NCC Pediatrics Continuity Clinic Curriculum: **Transgender and Gender Diverse (TGD) Youth**

Faculty Version

Goals and Objectives:

1. Provide a patient-centered, inclusive healthcare environment that supports the well-being of TGD children
2. Respond to common caregiver questions regarding healthy trajectories of gender identity development
3. Provide high quality resources and evidence-based advice to help families support a child who expresses a transgender or gender diverse (TGD) identity
4. Make appropriate referrals when indicated for children seeking medical interventions for gender affirmation.

Pre-Meeting Preparation:

Required Reading:

1. Primary Care Considerations for Transgender and Gender-Diverse Youth *(PIR 2020)*
2. "Trans Teen Shares Her Story" *(PIR 2016)*
3. Skim the "LGBTQIA+ Glossary of Terms for Health Care Teams" and read at least 10 definitions for terms you did not previously know.

Conference Agenda:

- *Review* Quiz
- Complete Cases

Extra-Credit:

See the following articles for more in-depth knowledge or just in time references on this topic:

- Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents *(AAP2018)*
- Providing Affirmative Care to Transgender and Gender Diverse Youth: Disparities, Interventions, and Outcomes *(Current Psych Reports, 2021)*
- The Endocrine Society's Gender Dysphoria/Gender Incongruence Guideline Resources *(American Society of Clinical Endocrinologists, 2017)*
- Standards of Care for the Health of Transgender and Gender Diverse People [8th Version] *(World Professional Association for Transgender Health, 2022)*
- Caring for Military-Affiliated Transgender and Gender-Diverse Youths: A Call for Protections *(AJPH, March 2023)*

Patient Education: **NCC Pediatrics Gender Diverse Youth Handout with Resources**

Primary Care Considerations for Transgender and Gender-Diverse Youth

Jason R. Rafferty, MD, MPH, EdM,*†‡ Abigail A. Donaldson, MD,†‡ Michelle Forcier, MD, MPH†‡

*Thundermist Health Centers, Woonsocket, RI
†Rhode Island Hospital/Hasbro Children's Hospital, Providence, RI
‡Warren Alpert Medical School of Brown University, Providence, RI

Practice Gap

Pediatric primary care providers must recognize that developmentally appropriate, gender-affirming approaches to the care of transgender and gender-diverse youth are necessary to reduce comorbidities, including high rates of suicide.

Objectives

After completing this article, readers should be able to:

1. Describe the developmental context for emerging gender identity in children.
2. Identify ways in which clinicians can explore gender development as a part of routine pediatric care.
3. Recognize that early identification and affirmation of gender identity is essential to engaging supports and promoting positive mental health outcomes.
4. Describe approaches and options for care available to transgender and gender-diverse youth and their families.
5. Recognize the potential medical and mental health disparities and risks faced by this historically marginalized population.

AUTHOR DISCLOSURE Dr Forcier is a paid consultant for Planned Parenthood and receives author royalties from *UpToDate*. Drs Rafferty and Donaldson have disclosed no financial relationships relevant to this article. This commentary does contain a discussion of an unapproved/investigative use of a commercial product/device.

ABBREVIATIONS

FDA	Food and Drug Administration
GnRH	gonadotropin-releasing hormone
HEEADSSS	Home, Education/Employment, Eating, Activities, Drugs, Sexuality, Safety, Suicide, Strengths
PPCP	pediatric primary care provider
TGD	transgender and gender diverse

INTRODUCTION

Pediatric primary care providers (PPCPs) establish care with patients at birth and manage individuals throughout childhood, adolescence, and young adulthood. Thus, pediatricians are uniquely situated to screen, identify, and care for transgender and gender-diverse (TGD) youth. Large, systematic prevalence studies of TGD identity in children have not been conducted. (1) A 2016 national survey estimated that 0.6% of adults in the United States identify as transgender. This is approximately 1.5 million people and is twice the prevalence found a decade earlier. (2) Estimates suggest that today's adolescents identify as transgender more often than adults. (1)

As children and adolescents become increasingly aware of gender diversity, PPCPs should be attentive to physical and emotional cues that point to

gender-related distress. Early identification of potential distress, supported exploration of identity, and affirmation foster healthy growth and development in a particularly vulnerable population. It also leads to positive long-term health outcomes, including decreased morbidity and mortality. (3)(4) Although the American Academy of Pediatrics recommends that TGD adolescents be supported and affirmed in their gender, (5)(6) most PPCPs still lack confidence and sufficient knowledge to provide care for TGD individuals. (7) Pediatric providers should orient themselves to this important emerging area of pediatric practice and take steps toward use of a gender-affirming, developmentally appropriate framework that can improve early identification and positive health interventions for a historically vulnerable population. (6) This article provides a general overview of assessment and management planning for TGD youth in the primary care setting.

