

TRANSGENDER AND GENDER NON-CONFORMING YOUTH

2018 edition

Jack L Turban, Annelou LC de Vries, Kenneth J Zucker &
Shervin Shadianloo



Photo Gillian Laub, Le Monde, 10.12.2014

Jack L Turban
Division of Child & Adolescent
Psychiatry, Massachusetts
General Hospital, Boston, MA,
2114, USA

Conflict of interest: none
declared

Annelou LC de Vries
Department of Child and
Adolescent Psychiatry, Center
of Expertise on Gender
Dysphoria, VU University
Medical Center, Amsterdam,
The Netherlands.

Conflict of interest: none
declared

Kenneth J Zucker
Professor, Department of
Psychiatry, University of
Toronto, Toronto, Ontario,
Canada

Conflict of interest: none
declared

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Transgender and gender nonconforming youth include children and adolescents who experience a marked incongruence between the gender assigned at birth and their gender identity (American Psychiatric Association, 2013). Over the past decade, there has been a remarkable increase in attention to transgender issues across the lifespan. Television has begun to highlight transgender individuals from childhood to adulthood (Zucker, 2007; Morrison, 2010). News outlets from *The New York Times Magazine* to *Le Monde* have explored the life experiences of transgender youth (Padawer, 2010; Rosin, 2008; Chayet, 2014). Legislative bodies have examined transgender rights through restroom access, hate crime legislation, insurance regulations, and anti-discrimination policies, with physicians playing key roles in these discussions (Schuster et al, 2016). These initiatives have ranged from protection of rights for transgender patients to discriminatory policies that put the wellbeing of transgender children at risk. In India, The Rights of Transgender Bill 2014 was recently introduced. The Canadian Senate passed Bill C-16 to expand anti-discrimination laws to cover transgender individuals. Legislation in the United States has fluctuated between Obama-era protections for transgender patients and Trump era restrictions, most recently a proposed ban on transgender service people in the military.

Parallel to this growing attention, there has been a marked increase in the establishment of specialized gender identity clinics for children and adolescents in North America and in Europe (Hsieh & Leininger, 2016), which likely reflects the marked increase in referrals that has been noted internationally (Aitken et al, 2015; Chen et al, 2016). The scientific literature on gender incongruence has expanded as well, with an influx of new studies on co-occurring psychological functioning, long-term follow-up studies, biological correlates, and outcomes of medical interventions. Practicing child and adolescent psychiatrists should be familiar with the basics of this field to appropriately assess and help these patients.

TERMINOLOGY AND DEFINITIONS

Terminology in this specialized area is continuously evolving. This section describes terms and definitions that are in common usage in 2018, but different regions, cultures, and families may have their own preferred terminology (see Table H.3.1).

The term *gender assigned at birth* refers to a newborn's gender (boy, girl, indeterminate), as generally declared by a medical professional. Other relevant terms include *natal sex* and *birth sex*. The term *biological sex* is somewhat vague, as it is unclear whether it would be based on karyotyping of the sex chromosomes, internal reproductive structures, the configuration of the external genitalia, etc. The vast majority of newborns are assigned the gender of boy or girl through prenatal diagnostics or, at birth, based on genital anatomy. A small number of newborns may be classified as having a "disorder of sex development" or what others have called "differences of sex development" (Hughes, 2006), congenital conditions in which biological parameters of sex (e.g., the sex chromosomes, the gonads, the configuration of the external genitalia, etc.) are incongruent with one another. These conditions include complete or partial androgen insensitivity syndrome, mixed gonadal dysgenesis, 5-alpha-reductase deficiency, penile agenesis, and congenital adrenal hyperplasia, among others. Such patients may

Shervin Shadianloo

Department of Child and Adolescent Psychiatry, Center for Transgender Care, Hofstra Northwell School of Medicine, 75-59 263rd St Glen Oaks, NY 11004, USA

Conflict of interest: none declared

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experience gender identity issues different from those experienced by individuals without a disorder of sex development (Meyer-Bahlburg et al, 2016).

Experienced gender or gender identity refers to one's sense of self as a boy, as a girl, or some alternative gender that is different from the traditional boy-girl dichotomy (e.g., "gender fluid," "agender," or "non-binary"). Other terms include *affirmed gender* (typically used for individuals who have transitioned socially to living as the desired gender). For the majority of individuals, experienced gender matches the gender assigned at birth. These individuals are referred to as *cisgender*. For some patients, experienced gender is opposite to the gender assigned at birth, and are referred to as *transgender*.

Gender expression refers to the way in which one presents to the outside world in a gendered fashion and may include pronoun use, clothing, and other external markers. *Gender nonconformity* refers to a person's gender expression that differs from socially anticipated gender expressions, which are binary in many cultures. These anticipated gender expressions vary from culture to culture and may vary from time to time within a single culture. *Gender expression* is different from *gender identity* in that an individual may carry and express themselves in a way that is not expected in their culture but continue to identify as their gender assigned at birth.

This may also be part of the psychosexual development of a child before, during and after puberty. The term *gender role* is also used in a similar way to *gender expression* but may be limited to behavior and is less inclusive than *gender expression*.

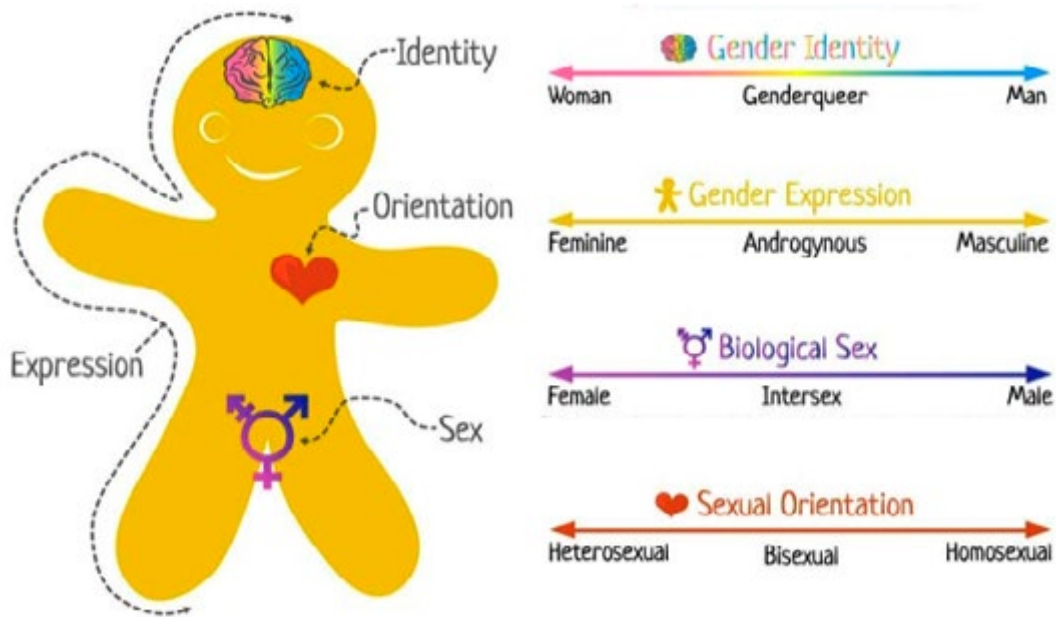
Transgender and *gender variant identities* are sometimes used as terms for individuals whose experienced gender does not strictly match the gender assigned at birth. Persons who experience psychological distress in relation to their gender identity may be referred to as *gender dysphoric*. "Gender dysphoria" is the diagnostic term adopted in the DSM-5 (see below) (American Psychiatric Association, 2013).

