could underreport rates of non-cisgender identities. Sex assignment at birth has become increasingly nuanced and focused on patient-specific recommendations (Kolesinska et al., 2014). Early and irreversible interventions may limit opportunities for gender affirmation later in life, which supports deferral of surgeries until the person's gender identity and ability to participate in the decision are established.

Parental Considerations

As is discussed in Chapter 11, much of the psychosocial research on intersex issues focuses on the mental health of parents. This work suggests that parents of children with genital difference experience stress similar to parents of children with chronic illness and, in some cases, also have de-

pression, anxiety, and decreased mental health quality of life (Wisniewski, 2017). Parents report fearing that their children will be teased, excluded, or stigmatized because of their genital differences (Wisniewski, 2017), and reduction of parental distress is often cited as a benefit of early genital surgery. However, there have been no studies examining experiences of bullying among children with intersex traits, and thus no evidence is available to indicate that surgery reduces the risk of bullying. Surgeons may be more likely to find a child's preoperative genital appearance unsatisfactory than parents (Nokoff et al., 2017), and this possibility raises the question of whether parents' perceptions of their child's genitals are influenced by the medical team's implicit bias. Overall, there is no evidence that genitoplasty directly targets parental distress, nor is there evidence that parental distress is intolerable or cannot be addressed in other ways (Roen, 2019).

An important consideration around parents is the process by which they make decisions about their child's health care. One ethical concern involved in this process is informed consent. Ethicists generally assume that parents can give informed consent for their child's health care as actors in the child's best interests (AMA, 2018). However, some scholars have suggested that, because the uniqueness of intersex surgery might affect a child's fundamental human rights, a court order might be required for the parent to give informed consent (Dalke et al., 2020). Evidence has also challenged the integrity of informed consent at a micro-ethics level. One study of self-identified DSD clinics found gaps in informed consent processes: more than two-thirds of the clinics did not document discussion of risks of surgery, including additional procedures, sexual dysfunction, psychosocial distress, gender uncertainty, and that interventions could be deferred until a later time (Rolston et al., 2017). Even with sufficient information, the informed consent process may not be adequate when carried out with parents of a minor child, given the distress that parents experience (Tamar-Mattis et al., 2013). Many families lack access to psychological services to assist in information processing despite multiple consensus recommendations for such services (Rolston et al., 2017). There are emerging data suggesting that the way information is framed can bias families' decision making. For instance, adopting a position of equipoise and patient-centeredness can unintentionally move families toward the surgeon's recommended course of action (Timmermans et al., 2018), and several studies have suggested that families feel as though their options are "surgery or nothing" (Roen, 2019).

Alternatives to Genital Surgery

There is very little research regarding alternatives to surgical intervention. Some doctors have suggested that gonadotropin-releasing hormone analogs can be used in place of gonadectomy for pubertal suppression in

children whose gender identity or pubertal development is uncertain and that hormonal management of CAH can reduce the size of a clitoris as an alternative to surgery (Mouriquand et al., 2016). Vaginal dilation may be an option in place of vaginoplasty for some. The contours of psychosocial support, including limiting genital exams and engaging patients and families over time to involve them in decision making, are beginning to emerge but as yet have minimal supporting data (Roen, 2019). This approach offers the possibility of helping families and young people learn to cope with and reduce the distress that surgery seeks to, but may not, avert.

In an appraisal of the literature and expert opinion, the Endocrine Society has recommended that parents be counseled on the risks and benefits of surgery and be permitted to make what they feel is the best decision for their child (Speiser et al., 2018). Timmermans and colleagues (2018) found that this approach biases families toward surgery. A growing number of consensus groups and professional medical organizations, including the American Academy of Family Physicians[17] and Physicians for Human Rights,[18] have interpreted the risk-benefit ratio as unfavorable for early genital surgery in instances where the individual is too young to participate in the consent process (Elders, Sacher, and Armona, 2017; Krege et al., 2019; Toler and GLMA Policy and Government Affairs Committee, 2016). These organizations advise the provision of psychosocial support for both parents and children and deferral of early genital surgeries until the child can participate in the decision.

Several international human rights groups have identified early surgery in the absence of informed consent as a violation of the child's human rights to autonomy and an open future, and even as a kind of medical torture (Amnesty International, 2017; Human Rights Watch, 2017; United Nations General Assembly Human Rights Council, 2013; WHO, 2014). In July 2020, Lurie Children's Hospital in Chicago, Illinois, became the first hospital in the nation to publicly acknowledge the harms of early genital surgeries and to adopt a policy that "irreversible genital procedures should not be performed until patients can participate meaningfully in making the decision for themselves, unless medically necessary" (Shanley et al., 2020). Of note, while the statement committed to pausing all genital surgeries that were not medically necessary, it did indicate that there may be a difference in approach for individuals with intersex traits who have CAH relative to people who do not.