CLINICAL CASE

Alex is a 6-year-old, identified as a female at birth, who presents to the primary care clinic for a health supervision visit. The medical record notes: "Mom reports that Alex has mostly boys as friends, has an interest in activities that are traditionally male, and sometimes wears brother's clothes." At this 6-year visit the PPCP explains that most children explore a range of gender expressions and identities as they develop. Several years later, at the 10-year health supervision visit, Alex has entered puberty, and Alex's mother reports discussing expected body changes at home. During the review of anticipatory guidance, the PPCP focuses on future pubertal changes. Throughout this conversation, Alex grimaces and hides behind a baseball cap. In response to this, the PPCP asks about Alex's feelings related to pubertal development, including changes in body, emotions, and social roles. Before Alex can respond, mom interjects that Alex never wants to talk about it and "wants to ignore puberty altogether."

DEFINITIONS AND BACKGROUND

Society's understanding and appreciation of the broad gender diversity that exists has evolved over time and across countries and cultures. Increasing numbers of persons—and youth in particular—are exploring gender, with all its varied identities and aspirations. Historically, TGD individuals have been discriminated against, marginalized, and denied appropriate medical care. With increased awareness and acceptance, TGD youth today are increasingly looking to their PPCP to help support, guide, and manage their gender care. (8) To effectively discuss gender concerns, PPCPs should be familiar with the appropriate (and evolving) vocabulary of gender care.

Gender is a defining and fundamental aspect of an individual's identity. It encompasses the inner sense of being male, female, a combination of both, or somewhere in between (*gender identity*) and the external way a person presents themselves to (*gender expression*) and is interpreted by (*gender perception*) the world. A person's *assigned gender* refers to the gender assignment made at birth, based on biological sex, including anatomy, genetics, and hormones. If a person's asserted gender identity aligns with their biological sex, they are considered *cisgender.* However, other people insist that their gender behaviors, appearance, and/or identity do not align with what is socially expected of their assigned gender. As this incongruence persists and is felt consistently over time, some gender-diverse individuals may label themselves with the broad umbrella term *transgender.* Traditionally, the medical community has associated a transgender identity with the terms *insistent, persistent,* and *consistent,* but many suggest that gender is more complex. More specific labels continue to evolve to capture the complexities of gender identity that people experience; for example, *gender fluid* means that one's gender may shift over time or in different circumstances, *nonbinary* means that one recognizes their gender to be something other than male or female, and *agender* means that one feels gender is a foreign concept to their identity. (9) Table 1 and the Figure provide an overview of these terms.

Significant discomfort, or *gender dysphoria,* may develop in a TGD individual due to the incongruence between gender identity and assigned gender. It can also result when one's gender identity does not align with socially prescribed roles and expectations based on the person's assigned biological sex at birth. (10) Gender dysphoria is highly associated with depression, self-harm, suicidality, and eating disorders. (11)

Gender-affirmative care focuses on developmentally appropriate, gender-inclusive management. It acknowledges an individual's unique gender experience within their developmental trajectory and accommodates understanding of gender diversity alongside gender questions and concerns. (12) A gender-affirmative care model naturally builds upon the family-centered, strengths-based focus of primary care pediatrics to foster open communication, empathy, and resiliency—all factors that are critical to supporting all children and adolescents in their journey to adulthood. (13)

Sexual orientation refers to a person's identity in relation to the gender(s) to which they are sexually and romantically attracted. As understanding of gender continues to evolve, so do the options and labels for sexual orientation. However, being gender diverse does not imply anything about who someone is attracted to, and providers need to be careful not to make assumptions. (6)