Sexual attraction or *sexual orientation* is a separate concept from gender identity. Sexual orientation refers to the type of individuals toward whom one is romantically or sexually attracted. Terms such as *androphilia* (attraction to males), *gynephilia* (attraction to females), *biphilia* (attraction to males and females), and *aphilia* (attraction to neither males nor females) have become more common, slowly replacing older terms such as heterosexual, bisexual, homosexual, and asexual, though this terminology can also be confusing as it does not explain if individuals are attracted to a specific gender assigned at birth, a specific gender identity, a specific gender expression, etc. In the scientific literature, the sexual orientation of individuals who identify as transgender has been described in relation to their experienced gender or their gender assigned at birth. For example, an adolescent female who identifies as male and is sexually attracted to females may be described as "heterosexual" in relation to experienced gender but as "homosexual" in relation to birth sex (Lawrence, 2010). From either a clinical or research perspective, it is critical to identify the frame of reference when describing a patient's sexual orientation. Most individuals who identify as transgender will describe their sexual orientation in relation to their gender identity, not their gender assigned at birth (e.g., a transgender woman who is attracted to men would likely consider herself to be heterosexual).

"Until I was about four or five I didn't know I wasn't a girl, to be honest with you. One of my earliest memories, about five years old, was being yelled at by a teacher for going to the toilet with the girls. About the same age I realised I was different to these other boys. At the age of nine I refused to have my hair cut. I didn't have it cut until I was 16, because having it cut was such a torment to me.

School was extremely difficult. I got bullied a lot. I was picked on for being too thin, for being feminine, for not liking football, for hanging round with girls, for having long hair. They mocked everything they could think of in terms of gender and sexuality."

The Guardian

Figure H.3.1 The “Genderbread Person”

The “genderbread person” is a tool designed by Sam Killermann to explain the distinctions between experienced gender (termed gender identity here), gender expression, gender assigned at birth (termed biological sex here), and sexual or romantic orientation. This educational tool may be useful for students new to the field and when explaining these phenomena to families with gender nonconforming and gender dysphoric children. These terms are further described in table H.3.1.

The “genderbread person” has been developed as an educational tool to clarify the distinctions among *gender assigned at birth*, *experienced gender*, and *sexual orientation* (Figure H.3.1). Note that as a published educational instrument, this graphic diverges somewhat from the contemporary terminology we describe. Nonetheless, this tool has proven useful for introducing this terminology to families and students new to the topics of gender and sexuality. The [gender unicorn](#) is another popular graphic that highlights the dimensional aspects of gender identity, gender assigned at birth, and sexual or romantic attraction.

UNDERSTANDING GENDER IDENTITY AND GENDER NON-CONFORMITY AROUND THE WORLD

Most of the current literature regarding gender non-conforming, gender variant and transgender youth is predominantly from Western countries. Given the intangible nature of gender, gender identity and its expression, cultural differences in how gender is understood and expressed may effect the approach to these individuals. National Geographic recently tackled the complex topic of gender in a [special issue](#).

To work with gender non-conforming, gender variant and transgender individuals from different cultures, or to apply current practice guidelines in different cultures, various factors need to be taken into consideration. Gender may be defined differently based on the language spoken. Language is the major mode of creating and describing concepts as well as the emotions associated with them.

Table H.3.1 Terminology

TERM	DEFINITION
<ul style="list-style-type: none"> Gender assigned at birth Natal sex Birth sex 	Gender assigned to an infant at birth, generally based on observed physical characteristics (genitalia etc.)
<ul style="list-style-type: none"> Experienced gender Gender identity 	Individuals' psychological understanding of their own gender
<ul style="list-style-type: none"> Affirmed gender 	Individuals' psychological understanding of their own gender, typically referring to living socially as that understood gender
<ul style="list-style-type: none"> Sexuality Sexual orientation 	Refers to the type of individuals towards whom one is romantically and/or sexually attracted
<ul style="list-style-type: none"> Gender incongruence 	Refers to individuals whose gender assigned at birth and gender identity do not match
<ul style="list-style-type: none"> Gender role 	A characteristic that is considered "male" or "female" by a particular culture
<ul style="list-style-type: none"> Gender expression 	An individual's outward presentation of their gender identity. Typical examples include, but are not limited to, clothing, hairstyles, and activities
<ul style="list-style-type: none"> Transgender 	Refers to individuals whose gender identity is incongruent with that assigned at birth. This term is often used for individuals who are transgender in a binary fashion but may also be used as an umbrella term for persons with any gender identity other than cisgender (see below).
<ul style="list-style-type: none"> Transsexual 	Typically used to refer to individuals who desire medical interventions to align their anatomy with their gender identity. This term has been used synonymously with transgender by some and has largely fallen out of favor
<ul style="list-style-type: none"> Transman 	A transgender individual who identifies as male (typically with a female gender assigned at birth)
<ul style="list-style-type: none"> Transwoman 	A transgender individual who identifies as female (typically with a male gender assigned at birth)
<ul style="list-style-type: none"> Gender dysphoria 	Refers to psychological distress in relation to one's experienced gender; is also the classification used in DSM-5 (when fulfilling certain clinical criteria). Note that not all patients with gender incongruence will experience dysphoria.
<ul style="list-style-type: none"> Cisgender 	Refers to individuals whose experienced gender matches the gender assigned at birth
<ul style="list-style-type: none"> Gender non-conforming Gender variant 	Refers to variation from developmental norms in gender role behavior that may be considered as non-gender stereotypical. This may include identifying as both genders or identifying with neither, among others. Some transgender individuals who identify on the gender binary (i.e., male or female) also identify with these terms.
<ul style="list-style-type: none"> Cross-sex hormones 	This term refers to the estrogen or testosterone treatment that induces the development of female and male secondary sex characteristics respectively
<ul style="list-style-type: none"> Gender affirming care 	Refers to treatments aimed at supporting a patient in that patient's gender identity. This may include mental health, medical, legal, and surgical aspects of care.
<ul style="list-style-type: none"> Gender identity exploration 	Refers to a process in which a patient is allowed to explore gender identity. Treatment should not have a gender identity (cisgender, transgender, or otherwise) as a goal of therapy. Rather, patients should be permitted to explore the different possibilities to better understand the best fit for them

Gender, being a core feature of identity, is influenced by the language spoken. In some languages the words for sex and gender are the same. This may make it harder to differentiate between gender identity versus anatomical sex. It is important to also note that some languages are grammatically gendered and some are not. In languages that are grammatically gendered (e.g., Spanish), use of pronouns can be an important topic and become a milestone in transitioning; however, this may vary if the language spoken is non-gendered. About one quarter of the world's languages are grammatically gendered. In these languages each noun is assigned to one gender, typically, masculine, feminine, neuter. Most cultures appear to have followed a binary anatomical sex and created their language and culture based on this presumed dichotomy. In contrast, other cultures have specific words to describe aspects of gender identity that may fall outside of a binary concept of gender such as *hijra* in India, *two-spirit* in some Native American tribes, and *men-women* in Balkan communities.

Historically, Middle Eastern, North African and European cultures recognized and had terms for transgender people. This includes *hijra* in India, *Mukhannath* in Islam and Arabic cultures, *Phrygia* in ancient Greek, and *Cybele* in ancient Roman. These individuals were often intersex people or natal males castrated for religious or other reasons. It is important to note that the recognition did not necessarily protect these individuals from stigma and marginalization, and in some places like India, *Hijras*, although believed to have power to remove a “bad spell” from newborns, were highly stigmatized. Meanwhile there have been new movements to support and protect transgender people in this region. The Rights of Transgender Persons Bill, which provisions anti-discrimination and employment for transgender people, was introduced in 2014 in India; it may result in positive changes in the future. Another example is the *Fatwa* from the Iranian Supreme Leader, Ayatollah Khomeini, after the 1979 Islamic Revolution, that allows transgender people to transition to their identified gender.