Overall, there is mixed evidence that surgery achieves its physical goals and scant evidence that it confers psychosocial benefit. The existing research does provide strong evidence of the risk of irreversible harm from

[17] See https://www.aafp.org/about/policies/all/genital-surgeries.html.
[18] See https://phr.org/news/unnecessary-surgery-on-intersex-children-must-stop/.

early genital surgery, including immediate postoperative complications and later revisions, as well as the potentially catastrophic risk of incorrect, surgically reinforced gender assignment. The absence of data on alternative affirming pathways means that there is very little evidence of benefit from deferring surgery. It also means, however, that there is very little evidence of harm from deferring surgery. Factoring in the human rights of children and evidence that individuals with diverse sexualities, bodies, and genders can and do thrive with affirmation and support from parents, peers, and communities, there is insufficient evidence of benefit to justify early genital surgery. Therefore, the deferral of surgery until a child can participate in the decision, except in scenarios with urgent medical need, such as urinary obstruction or immediate cancer risk, may optimize the benefits of informed consent, autonomy, and patients' physical, social, and emotional well-being.

SUMMARY AND CONCLUSIONS

Access to comprehensive, affirming, and high-quality health care services is a human right for all people. Ensuring access to care for SGD populations includes building supportive and protective structures at all levels, from the broad societal level to the level of individual provider practices. At the societal level, laws that guarantee access to health care services, health insurance coverage, and public health programs for all, regardless of sexual orientation, gender identity, and intersex status, are critical to the health and well-being of SGD people. Laws and policies that provide affordable, comprehensive health insurance coverage, such as Medicaid expansion by all states or some form of universal coverage, could combat health risks such as uninsurance and poverty among SGD populations.

CONCLUSION 12-1: Sexual and gender diverse populations need access to a full range of preventive, chronic, and acute health care services delivered in settings that are welcoming, affirming, and both clinically appropriate and culturally responsive.

Health services and procedures that are particularly important for the health and well-being of SGD populations include but are not limited to pre- and post-exposure prophylaxis for HIV; HIV treatment and care; abortion, fertility, and other reproductive health services; affirming mental and behavioral health care services; and gender-affirming care for transgender people. Transgender people, as well as lesbians and bisexual women, also need access to timely and anatomically appropriate preventive screenings.

Important aspects of providing culturally responsive and clinically appropriate care for SGD populations include but are not limited to creating affirming health care environments; using forms that are inclusive of diverse

identities and family structures; seeking to address social determinants of health and social needs; and requiring routine, high-quality cultural and clinical training on working with SGD populations for the health care and public health workforce. Efforts to promote quality of care and care coordination may have differential effects on populations experiencing disparities, making it important to assess the effects of these efforts on groups such as LGBT people, people with intersex traits, and intersectional groups such as LGBT people of color and people living with HIV. Entities that provide resources and guidance on affirming health care policies and environments for SGD populations include the Academy of Physician Assistants, GLMA: Health Professionals Advancing LGBTQ Equality, Association of American Medical Colleges, American Psychological Association, American Academy of Pediatrics, American Medical Association, National LGBT Health Education Center, and The Joint Commission.

CONCLUSION 12-2: Gender-affirming care, including puberty delay medications, mental health services, hormone therapy, and surgeries, is associated with improved mental and physical health for transgender people.

Gender-affirming care for transgender people, including non-binary and other gender diverse people, is an essential and medically necessary intervention to improve health and well-being. Provision of this care needs to be individualized and conducted in partnership between patients and their providers. Insurance coverage of gender-affirming services and procedures by public and private payers, according to the most updated expert standards in the field and without inappropriate age or other restrictions, is necessary to facilitate access to these services and to avoid discrimination on the basis of sex and gender identity.

CONCLUSION 12-3: Conversion therapy to change sexual orientation or gender identity and elective genital surgeries on children with intersex traits who are too young to participate in consent are dangerous to the health and well-being of sexual and gender diverse people.

Conversion therapy to change sexual orientation or gender identity can cause significant and life-long trauma. Elective genital surgeries on children with intersex traits who cannot participate in consent are similarly detrimental to health and well-being. The American Medical Association, American Academy of Family Physicians, American Academy of Pediatrics, American Psychiatric Association, American Psychological Association, GLMA: Health Professionals Advancing LGBTQ Equality, Physicians for Human Rights, the U.S. Department of Health and Human Services, and

the World Health Organization recommend that these procedures not be promoted or performed.

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