TABLE 1. **Common Gender Terms and Definitions with Examples from "The Gender Planet" (Fig) to Create a Child-Friendly Gender Interview**

TERM	DEFINITION	DEPICTION FROM "THE GENDER PLANET"
Assigned gender	An assignment made at birth based on biological sex characteristics, including anatomy, genetics, hormones, and other factors	The continent in which a person is born—usually "Ladyland" or "Manlandia"—which are large and diverse with different regions and subcultures (eg, Ladyland contains "feminine foothills," "tomboy town")
Gender identity	A deep internal sense of being female, male, a combination of both, somewhere in between, or neither	The continent, or more specific region/subculture, in which a person decides they want to settle, usually in a culture in which they feel affirmed
Gender expression	The external way a person expresses their gender (eg, clothing, hairstyle, etc)	Regional variations in dress, behavior, and customs
Gender perception	The way others interpret a person's gender expression	Stereotypes, prejudices, and assumptions about you and your region/subculture made my other regions/subcultures
Agender	One who does not identify with any gender and feels that gender is a foreign concept to their identity	Represented by a satellite well beyond the gender planet
Cisgender	A person whose asserted gender identity aligns with their biological sex	People who are born on one gender continent and settle there long-term
Gender diverse	People with gender behaviors, expressions, identities that differ from those that are socially expected based on their biological sex	Represents the wide diversity of regions and cultures represented on the gender planet; there is also a "Gender Diverse Island" where people identify as being a blend of different gender cultures and identities
Gender fluid	When a person's gender identity is not fixed, it may shift over time or in different circumstances	There is a "gender fluid" cruise boat that takes people from one continent to another, sometimes to explore or other places to settle; some people find they fit best on the boat itself
Nonbinary, genderqueer, etc	There are many labels that are used by people whose gender identity is something other than entirely male or female	These terms are represented by smaller varied islands: "Third Gender Island" (*other* than Manlandia and Ladyland); "Gender Neutral Island" (*in between* Manlandia and Ladyland); and a range of new islands (and terminology) that are being discovered
Transgender	When a person's asserted gender identity persistently, consistently, and insistently does not match their biological sex (eg, persons assigned female at birth may identify as male, transman, or transmasculine)	People who are born on one gender continent but cross borders to live and settle outside their assigned continent

"The Gender Planet" is used with permission from The Gender Book *(http://www.thegenderbook.com).*

CLINICAL APPROACH

Pediatric Approach to Gender in the Context of Child Development

Gender identity is expressed in a developmental process that begins in early childhood. Past studies suggest that infants and toddlers present rudimentary forms of gender understanding, even before gender-differentiating behaviors are observed. For example, infants as young as 3 to 4 months of age distinguish between male and female categories of faces, and by 6 to 8 months discriminate male and female voices. (14)

By 24 to 31 months, toddlers engage in verbal gender labeling and show gender-type toy awareness. (14) Some TGD children articulate an awareness of feeling "different" starting as early as preschool. By ages 3 to 5 years, gender is a highly salient influence on preferences related to play, peer groups, and clothing. TGD preschoolers typically demonstrate preferences, behaviors, and belief measures consistent with peers of their asserted gender. (15)

By 5 to 6 years old children develop gender consistency (understanding that gender is stable from infancy to adulthood) and stability (understanding that it does not change with fluctuation in role or appearance). This reinforces same-gender stereotyped play preferences and friend groups. (14)(15) Childhood play involving toys or roles that