It is beyond the scope of this chapter to review the concept of gender identity in all different cultures; we bring these examples to highlight the cultural variation about how gender identity is understood. There are many countries that have no literature on the care of gender non-conforming, gender variant, and transgender people. Transgender identity and gender non-conformity continue to be highly stigmatized around the world. In East Asia alone, perspectives vary significantly. Thailand has the highest number of gender affirming surgeries in the world. In China, there are limited if any services for transgender people.

Working with children and youth presenting with gender issues requires knowledge of the child's psychosexual development, cultural aspects of gender and its expression in that specific society and family unit, as well as their exposure and understanding of the expanding information and media awareness around gender non-conformity and transgender identity. In the case of working with immigrant families, understanding the interaction of the host and home cultures is also important.

HISTORY OF GENDER IDENTITY AND MEDICINE

John Money (1921-2006) was a psychologist and sexologist whose empirical and theoretical contributions regarding gender identity, gender role, and gender



Click on the picture to access Mermaids, UK site that provides information and support for children and teenagers with gender identity issues

development were innovative and of great influence, beginning in the 1950s. Money originally proposed a theory of “gender neutrality,” suggesting that gender identity was predominantly determined by social factors, including the gender assigned at birth and subsequent socialization processes (Money et al, 1957). Money proposed that, for individuals with a disorder of sex development, early surgical interventions to correct genital ambiguity were often needed so that a child could then be supported with rearing in the gender assigned at birth.

Over the past few decades, Money’s original theory of gender neutrality at birth has been challenged by various lines of evidence suggesting the importance of biological factors, particularly patterns of prenatal hormone exposure, that also contribute to gender identity formation and differentiation. For example, chromosomal females with congenital adrenal hyperplasia who were assigned female at birth are exposed to elevated levels of prenatal testosterone; many of these girls are “behaviorally masculinized” and a higher percentage than the general population develop gender dysphoria and transition from female to male (Dessens et al, 2005; Pasterski et al, 2015).

Perhaps the most widely cited case pertains to a biologically “normal” male (one of a pair of identical twins) who, after a circumcision accident at the age of 7 months that led to penile ablation, underwent a vaginoplasty and was socially re-assigned to female at the age of 17 months. Although this patient was described by Money as a “tomboy” during childhood, subsequent follow-up revealed that the patient rejected estrogen therapy at the time of puberty and subsequently transitioned back to living as a male (Colapinto, 2000; Diamond & Sigmundson, 2004). Tragically, he committed suicide at the age of 38 (The Associated Press, 2004). The “John-Joan” case, as it was called, has been used as evidence of the importance of biological factors in contributing to a person’s sense of gender identity. A subsequent summary of seven similar patients reared as female after traumatic loss of the penis have shown both male and female gender identities in adolescence and adulthood, further complicating the picture (Meyer-Bahlburg, 2005).

In the 1960s, research into the developmental histories of adults with “transsexualism” suggested that childhood cross-gender identification was common in these individuals (Green, 1974). This work was followed by research with children who showed patterns of gender-related behavior similar to the recalled patterns of transsexual adults (Green, 1974). During this period, there was much less attention given to adolescents with a marked history of cross-gender identification.

By the late 1990s, however, more attention was given to adolescents with a DSM diagnosis of gender identity disorder, including the possibility of treatment with gonadotropin releasing hormone analogs, as reported by a research team in the Netherlands (Cohen-Kettenis & van Goozen, 1998). This approach, described below, was ultimately outlined in the 2009 Endocrine Society Guidelines for the Treatment of Transsexual Persons (Wylie et al, 2009), and in the periodically updated World Professional Association for Transgender Health (WPATH) Standards of Care (Coleman et al, 2011). Research into these hormonal interventions has since garnered significant attention, including increased NIH funding to study the long-term benefits and risks of these treatments (Reardon, 2016).

“I have lived two thirds of my life as female and a third as male. I graduated from high school as a girl and from college as a guy; those five years were the most difficult yet joyous and rewarding of my life.

I was afraid to take this step toward medical transition; afraid I would lose everyone I loved, afraid of what I would look like, afraid of what people would say and what a freak they would think I am. I thought I would have to move far away and never talk to my parents, extended family, or friends again. I am happy to say I was very wrong.

It has taken a lot of time, patience, and communication, but for the most part I did not lose anyone I love, and the people I did lose were not real friends in the first place. Nothing has turned out like I thought it would when I first started transitioning; instead of being shunned and vilified by people from my past, I have been received warmly and lovingly. I have made many amazing friends and had many incredible experiences along the way.”

The New York Times

It should be noted that a large number of transgender individuals are rejected by their families. This leads to high rates of homelessness among them.

DIAGNOSIS AND ASSESSMENT

Assessment of youth presenting with gender-related concerns requires a developmental history that explores general psychological development, gender development, and a careful analysis of the child's environment and safety related to expressed gender non-conforming behaviors. Various developmental theories may provide assistance in understanding and categorizing children based on their age in regards to gender development. The DSM-5 has criteria for diagnosis of gender dysphoria in both children and adolescents. Gender dysphoria is a clinical diagnosis and requires in depth and longitudinal evaluation of these youth. Several scales have also been developed to help with the assessment of gender non-conforming youth (The Utrecht Gender Dysphoria Scale, The Gender Identity/Gender Dysphoria Questionnaire for Adolescents and Adults, among others), though none of these alone can establish a diagnosis. The evaluation of gender, in addition to the usual developmental and mental health evaluation of a child, needs to include a thorough chronological history of the child's gender expression and identity from parents and caregivers as well as a developmentally informed evaluation of the child's gender individually. The evaluator may use tools such as toys, books, drawing or playing materials to assist in the evaluation and gather information about behavior at school, with peers and at home.

Families play a key role in the evaluation. A child's gender variance has a significant impact on the family dynamics and may lead to conflicts and disruption of emotional attachments. It is important that these issues be identified and efforts be made to include all parties involved in the child's life regardless of the child's age.

Safety is a complex matter in the lives of gender non-conforming and transgender youth. Mental health practitioners need to be aware and look for overt and covert aggression and risk to the child due to being a sexual and gender minority, in addition to the usual safety issues. Bullying, risk of being kicked out of home, societal violence, and local legislation prosecuting or endangering a youth need to be considered and documented.

CLASSIFICATION

Gender identity diagnoses first entered the DSM in its third edition with three diagnoses: transsexualism, gender identity disorder of childhood, and atypical gender identity disorder (American Psychiatric Association, 1980). The essential feature of these three diagnoses was "an incongruence between anatomic sex and gender identity" (American Psychiatric Association, 1980). Revisions in the DSM-III-R were modest, though, in this edition, exclusion of individuals with schizophrenia or a disorder of sex development was removed, noting that individuals with either of these diagnoses could also have a "gender identity disorder" (American Psychiatric Association, 1987).

In the DSM-IV, the three diagnoses from DSM-III were collapsed into the overarching diagnosis "gender identity disorder," with distinct criteria sets for children versus adolescents and adults (American Psychiatric Association, 1987). This edition also added a criterion stating "The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning" (Vance et al, 2010).