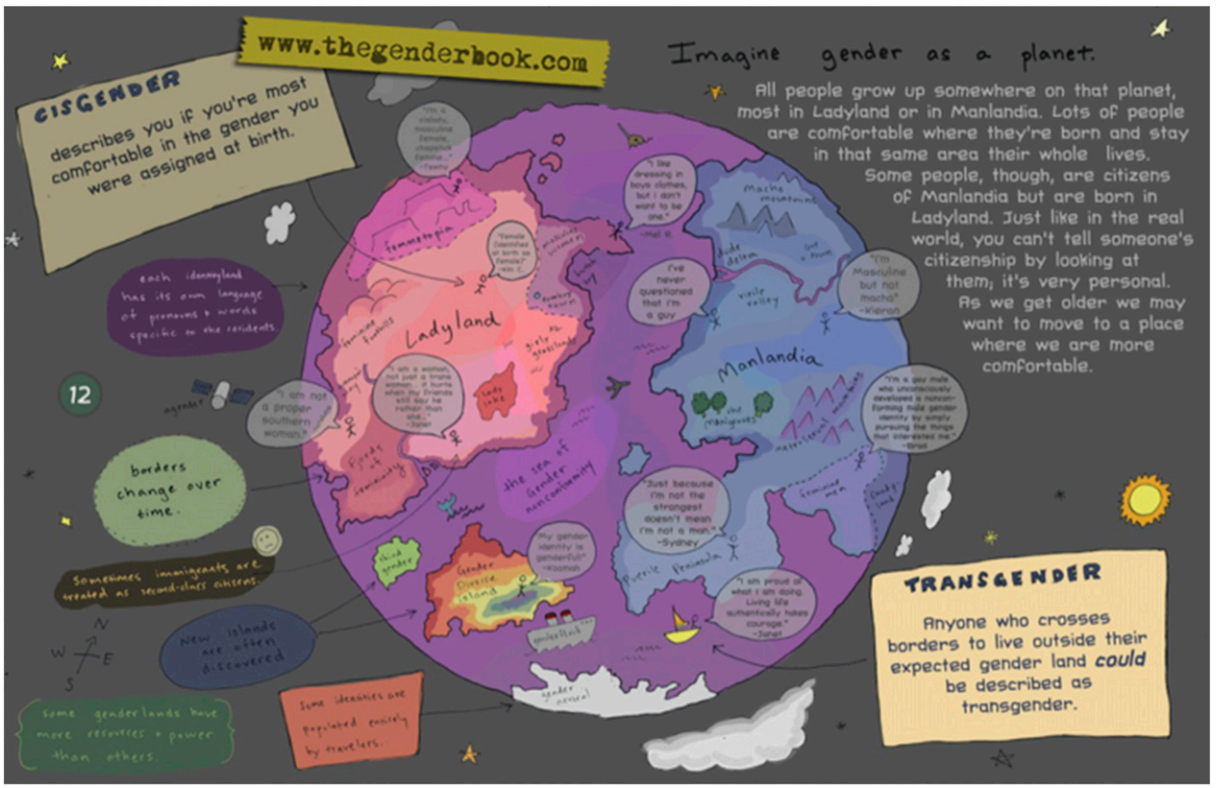

Figure. "Imagine gender as a planet." This depiction uses the analogy of a planet with different continents, cultures, and migration patterns to depict the complexity of gender diversity. See Table 1 for relationship to specific terms. Reprinted with permission from *The Gender Book* (http://www.thegenderbook.com).

go against gender stereotypes is a normative experience in early school-age children: all children experiment with different dress, makeup, toys, activities, and make-believe roles. Often the externally imposed environment drives children toward stereotyped preferences (ie, peer exclusion and parental expectations). (16)(17) For TGD youth, such pressures drive their preference "underground," or force them to suppress their genuine sense of self, which over time leads to low self-esteem, shame, and depression. (3)

The onset of puberty—particularly the emergence of physical features that affect how one's gender is perceived (eg, development of breasts and menses or male pattern hair and masculine habitus)—can be distressing for many adolescents, especially if such physical changes are at odds with one's gender identity. TGD adolescents often present with a sense of urgency and heightened distress as they undergo these permanent physical changes at odds with their inner experience of gender and self. TGD adolescents are at particularly high risk for social withdrawal, self-injurious behaviors, and restrictive eating disorders. (10)(11)(18)(19) Many may not directly present with gender concerns but instead their distress will manifest as declining academic progress or high-risk behaviors, such as substance use. (10) Adolescence is also a time of heightened attention to relationships, sexuality, and romantic partnership, adding complexity to the task of gender identity articulation and assertion. Menses, erections, orgasms, masturbation, and peer pressure to have sex can be overwhelming and extremely distressing for TGD youth. (20)

Traditionally, gender development has been understood as a linear trajectory, but emerging research conceptualizes it as an ongoing process that is revisited and reevaluated throughout the life span. (21)(22) It can also interact with other aspects of identity development, such as realizing one's sexual orientation. Although developing a gender identity and a sexual orientation are distinct processes, they are not experienced in parallel. Rather, they can overlap, intersect, and complicate each other. Exploring one's sexual orientation may expand one's exposure to gender diversity, raising questions about their own gender identity, and evolving gender identities perpetually challenge the understanding of one's sexual and romantic attractions. (21)

Table 2 provides some developmentally appropriate questions for patients and parents that may help PPCPs explore gender and identify gender dysphoria in children and adolescents.