Table H.3.2 Summary comparison of diagnostic criteria for gender dysphoria in children and in adolescents and adults according to DSM-5

GENDER DYSPHORIA IN CHILDREN	GENDER DYSPHORIA IN ADOLESCENTS AND ADULTS
<p>A marked incongruence between one's experienced/expressed gender and assigned gender (one of which must be a strong desire to be of the other gender or an insistence that one is the other gender or some alternative gender different from one's assigned gender), of at least 6 months' duration, as manifested by at least six of the following.</p>	<p>A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by at least two of the following:</p>
<ul style="list-style-type: none"> • In boys (assigned gender), a strong preference for cross-dressing or dressing as female; or in girls (assigned gender), a strong preference for wearing only masculine clothing and a strong resistance to wearing feminine dresses. • A strong preference for cross-gender roles in make-believe play or fantasy play. • A strong preference for toys, games, or activities stereotypically used by the other gender. • A strong preference for playmates of the other gender. • In boys (assigned gender), a strong rejection of masculine toys, games, and activities and a strong avoidance of rough-and-tumble play; or in girls (assigned gender), a strong rejection of feminine toys, games, and activities. • A strong dislike of one's sexual anatomy. • A strong desire for the primary and/or secondary sex characteristics that match one's experienced gender. 	<ul style="list-style-type: none"> • A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics). • A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics). • A strong desire for the primary and/or secondary sex characteristics of the other gender. • A strong desire to be of the other gender (or some alternative gender different from one's assigned gender). • A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender). • A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender).
<p>The condition is associated with clinically significant distress or impairment in social, school, or other important areas of functioning.</p>	

DSM-5 renamed gender identity disorder as “gender dysphoria,” aiming to decrease stigma associated with the diagnosis while maintaining a diagnosis that could be used to secure access to care for those who needed it (Vance et al, 2010). DSM-5 removed sexual orientation subtyping but noted in the text its relevance in understanding variations in developmental trajectories, and for research on biological factors and long-term outcomes (American Psychiatric Association, 2013). DSM-5 also made the childhood diagnosis stricter, requiring more than just gender non-conforming behavior. The new criteria require that a child express an actual desire or insistence in being of the other gender. The adolescent and adult criteria simultaneously became more inclusive, allowing for non-binary gender identities that would allow for gender variant, but not strictly binary, transgender adolescents and adults to receive the diagnosis and subsequently access to care.

Current DSM-5 criteria for gender dysphoria in children require a marked incongruence between one’s experienced/expressed gender and assigned gender, of at least six months’ duration, as evidenced by at least six of eight criteria, one of which must be a strong desire to be of the other gender or an insistence that one is the other gender (or some alternative gender different from one’s assigned gender). Additionally, the patient must experience clinically significant distress or impairment in social, school, or other important areas of functioning as introduced in the DSM-IV (see Table H.3.2). DSM-5 criteria for gender dysphoria in adolescents and adults are similar, though with different requirements for the manifestation of gender dysphoria. This diagnosis requires at least two of six manifestations (see Table H.3.2).

Some have argued for use of the term “gender incongruence,” including the Working Group on Sexual Disorders and Sexual Health for the forthcoming 11th edition of the International Classification of Diseases (ICD-11). This group suggested that the term “gender incongruence” highlights that not all transgender individuals experience dysphoria. The group notes that the term gender dysphoria might increase inappropriate stigmatization and pathologization. The group recognizes the necessity of diagnosis only for the purpose of preserving access to medical care. The group additionally argues that this diagnosis be moved out of the chapter on mental health and behavioral disorders and into another section, provisionally termed “conditions related to sexual health” (Drescher et al, 2016), though this brings up an additional issue of conflating gender identity with sexuality, as described in the terminology section above.



Click on the picture to access the site of the Gender Identity Research and Education Society (GIRES)

EPIDEMIOLOGY

A range of methodological challenges including, but not limited to, shifting terminology and stigma associated with self-identification, have made it difficult to establish the true prevalence of gender dysphoria or gender incongruence.

Prevalence in Adults

In adults, most studies have used the number of individuals that seek clinical care for gender affirming treatment as a proxy for determining prevalence in a certain country or catchment area. A recent meta-analysis based on 21 studies that applied this method concluded that the prevalence of transsexualism (the definition used in most of these studies) was 6.8 trans women in 100,000 gender

at birth assigned males (1:14,705) and 2.6 trans men in 100,000 gender at birth assigned females (1:38,461) (Arcelus et al, 2015). A time trend was also found, with recent studies reporting higher prevalence rates. These studies are, of course, limited by the fact that they do not include transgender individuals who do not seek gender affirmative healthcare. Indeed, much higher prevalence rates—ranging from 4.2 % having an ambivalent gender identity, to around 0.5 % identifying as transgender and considering medical interventions—are suggested by recent studies that have used broader definitions and probability samples (Conron et al, 2012; Kuyper & Wijzen, 2014; van Caenegem et al, 2015). A recent population-based survey in the US found that 0.6% of adults self-identified as transgender, with rates ranging from 0.3% to 0.8% in the states for which data were available. Compared to older age groups, young adults aged 18 to 24 were more likely to identify as transgender (Andres et al, 2016).

Prevalence in Children and Adolescents

Although formal epidemiological studies of gender dysphoria (previously known as gender identity disorder) in children and adolescents have not been conducted, looser or more liberal definitions of “caseness” have been examined in several studies. In a random sample of 2,730 Grade 6-8 students from San Francisco, Shields et al (2013) found that 1.3% self-identified as “transgender” in response to the question “What is your gender?” with the other response options being female or male. In a random sample of 8,166 high school students from New Zealand, Clark et al (2014) found that 1.2% self-identified as transgender and 2.5% reported that they were not sure about their gender, in response to the question “Do you think you are a transgender?” which was followed by a definition of the term. Interestingly, another 1.7% reported that they did not understand the question. In a study of 80,929 American high school students from the 2016 Minnesota Student Survey, 2.7% self-identified as transgender or gender non-conforming (Rider et al, 2018).

Gender Assigned at Birth Ratio

Of pre-pubertal children referred to gender identity clinics, the majority has a male gender assigned at birth. Among 577 Canadian children referred to a gender identity clinic between 1976 and 2011, the male-to-female ratio was 4.49:1 (Wood et al, 2013). This was significantly higher than the 2.02:1 ratio in the Netherlands (Aitken et al, 2015). These differences are theorized, in part, to be a reflection of increased parental anxiety regarding gender-variant behavior in males compared to females, particularly in North America. For adolescents with gender dysphoria, the gender ratio is much closer to 1:1 and appears to be more consistent across nations (Aitken et al, 2015). However, it is of note that there has been a recent temporal shift from more birth-assigned males prior to 2006, to more birth-assigned females from 2006 to 2013, though the ratio remains closer than 2:1 in either direction (Aitken et al, 2015).

BIOLOGICAL AND PSYCHOSOCIAL DETERMINANTS

The etiology of cross-gender identification and behavior continues to be elusive. While psychological and social factors were once the main focus of study, attention has shifted more recently to biological mechanisms. At present, the

evidence suggests that both psychosocial and biological elements are involved. A single mechanism is unlikely and gender dysphoria most likely results from a complex interaction between these factors (Steensma et al, 2013a).

Biological Factors

Twin studies suggest a strong heritable component with additional environmental contributors. In a large-scale CBCL study of Dutch twins (N=23,393) aged 7 and 10 (Coolidge et al, 2002), monozygotic (MZ) and dizygotic (DZ) twins were compared; genetic factors contributed to 70% of cross-gender behavior (as assessed via the two CBCL gender items). Another study of 314 MZ and DZ twins (mean ages 9.4 and 10.1 years, respectively) roughly replicated this finding, with genetic factors contributing up to 62% of the variance on a DSM-IV-based gender dysphoria scale (Coolidge et al, 2002).

Many studies, both in animals and humans, have shown that differences in brain anatomy and function in males and females underlie the sex differences in their behavioral characteristics (Hines, 2011). Sex hormones play an important role in these differences. The *organizational effect*, predominantly prenatally but also during puberty, leads to the sex differences in brain structures (Ruigrok et al, 2014; Giedd et al, 2012). On average, males have larger brain volumes, more white matter, gray matter, and cerebrospinal fluid than females, although when corrected for total volume, females have more gray matter and a larger volume of the cortex (Ruigrok et al, 2014; Guillamon et al, 2016).

The sexual differentiation hypothesis suggests that transgender individuals may have brain structures and brain functioning more closely aligned with their gender identity than with their assigned gender at birth (Swaab & Garcia-Falgueras, 2009). Post-mortem studies have suggested a sex reversal in several hypothalamic nuclei in transsexuals (Kruijver et al, 2000; Zhou et al, 1995). More recent neuroimaging techniques have allowed the *in vivo* study of brain morphology and functioning of larger numbers of adolescents and adults with gender nonconforming feelings (Kreukels & Guillamon, 2016). Before they received any medical gender affirmative treatment, brain anatomy with regard to volume, gray and white matter, and cerebrospinal fluid did not differ compared to their birth-assigned sex. Differences have been found with regard to white matter microstructure showing that transgender individuals lie between males and females (Guillamon et al, 2016). In the realm of functional neuroimaging, task-related studies show that transgender people may have either similar reactions as those of their experienced gender (e.g., smelling odorous steroids; Berglund et al, 2008) or activity different from their assigned gender as well as their experienced gender (e.g., mental rotation; Schoninget al, 2010), or not different from their assigned gender (e.g., verbal fluency; Soleman et al, 2013). Overall, results in the realm of neuroimaging are mixed.

In animal studies, where prenatal hormones can be manipulated, the strong effect of prenatal testosterone on gender role behavior is clear (Hines, 2011). The effects on gender identity, however, can only be studied in humans. Individuals with a disorder of sex development may be exposed to high levels of prenatal testosterone, and individuals with two X chromosomes with congenital adrenal hyperplasia (Merke & Bornstein, 2005) indeed have higher rates of gender dysphoria and cross-gender identification (Pasterski et al, 2015). However, the



In the US, the Trump administration withdrew in 2017 a federal guidance issued by the Obama administration in May 2016 requiring transgender students to have unfettered access to bathrooms and locker rooms matching their gender identity.

majority of female-raised individuals with congenital adrenal hyperplasia (~95%), appear to develop a female gender identity (Dessens et al, 2005). Other evidence for the importance of prenatal testosterone comes from studies in XY individuals with complete androgen insensitivity syndrome who lack the receptors necessary to respond to endogenous testosterone. The vast majority of these patients develop a female gender identity, suggesting that downstream testosterone signaling may be important for the development of a male gender identity (Mazur, 2005). Some have noted that these patients were reared unambiguously as females and that social factors may have played a strong role in their female identity formation (Hines, 2009). Some studies have shown that those with complete androgen insensitivity syndrome have lower scores on female identity scales (Richter-Appelt et al, 2005) and there are case reports of gender dysphoria ultimately leading in these patients to gender affirming surgeries (T'Sjoen et al, 2011). This could be secondary to the psychological stress of learning about the diagnosis, as well as the possibility of undetected functional androgen receptors (Steensma et al, 2013a). Overall, studies of gender identity in individuals with disorders of sex development, while implicating androgens in the development of gender identity, have yet to show a direct relationship.

Psychosocial Factors

Past literature has investigated the potential role of parental characteristics on the development of gender dysphoria (maternal wish for a child of the opposite gender, paternal absence, and parental psychological functioning, among others). None of these hypotheses have been validated (Steensma et al, 2013a). Mothers of gender dysphoric boys have been noted to have higher scores on the Beck Depression Inventory and the Diagnostic Interview for Borderlines (Marantz & Coates, 1991), but these higher scores might be due to external pressures placed on these parents by unaccepting social environments and such studies cannot determine the direction of causation. One study noted that gender dysphoric boys were rated as more feminine and “beautiful” by blinded college students (Zucker et al, 1993), while another study of gender dysphoric girls showed that these girls were rated as less “cute” (Fridell et al, 1996), raising the question of whether perceived physical appearance and resultant social treatment may contribute to gender incongruence. An alternative interpretation of this data is that those with a more male gender

identity might alter their appearance to appear more “masculine” (e.g., culturally masculine haircuts), while those with a more female gender identity alter their appearance to look more “feminine” (McDermid et al, 1998). Some have suggested that a lack of parental limit setting, particularly around cross-gender behavior, is associated with gender dysphoria (Zucker & Bradley, 1995), though this does not prove causation, as more insistence on cross-gender behavior (i.e., transgender identity or stronger cross-gender behavior preferences) may make this limit setting more difficult. Overall, there have been no proven causative psychosocial factors in the development of gender incongruence

CLINICAL COURSE

Persistence of Gender Dysphoria from Childhood to Adolescence

The natural history of gender identity for children who express gender nonconforming or transgender identities is an area of active research (Olson, 2016). To date, the long-term follow-up studies of clinic-referred children have been based on samples that have included children who were either threshold or sub-threshold for the gender identity diagnosis in DSM-III, III-R or IV and some of the earliest studies began prior to the availability of formal diagnostic criteria.

These follow-up studies have classified participants as either “persisters” or “desisters” with regard to gender dysphoria using various metrics (semi-structured interviews based on DSM criteria for gender identity disorder, dimensional scores on standardized questionnaires, etc.). Ristori and Steensma (2016) summarized 10 follow-up studies and reported that the percentage of participants classified as persisters ranged from 2% to 39% (collapsed across natal boys and girls). In one study (Wallien & Cohen-Kettenis, 2008), the percentage of natal girls who were “persisters” was substantially higher than the percentage of natal boys (50% vs. 12%), but in two other studies from the same clinic the percentage was similar across natal sex (Drummond et al, 2008; Singh, 2012).

One criticism of these studies is that either formal diagnostic criteria were not used (because they were not available at the time of the study) or that subthreshold cases were included. These subthreshold cases may have included individuals with cross-gender interests or behaviors who did not actually identify as transgender. It is perhaps not surprising that these patients did not identify as transgender at follow-up. Some studies have found that threshold cases were more likely to be classified as persisters (Steensma et al, 2013b), but other have not (Singh, 2012). It has also been suggested that more recent cohorts (after the year 2000) have found higher rates of persistence (12% to 39%) (Zucker & Bradley, 1995; Wallien & Cohen-Kettenis, 2008; Drummond et al, 2008; Singh, 2012) than older cohorts (2% to 9% prior to 2000) (Green, 1987; Zuger, 1984), suggesting that, as society becomes more accepting of these individuals, fewer report “desisting,” which may represent going back into the closet due to social pressures rather than a true desistence of cross-gender identification. Comparisons of persisters with desisters have found that the intensity of gender dysphoria (using dimensional metrics), older age at the time of assessment in childhood, a lower social class background, and having a female gender assigned at birth are associated with higher rates of persistence (Steensma et al, 2013b). Despite this work, it remains difficult to

predict the likelihood of cross-gender identification persistence from childhood into adolescence for an individual child (Steensma et al, 2013b).

Persistence of Gender Dysphoria from Adolescence to Adulthood

In contrast to the low rates of persistence from childhood into adolescence, it appears that the majority of transgender adolescents persist in their transgender identity (Cohen-Kettenis & Pfäfflin, 2003). In a study of 55 transgender adolescents receiving gender affirmative care, 100% continued to identify as transgender in young adulthood (deVries et al. 2014). Larger longitudinal studies such as this are needed.

Childhood Gender Variant Behavior and Sexual Orientation

Childhood gender variant behavior has been found to be a strong predictor of a same-sex sexual orientation in adulthood (using gender assigned at birth as a reference point). In a study of 879 Dutch boys and girls, gender variant behavior was assessed using the CBCL and sexual orientation was assessed 24 years later (Steensma et al, 2013c). It was found that the prevalence of a same-sex sexual orientation was, depending on the domain (attraction, fantasy, behavior, and identity), between 8.4 and 15.8 times higher in the gender variant subgroup as compared to the non-gender-variant subgroup. In summary, the current literature, though limited, suggests that the majority of gender nonconforming pre-pubescent children will grow up to endorse identification as cisgender individuals with either a bisexual or a same-sex sexual orientation (Wallien & Cohen-Kettenis, 2008; Singh, 2012; Green, 1987).