TABLE 2. **Practical Examples of Phrasing for Introducing a Gender History and Discussing Gender in Primary Care Settings**

FOR PROVIDERS FRAMING THE INTERVIEW	RANGE OF QUESTIONS TO EXPLORE GENDER	POTENTIAL RESPONSES PROMPTING ANTICIPATORY GUIDANCE AROUND GENDER DIVERSITY[a]
Prepubertal Children		
Child interview		
As your provider, I would like to ask you some questions about your body, preferences, and the things you do. We all have certain things we like and don't like which makes us unique. I want to learn some things about you. There are no right answers to these questions and it is okay not to know the answers.	• How do you like to play when you are alone? What do you like to do with others? • What are your favorite toys, games, characters in plays, books, or movies? • Do you have any questions or problems with your body? What are 2 things that you like about your body? Is there anything you don't like? • Has anyone ever teased you about the way you look, how you play, or what you like to do? • Are you a boy, girl, or something else? Is that okay with you? What are 2 things you like about being a boy, girl, or something else? What are 2 things you don't like? • What do you expect from your life as an adult? What do you want to do? Do you want to be a parent or have a family?	• Plays with toys, games, or dresses that would not be expected based on biological sex • Any concerns about their body, particularly if related to sex-defining characteristics (genitals, breasts, muscle mass, etc) • Predominant identification with personal identity, roles, or peer groups that are not aligned with biological sex • If the child has any specific concerns/fears related to their gender

Continued

TABLE 2. (Continued)

FOR PROVIDERS FRAMING THE INTERVIEW	RANGE OF QUESTIONS TO EXPLORE GENDER	POTENTIAL RESPONSES PROMPTING ANTICIPATORY GUIDANCE AROUND GENDER DIVERSITY[a]
Parent interview		
Children grow and develop in many ways, including their sense of self. We all have a sense of gender: the feeling of being male, female, or sometimes something else. I want to ask you some questions about your child's gender development so we can work together to best support your child's emerging identity and unique self. *It is okay to have questions and concerns, and I want you to know that you can come to me as a resource.* *Pediatricians now understand that no matter the gender of the child, parental support is one of the most important factors in safe, healthy, and happy development.*	• Describe your child's: - general gender development including: - expression and exploration of their gender	• Persistent, insistent play patterns, peer associations, or gender expression that is other than expected based on biological sex
	• Do you have any concerns about your child's gender development (who they play or identify with; favorite activities; preferred books, movies, characters, etc)?	• Parents express concern about gender, gender of peer associations, gender expression, or their child's gender development
	• Do you have concerns about the safety and well-being of your child? - Who can they talk to about problems and difficulties? - Have you had discussions about touch, consent, and safety?	• Child has few social supports and/or peer friendships
	• What hopes and dreams do you have for your child? What fears or concerns?	• Parents report little/no communication with their child about gender
	• How do you feel about gender and gender roles given your own childhood, family background, culture?	• Any concerns/fears about the child's safety related to their gender

Continued

TABLE 2. (Continued)