COEXISTING PSYCHIATRIC CONDITIONS

Children and adolescents with gender incongruence exhibit higher internalizing and externalizing psychopathology compared to non-referred controls, with internalizing psychopathology being more common, particularly in birth-assigned boys (Steensma et al, 2014; de Vries et al, 2016; Wallien et al, 2007; Skagerberg & Carmichael, 2013). One hypothesis is that this problem behavior is a result of stress due to being a minority and dysphoria toward their gender assigned at birth. These individuals are subjected to rates of peer bullying as high as 80% (Holt et al, 2016; Kaltiala-Heino et al, 2015; McGuire et al, 2010), and poor peer relations is one of the strongest investigated predictors for behavioral and emotional problems in gender nonconforming youth (de Vries et al, 2016). In a study of 105 gender dysphoric Dutch adolescents whose parents completed the Diagnostic Interview Schedule for Children, 32.4 % had one or more psychiatric disorders, with 21% suffering from anxiety, 12.4% from mood disorders, and 11.4% from disruptive disorders (de Vries, 2011).

Chart review studies of gender nonconforming youth presenting to specialized gender identity clinics have shown similarly high or even higher rates of psychiatric conditions: mood (12.4-64%), anxiety (16.3%-55%), and disruptive disorders (9-11.4%) (Holt et al, 2016; Kaltiala-Heino et al, 2015; de Vries et al, 2015; Olson et al, 2015; Spack et al, 2010; Khatchadourian et al, 2014). The range of prevalence across studies may be the result of cultural differences, varying diagnostic criteria, and differing ages at assessment. These psychiatric conditions appear to become more common in gender nonconforming individuals with

increasing age. Some studies have shown that older transgender youth suffer a greater burden of co-occurring psychiatric conditions (McGuire et al, 2010), and that gender nonconforming adults suffer a greater burden of co-occurring psychiatric conditions compared to adolescents (de Vries et al, 2011b).

Self-harming Behavior and Suicidality

Self-harming and suicide attempts are very prevalent among gender nonconforming youth. Gender clinics report high rates of past suicide attempts by patients presenting for care: Boston (9.3%, mean age 14.8; Spack et al, 2012), London (10%, mean age 13.5; Holt et al, 2016), Los Angeles (30%, mean age 19.2; Olson et al, 2015). Rates of self-harm and suicidality also appear to increase with age within this population (Aitken et al, 2016).

Autism Spectrum Disorder

A number of studies show that autism spectrum disorder (ASD) symptoms are over-represented among transgender individuals. The rate of ASD among the general population is estimated at around 1% (Lai et al, 2014). Clinical-level rates of ASD symptomatology in transgender adults have been reported in 5-20% (Jones et al, 2012; Pasterski et al, 2014; Pohl et al, 2014). It is important to note, however, that these studies measure autism symptomatology and did not necessarily make a diagnosis of true ASD. These scales can be elevated in non-ASD conditions including anxiety and depression. Social deficits among transgender youth may be secondary to social ostracism and not due to an underlying ASD. Two studies found increased gender variance (5.4%, 11.3%), defined by a positive response to “wishes to be of the opposite sex” on the CBCL or YSR in referred children, adolescents, and adults with ASD compared to non-referred controls (Strang et al, 2014; van der Miesen et al, 2016a). However, the same was true for an ADHD referred control group (Strang et al, 2018), raising the issue that a higher probability of gender variance is characteristic of clinic referred samples in general. It is also possible that youth with ASD may have rigid thinking that makes them (or their parents) more likely to endorse the CBCL items of “sometimes or often” wanting to be the opposite sex due to gender-atypical interests. This does not necessarily suggest a core gender identity that diverges from their gender assigned at birth (Turban & van Schalkwyk, 2018).

Clinically, the co-occurrence of gender dysphoria and ASD may complicate transgender care, as diagnosing gender dysphoria can be difficult (e.g., in the context of the rigid thinking characteristic of ASD). Additionally, language difficulties can make expression of gender dysphoria difficult for patients with ASD. Nonetheless, a comprehensive narrative review of the literature has shown a role for transition with pubertal blockade and cross-sex hormonal therapy in these patients following an extended diagnostic process (van der Miesen et al, 2016b). Using a [Delphi method](#), a group of experts on ASD and gender dysphoria published initial clinical guidelines for the assessment and treatment of patients with both conditions co-occurring (Strang et al, 2018). Careful diagnosis of both conditions by specific specialists, collaboration between clinicians from both fields, and risk assessment and safety issues are part of the suggested management protocol.



Click on the image to access the 2017 endocrine society guidelines

THERAPEUTICS

Treatment of Prepubescent Children

The treatment for children with gender dysphoria has been the subject of intense controversy recently (Drescher & Byne, 2012). As noted below, there are three broad approaches that have been delineated in the literature:

- The oldest—characterized by Dreger (2009) as the “therapeutic model”—consists of efforts, either directly (e.g., via specific suggestions that parents can implement in the day-to-day environment) or indirectly (e.g., via psychodynamically-informed approaches that treat the putative underlying “causes” of the gender dysphoria) that actively attempt to reduce cross-gender identification.
- An intermediate approach—described by some as “watchful waiting” (Drescher & Byne, 2012)—in which no direct efforts are made to “prohibit” a child’s gender-variant behavior, but that also advises parents to keep options open about the child’s long-term gender identity and to avoid early social transition.
- More recently, an approach—characterized by Ehrensaft (2012) as the “affirmative model”—that considers all outcomes of gender identity to be equally valid and desirable and allows children who express a desire to socially transition to do so after careful counseling.

These approaches have been discussed in great detail in three reports (American Psychological Association, 2015; Adelson, 2012; Byne et al, 2012), in a special volume of the *Journal of Homosexuality* (Drescher & Byne, 2012), and in various other essays and case reports, the references for which can be found in these major reviews.

For the non-specialist, there are several key issues to keep in mind when appraising this literature:

- Some of these approaches may be influenced by particular theoretical formulations regarding the determinants of gender dysphoria and these formulations guide or influence recommended treatment plans.
- There are no randomized controlled trials comparing the effects of these treatments with regard to both short-term and long-term outcomes. Indeed, Byne et al (2012) noted that, by and large, “the highest level of evidence [...] can best be characterized as expert opinion.”
- With some rare exceptions (Meyer-Bahlburg, 2002), there are no manualized or even semi-manualized treatments that a clinician can follow in developing a therapeutic plan.

Thus, clinicians need to educate themselves by reading about the therapeutic model that they intend to follow and tailor it on a case-by-case basis. Below, we provide brief summaries of these three treatment approaches.

Promoting Identification with the Gender Assigned at Birth

This approach aims to reduce through psychosocial interventions the child’s cross-gender identification and gender dysphoria. These treatments

(described in the literature since the 1960s) have been quite varied. They include classical behavior therapy, psychodynamic therapy (including psychoanalysis and dynamically-informed play psychotherapy), parental counseling, and parent-guided interventions in the naturalistic environment (e.g., encouragement of peer relations of the same natal sex) (Meyer-Bahlburg, 2002). None of these treatments have been found to be effective and are not recommended.

The underlying assumption of all these approaches rests on the view that gender identity is not yet fixed in childhood and may be malleable through psychosocial treatment. There is also an implicit assumption or value judgment that might be inferred from this approach, namely, that all things considered, a child's long-term adaptation might be easier if he or she could come to feel content with a gender identity that matches their natal sex.