FOR PROVIDERS FRAMING THE INTERVIEW	RANGE OF QUESTIONS TO EXPLORE GENDER	POTENTIAL RESPONSES PROMPTING ANTICIPATORY GUIDANCE AROUND GENDER DIVERSITY[a]
Peripubertal/Postpubertal Adolescents		
Adolescent interview		
Gender identity is something that all people have. It is a key component of who we are. There are some common labels people use to describe their gender, such as "boy" or "girl," but sometimes gender identity can be more complicated, and the simple labels of "boy" or "girl" do not fit. As your medical provider, I would like to better understand your gender identity. You don't need to have all the answers—it is okay if you are still figuring things out or if things change. I also want you to know that this topic is not one we have to share with your parents unless you want to, as it is part of how we deliver confidential care.	• Do you have any questions or concerns about puberty or the way your body is changing? Is anything about those changes causing you to be sad, uncomfortable, or angry? What did you like or not like about puberty?	• Identifies gender labels other than cisgender, particularly if any concern or discomfort is reported
	• How would you describe your gender? What do you like about your gender? What do you not like about it? What does your gender identity mean to you?	• Strong dislike of physical pubertal changes (facial hair, breasts, menarche) and/or dysphoria over genitals (hates structure, function)
	• Does the way you express yourself on the outside match the way you feel about yourself on the inside?	• Future desire for physical features or roles often not associated with biological sex
	• Who (if anyone) do you talk to about your gender? If you had concerns about your body or gender, who would you go to for support?	• Lack of social support
	• Have you ever had thoughts of wanting to harm or kill yourself due to discomfort with your gender or who you are?	• Any safety concerns
	• Have you ever tried to change your body to better align with your gender? If so, what have you tried?	• May indicate nonbinary identity
	• How do you see yourself and your life when you are "all grown up"?	• Wears clothing, hair, jewelry, accessories typically associated with both genders • Would like to pass as neither male nor female, or shifts between gender identities • Rejects gender binary and traditional gender concepts

Continued

TABLE 2. (Continued)

FOR PROVIDERS FRAMING THE INTERVIEW	RANGE OF QUESTIONS TO EXPLORE GENDER	POTENTIAL RESPONSES PROMPTING ANTICIPATORY GUIDANCE AROUND GENDER DIVERSITY[a]
Parent interview		
In adolescence, one of the core developmental tasks is establishing a more complete sense of self, which includes gender identity. As your child's experiences and insight regarding their gender progresses through adolescence, this reflective process can become more difficult and even distressing. I will continue to ask you and your child questions about gender over time because this is a normal developmental process, and talking about it in the medical setting can establish support for the process of exploring gender identity and demonstrates awareness that this is a complicated, often fluid process over time. We all have a concept of gender: the feeling of being male, female, or sometimes something else. Most youth explore and express their gender with their clothing, makeup, hairstyle, or interests. It is typical for children to explore gender roles and expression as they grow into their adult identities.	• Do you have any concerns about your child's gender development? • How do you feel about gender and gender roles given your own childhood, family background, culture? • Has there been any change in your child's gender expression with the onset of puberty? Does your child express concerns or worries about puberty? • Do you talk to your child about keeping their body healthy and safe? Do you have any concerns about the overall safety and well-being of your child? • Who are your child's closest friends? Do you have any concerns about your child's friends, peers, or adult supports? • Does your child have people in his or her life who they can go to if they are struggling? Have you discussed this with your child? • What hopes and dreams do you have for your child? What fears or concerns?	• Persistent, insistent, consistent play patterns, peer associations, or gender expression other than expected based on biological sex • Parents' concerns about gender, gender identity, gender expression • Few social supports, friendships • Engaging in high-risk behaviors • Poor communication between the parent and adolescent • Any concerns/fears about the adolescent's safety related to gender

[a]*Gender exploration is a normal part of development, and no response can reliably predict a transgender and gender-diverse identity. However, anticipatory guidance on gender helps establish that discussions related to gender are normal and appropriate throughout development and acknowledges that gender identity may change over time.*

Screening for and Identifying TGD Youth

There is no way to predict which subset of gender-questioning or nonconforming children and adolescents will identify as transgender adults. (18)(23) TGD youth report an awareness of difference in their gender experience at an average age of 8.5 years but delay communicating or disclosing until an average of 10 years later. (8) Throughout development, TGD youth tend to describe their identity as consistent, persistent, and insistent despite various challenges and pressures to suppress it. (12)(24) Understanding that a clear concept of gender identity can take time to develop for many children and adolescents, PPCPs should inquire at all annual visits (and whenever concerns arise) to support patients and families in early identification of gender dysphoria. As children enter preadolescence, PPCPs should consider establishing some time alone with the patient during the annual health supervision visit to assess gender and other concerns the patient may have in private. Some parents may not be comfortable with this separation; however, early identification allows for timely mobilization of necessary emotional and social supports, treatment planning, and increased engagement in care. Early identification of gender dysphoria can also help establish a treatment plan well in advance of puberty to increase the likelihood that the youth's ongoing development will be congruent with their asserted gender identity. (6)

PPCPs can model nonjudgmental communication and understanding for TGD youth and their families by actively listening to a child's personal gender narrative. The PPCP serves a critical role as a trusted adult who can acknowledge and normalize any questions, concerns, or hesitation regarding gender identity development. A gender-affirmative approach centers on unconditional safety, respect, and empathy in eliciting the gender narrative. (13)(25)(26)(27) Table 1 can help guide PPCP inquiry about gender and gender identity.

SPECIAL CONSIDERATIONS IN ADOLESCENTS

Confidentiality

Confidentiality is a consideration for all adolescents but may be particularly important to TGD youth. Establishing some time alone between the adolescent and the PPCP is standard practice for adolescent care; PPCPs should review confidentiality with adolescent patients and their parents at regular intervals to support this practice. Adolescents may be reluctant to reveal their gender questioning and/or diverse identity to family members and may feel unsafe to do so. Understanding that the clinic setting is a safe place to explore and discuss gender identity in confidence may help the adolescent feel more comfortable exploring these questions and concerns with the PPCP. (28)

Psychosocial Assessment

Thoughtful psychosocial history-taking and assessment are key components of any adolescent or young adult examination; however, for TGD youth this assessment is critical to understanding the complexity of each individual, including comorbid concerns. The HEEADSSSS psychosocial interview is a standard assessment tool for adolescent psychosocial wellness that can help guide a gender interview in an open and supportive manner. HEEADSSSS is an acronym for the domains that can be assessed: Home, Education/Employment, Eating, Activities, Drugs, Sexuality, Safety, Suicide, Strengths (Table 3). Using open-ended, nonjudgmental questions can facilitate a more honest conversation with the adolescent patient. For example, asking adolescents how they feel about their gender, in general, and allowing them to define the labels they use may yield more information than just asking if they identify as male or female based on the provider's assumptions of what those specific labels mean.

PPCPs who have established relationships with TGD youth and their parents are in an ideal position to assess home, school, and work environments and to build on sources of support while assessing for potential sources of rejection, abuse, or safety concerns. Within the psychosocial assessment there are several areas of concern for TGD youth. For example, many TGD youth experience feelings of "otherness" and isolation, so it is essential to ask whether they feel safe disclosing their identity to friends, family, and/or other supportive adults. This should be followed by inquiring about the reasons why they do or do not feel safe disclosing their gender identity in these settings to better assess safety and support and to promote healthy adolescent development. (6)(11)(18)(24)(28)

Transgender people experience disproportionately high rates of interpersonal violence of all types, by both strangers and people they know (family, romantic partners). Research has shown that most TGD people will experience violence in their lifetimes. This risk starts at an early age through bullying and intimate partner/dating violence, and it persists throughout the life span. (29)(30)(31) Likewise, 40% of transgender people have attempted suicide in their lifetime, which is 9 times the rate among all people in the United States. (30) Therefore, safety assessments should be conducted frequently, including specific inquiry about exposure to violence, bullying, and thoughts of self-harm or suicide.

Body dissatisfaction is common among TGD youth, and individuals may experiment with weight or exercise

TABLE 3. **HEEADSSSS Psychosocial Tool for Assessing Resiliency and Risk Among TGD Youth, With affirming Interventions**