Critics of this approach have argued that there is nothing inherently “wrong” with a cross-gender identity and have challenged the view that trying to change such an identity is warranted. Indeed, there are now several US states and one province in Canada that have legislated that it is inappropriate to try and change a minor's gender identity when the minor is unable to consent to the treatment. Exempt from this directive is “identity exploration,” which is different in that it does not consider cis-gender identification to be a preferable outcome (Green, 2017). Critics have also noted that some of the earliest proponents of this treatment held the belief that it might reduce the odds of the child later development a same-sex sexual orientation (Pleak, 1999), although others rejected this as unethical (Zucker, 1990). Another concern has been that these treatments might cause a child to feel shame or other negative and maladaptive feelings (Adelson, 2012).

Watchful Waiting

The second approach takes an intermediate therapeutic position. On the one hand, it does not recommend an early gender social transition on the grounds that the extant follow-up studies have suggested that the majority of children with gender dysphoria may desist for one reason or another (see above for the limitations on these studies). On the other hand, it does not explicitly recommend any type of limit-setting on the child's gender variant behavior, with the exception that in certain environments it might be risky or dangerous to display such behavior, which Hill and Menvielle (2009) described as the “only at home” rule.

This approach also does not favor one type of long-term outcome over another, noting that it is difficult to predict outcome for an individual child and that the more important focus should be on the child's general psychosocial adjustment and wellbeing. This approach does, however, include recommendations to parents to encourage in their child a variety of gender-related interests and social affiliation with children of both genders. In some respects, the “watchful waiting” label is a bit of a misnomer because clinical protocols appear to include information provided to the parents that is more than “wait-and-see.” As noted by de Vries and Cohen-Kettenis (2012), appropriate limit-setting with good explanation of why the limits are set may be helpful, so that the child will learn “that not all desires will be met,” which is important because “someone's deepest desire or fantasy to have been born in the body of the other gender will never be completely fulfilled.” Although social transition according to this approach is not recommended at a very young age, an increasing number of children have already socially transitioned



Click on the image to view a clip about the treatment issues facing transgender adolescents in Australia.

when they come to gender identity clinics (Steensma & Cohen-Kettenis, 2011). Some of these children may have no clear memories of a time when they were socially living in the birth assigned gender and have stopped talking about being born different from their experienced gender. In these cases, it is encouraged that parents create an open situation where the child has the possibility of returning to the birth assigned gender. It is discussed with the child that, when gender identity feelings change, it is nothing to be ashamed of, that nobody will be angry, that the child may speak out, and that it is good to have tried. A form of psychotherapy that helps the child to verbalize his or her feelings may be advised so that, by the time the child may come back for the administration of gonadotropin releasing hormone analogs, the child is able to talk about his or her feelings and can give informed consent.

Affirmative Approach

The affirmative approach theorizes that clinician and parental attempts to push children with gender incongruence to conform with their gender assigned at birth might produce shame and stigma that can ultimately lead to psychopathology (Ehrensaft, 2012). It considers all outcomes of gender identity to be equally desirable and affirms any gender identity the child expresses.

Though similar to the watchful waiting model, an important difference is in its attitude regarding early social transition. In the affirmative model, prepubertal children who express a desire to socially transition and live full time in their experienced gender (i.e., using cross-gender pronouns, a cross-gender name, cross-gender clothing, etc.) are allowed to do so. The approach to social transition must be carefully individualized with a nuanced understanding of the child's gender identification and the level of support within the child's community; there must also be an open discussion with the child highlighting that, despite the social transition, the patient is free to transition back at any time (Edwards-Leeper et al, 2016).

This transition back to living as one's birth gender can be difficult (Steensma & Cohen-Kettenis, 2011), though this must be weighed against the potential negative consequences of refusing to affirm a child's identity and desire to transition socially. The affirmative model hypothesizes that lack of affirmation might lead to shame and consequent psychopathology. The therapeutic relationship in these cases could also be negatively affected if the clinician strongly discourages an early transition for a patient who persists in cross-gender identification.

Critics of social transition in prepubertal children have questioned whether early social transition increases the rate of persistence of gender incongruence from childhood into adolescence. Indeed, a multivariate regression analysis revealed that early social transition was associated with persistence (Steensma et al, 2013b). However, the direction of this association cannot be determined in this study. While some believe that prepubertal social transition makes children more likely to persist, the alternative interpretation is that those likely to persist are also more likely to undergo early social transition, due to currently unidentified factors. Additionally, this raises the ethical question of whether persistence should be considered an undesirable outcome. The affirmative model suggests that all outcomes of gender identity are equally desirable.

Some people call it “transgender regret.” When you change from one gender to another and then feel, somehow, you’ve made a mistake. Others call it “detransitioning” or a “reversal”. Zahra Cooper calls it, simply “going back”, as she told the [New Zealand Herald](#). [...] For four years, she struggled between the genders, being bullied at school and online for being “weird”. At 18, she asked her family to start calling her “Zane” and using male pronouns. She began to think about formally transitioning — taking hormones to become more masculine. [...] In December 2015, Zahra began taking testosterone, at first swallowing pills three times a day, and then via injection. After what seemed such a long wait for treatment, she expected to feel elated. But the euphoria many trans people describe at that point never really set in. “I started getting really angry from the testosterone, which is a side effect,” she says. “But then I started getting depressed. I was like, why am I depressed? I should be happy.” As the physical changes began, Zahra grew more and more anxious. She fought with family, often storming out of the house. “I was getting a deeper voice, facial hair and many other changes but I just wasn’t happy with them,” she says. “I didn’t feel like myself.” Then eight months in, things hit crisis point. Zahra tried to kill herself. Twice. [...]

Zahra had begun dating a transgender boy called Tyson Kay. Tyson is 17. He too was assigned female at birth, and at the time of Zahra’s breakdown was in the middle of his own transition to male. “I didn’t know how he would feel,” she says. Going off testosterone meant more mood swings, and an unpredictable end result. She didn’t know whether he would want to hang around, and worried over how to break the news. In the end, Zahra texted him saying: “I’m going to transition back”.

Separate from the question of persistence is the question of mental health outcome following social transition. There is a paucity of literature studying the effect of prepubertal social transition. One study examined 73 American prepubertal children who were transgender in a binary fashion and allowed to transition socially. Parents of these children completed short rating scales for anxiety and depression at an unspecified time following the transition (Olson, 2016a). Data from these scales revealed that these children had notably lower rates of internalizing psychopathology than previously reported for children who did not transition. Furthermore, socially transitioned children in this study showed developmentally normal levels of depression and only minimally elevated (subclinical) levels of anxiety. It is important to note that families in this study had a relatively high income, raising the question of whether this cohort is representative of a broader socio-demographic population (Olson, 2016a). Though this early work suggests that socially transitioned children have better mental health metrics than children who did not socially transition, future research is needed to fully understand the dynamic and long-term effects of social transition in a broader population (de Vries et al, 2014).

Treatment of Adolescents

Once children reach puberty, transgender identity persists in the majority of cases and medical intervention is often considered. At present, the effectiveness of an approach that includes puberty suppression followed by hormone administration and surgery has been evaluated in two studies in the same cohort of Dutch adolescents. The first study evaluated gender dysphoria and psychological functioning at two times, first, when the 70 adolescents entered the clinic (mean age, 13.65 years) and, second, just before they started hormone treatment (mean age, 16.64 years). Of interest, while adolescents improved with regard to psychological functioning on several domains, gender dysphoria did not improve and all adolescents went on with the next step of gender affirming hormones (de

Table H.3.3. Summary of Treatment for Transgender Youth

TIMING	INTERVENTION
Pre-pubertal	No endocrine intervention recommended. Patient should have regular psychotherapy to discuss gender identity and assess possible future need for hormonal intervention
Early signs of puberty	Pubertal blockade with gonadotropin-releasing hormone analogs to prevent the development of secondary sex characteristics and provide additional time for psychotherapy and consideration regarding partially reversible interventions
Age 14+ or 16+ (depending on the center and patient)	Cross-sex hormonal therapy with estrogen or testosterone. Less frequently, with other endocrine-acting medications that have less favorable side effect profiles.
Age 18 (for most centers)	Gender affirming surgeries may be considered. Note that some surgeries may be performed earlier for select patients.

Vries et al, 2011a). The second study added a third assessment, around one year after gender affirmative surgery, when the first 55 adolescents who had been in this treatment protocol had reached young adulthood (mean age, 20.70 years). This time, gender dysphoria had resolved and psychological functioning measures had improved further, with scores comparable to normative samples. The same accounted for quality of life, subjective happiness, and satisfaction with life (de Vries et al, 2014). These results are promising and suggest that starting treatment at a relatively young age is possible. However, the results come from only one clinic and concern a highly selected cohort that received support from their parents—and often from their school and social environment—that started treatment only after extensive assessment, and that had mental health counselling during the years of treatment. Whether the same positive results can be expected for the larger number of adolescents who are currently being treated in clinics and who vary considerably in their quality of care and approach has yet to be determined.

Assessing Eligibility

According to Endocrine Society Guidelines, hormonally-based medical intervention may be initiated at the earliest signs of puberty (i.e., Tanner 2 or 3) with pubertal blockade (Hembree et al, 2017). Other conditions for eligibility include meeting criteria for gender dysphoria, experiencing dysphoria toward early pubertal changes, having adequate psychological and social support for treatment, understanding the risks and benefits of treatment, and not suffering from a psychiatric comorbidity that would interfere with treatment (Wylie et al, 2009). To assess eligibility, most clinics offer assessment by a mental health professional that sees the adolescent and his or her family over a longer period of time before decisions regarding medical interventions are made. This time is used to prepare the adolescent for the long period of medical treatment and weigh the pros and cons of treatment so that an informed decision can be made. Although many

adolescents come with a clear wish for medical treatment, some are not sure yet and want to explore their gender dysphoric feelings more broadly. Sometimes co-occurring psychiatric difficulties like ASD with rigid thinking, severe depression with acute suicidality, or anxiety with worrisome avoidance and school refusal, complicate the diagnostic work and make attending regular check-ups and taking medication impossible. Treatment of these psychiatric disorders may then be necessary before endocrine intervention. The importance of parental support for the psychological well-being of these adolescents is widely acknowledged (Simons et al, 2013). The time used for assessment may also be helpful to address parents' concerns and improve adolescent-parent relationship. The time needed before medical intervention is provided will vary for each individual, but tends to be longer when other psychosocial conditions are present (Costa et al, 2015; de Vries et al, 2011b).

Reversible Interventions (Pubertal Blockade)

The first intervention (implemented at Tanner stages 2 or 3) is pubertal blockade with gonadotropin-releasing hormone analogs.

Partially-Reversible Interventions (Cross-Sex Hormonal Therapy)

According to Endocrine Society guidelines, around the age of 16, patients may choose to move onto the next intervention: cross-sex hormonal therapy with estrogen or testosterone. Some researchers have noted that cross-sex hormones can be instituted earlier, as delaying puberty outside the developmentally appropriate age may cause social problems for these youth (Rosenthal, 2014). The newly-

Gonadotropin Releasing Hormone Analogs (Puberty Blockers)

Gonadotropin-releasing hormone is produced by neurons in the hypothalamus. This hormone is secreted at very low levels in prepubertal children. At the initiation of puberty, release of gonadotropin-releasing hormone becomes cyclical. This cyclical release results in production of follicle stimulating hormone (FSH) and luteinizing hormone (LH) by the anterior pituitary. These hormones then enter the peripheral circulation where they trigger the production of sex hormones (estrogen in natal women and testosterone in natal men). These hormones then initiate the irreversible development of secondary sex characteristics.

Gonadotropin-releasing hormone analogs (either as implants, depot injections, or regular injections) maintain high levels of gonadotropin-releasing hormone in circulation. Without physiological cyclical fluctuations in gonadotropin-releasing hormone analogs, FSH and LH are not released and all downstream signaling is prevented. This allows the patient to remain in an early pubertal state.

Pubertal blockade prevents the development of irreversible secondary sex characteristics (voice deepening, breast development, etc.) and provides additional time for gender dysphoric children to decide if they wish to fully transition physically into the body of the opposite sex. Therefore, it does not need to be considered actual gender affirmative medical treatment, but rather may function as an extended diagnostic phase. If the gonadotropin-releasing hormone analogs are discontinued, their effects are reversible. The patient undergoes natal puberty if the gonadotropin-releasing hormone analogs are discontinued. Follow-up studies into young adulthood on the first cohort of puberty-suppressed adolescents are reassuring in regard to side effects. Although there was some decrease in bone density, there were no further concerns regarding liver and kidney functioning and lipid profile (Klink et al, 2015; Schagen et al, 2016). Some clinicians advise to evaluate bone age every three months and regular blood monitoring to ensure that puberty is sufficiently suppressed (Wylie et al, 2009).

released 2017 Endocrine Society Guidelines agree with this approach. Additional criteria for cross-sex hormonal therapy are identical to those for gonadotropin-releasing hormone analogs in the Endocrine Society Guidelines.

Cross-sex hormones will initiate the development of secondary sex characteristics of the desired puberty. These interventions are mostly irreversible and carry a more significant side effect profile. The most prominent side effect of estrogen therapy is hypercoagulability, though clinicians prescribing these medications should be aware of the full spectrum of side effects. Of note, hypercoagulability can be particularly problematic for patients undergoing high-risk surgery such as vaginoplasty. Patients on these medications should be regularly monitored for serum hormone concentrations as well and maintained within normal testosterone and estrogen serum concentrations for their desired gender. Spironolactone has been used for its anti-androgenic properties in select cases but is generally not considered a first line treatment given its unfavorable side-effect profile as a diuretic (Wylie et al, 2009).

Irreversible Interventions (Gender Affirming Surgeries)

At the legal age of adulthood, patients may choose to undergo a variety of surgical interventions, including vaginoplasty, phalloplasty, scrotoplasty, breast augmentation, facial reconstruction, hysterectomy, and reduction thyroid chondroplasty, among others. Patients should be carefully counseled on the risks and benefits of surgery. Specific surgical interventions are many and are out of the scope of this chapter. Of note, some surgical interventions may be considered earlier in the course of treatment. In the World Professional Association for Transgender Health (WPATH) Standards of Care, mastectomies are being considered earlier than age 18 (Coleman et al, 2011).

Fertility Considerations

There is a paucity of research on the effects of pubertal blockade and cross-sex hormonal therapy on future fertility. Interested patients should be counseled on fertility preservation options early in treatment and before starting hormonal treatment.

CULTURAL ASPECTS

In providing care for transgender and gender nonconforming people, one will need to consider the local legal situation, family dynamics, and patients' and their families' attitudes, and adjust the services accordingly. When treating immigrant families and ethnic minorities in Western countries, it is important to understand the family's culture and how they have been influenced by the host culture in regards to sexuality and gender. One may not assume that immigration necessarily altered background cultural concepts about sexuality and gender including stigma — in many cases they become more rigid. Legal issues remain very important in providing care as, even in the United States, there have been several recent setbacks in the legal protection of transgender and gender nonconforming individuals.

SUMMARY

Gender nonconforming and gender dysphoric youth represent a vulnerable demographic with high rates of co-occurring psychiatric conditions and suicidal behavior, likely secondary to minority stress and dysphoria related to living in a

body that does not match one's experienced gender. Prepubescent children with gender variant behavior or identification are best supported with psychotherapy and socio-familial interventions. For those children who continue to have strong cross-sex identification in adolescence, pubertal blockade and cross-sex hormone therapy to align patients' bodies with their experienced identities have been shown to improve mental health outcomes.

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