DOMAIN	ADAPTED FOR TGD YOUTH	AFFIRMING INTERVENTIONS[a]
H Home environment	• Who (if anyone) in your family have you disclosed your gender identity to? • Who is supportive and understanding? Who might struggle with it or may not be supportive? • Are there safety concerns at home?	• Explore ways to disclose gender identity to family (in writing, in person), with support when appropriate and safe to do so • Connect patient/family with counseling, support resources • Assess risk of homelessness, abuse, other safety concerns
E Education and/or employment	• Have you disclosed your gender identity to anyone at school or work (teachers, counselors, co-workers, friends/peers)? • Have appropriate accommodations been made to affirm your gender (name use, bathroom/locker room use, etc)? • What resources support you (genders and sexualities alliance, peer/adult allies, etc)? • Are there safety concerns at school, at work, or in the community?	• Work with the family, school, employer to develop a gender plan with appropriate accommodations • Advocate for gender-inclusive antibullying policies in local schools and community
E Eating and dietary concerns	• How do you feel about your body, body shape, weight, and the way you present yourself to others? • Have you ever changed your diet or exercise behaviors to deal with body dissatisfaction? • Do you ever make yourself vomit or take any substances or supplements to try to change the shape/composition of your body?	• Understand that disordered eating and body image are more prevalent in TGD youth • Offer medical, dietary, and psychiatric referrals when appropriate
A Activities	• Have your peers been helpful, hurtful, or somewhere in between? • What activities are you interested in? • Are school and activity settings safe and affirming environments for you?	• Discuss safe ways to disclose to peers, team members, coaches • Ensure appropriate accommodations • Advocate for gender-inclusive sports and extracurricular policies • Provide gender education to coaches and communities
D Drugs and substance use	• Some gender-diverse teens may use substances to cope with feeling different and other stressors. What substances have you tried? Are there any that you use regularly? • Has substance use ever affected home, school, or friendships? • Do you have any concerns about your substance use?	• Discuss healthy ways to manage stress and dysphoria • Motivational interview with focus on the larger context of gender and future related goals • Appropriate referral when concerned
S Sexuality	• Who are you attracted to, if anybody? • Do you have a label to identify your attractions, and what does that label mean to you? • If you are in a relationship(s), do you feel supported? Are there any safety concerns? Do you ever feel pressure to engage in sexual or other activities by your partner(s)? • What types of sexual activities do you engage in or are you curious about? Do your relationships, sexual activity, or use of certain body parts for sex create any discomfort based on your gender identity?	• Supportive discussions about healthy relationships, sexuality • Offer contraception, sexually transmitted infection prevention, vaccination, other preventive services • Provide education about gender-inclusive approaches to sexual health issues

Continued

TABLE 3. (Continued)

DOMAIN	ADAPTED FOR TGD YOUTH	AFFIRMING INTERVENTIONS[a]
S Safety	• Do you feel safe at home, school, work; in your relationships; and in the community? • Have you ever been hurt (verbally, physically, or sexually) because of your gender?	• Assess risk of abuse and any safety issues • Provide education on personal safety • Advocate for policies to promote safety of all youth, including antibullying policies
S Suicide, depression, and mental health	• How do you feel about your gender (proud, confused, angry, sad, ashamed, or any number of other emotions)? • Describe the times where you have felt down, angry, worried, or bad about who you are. Do these or any other emotions get in the way of your everyday life? • Have you had feelings of wanting to hurt or kill yourself or others? Have you ever acted on these feelings? • When you are struggling emotionally, what do you do to cope and who can you go to for support?	• Understand that anxiety, depression, suicidality, and self-harm are more prevalent in TGD populations • Provide anticipatory guidance bolstering stress management and positive supports • Offer services to help youth cope with the effects of minority stress • Advocate for improved mental health resources and access
S Strengths and resiliency	• What do you like about yourself? What are you good at? What are your personal values? • What are your hopes and dreams for the future, particularly in terms of gender, relationships, and ways you want to contribute to the world?	• Celebrate skills, interests, and aspirations; provide counseling and resources to help foster these resiliency factors • Use a strengths-based approach that emphasizes positive attributes when communicating with the youth and the family

TGD=transgender and gender diverse.
[a]See the Resource list for links and practical examples.

manipulation to suppress development or achieve a physical appearance that is more consistent with their asserted gender. Emerging evidence suggests that TGD individuals are more likely to engage in disordered eating behavior compared with cisgender peers. (11)(19)(32)(33) Therefore, PPCPs should be alert to changes in nutrition and exercise habits and should screen for disordered eating behavior. Weights should be obtained at all visits and trends followed over time to help identify more secretive behaviors. Body dissatisfaction in TGD youth can co-occur with depression, victimization, and substance use or experimentation. (8)(10)(11)(28) Providers should, therefore, screen for drug, alcohol, and tobacco use alongside other psychosocial risks.

For all sexually active adolescents and young adults it is important to take a thorough sexual history. For the TGD patient, this should include inquiring about—and using—the labels that they might use for their genitalia to make the discussion more comfortable and avoid triggering dysphoria. (34) It is critical to ask about sexual behavior to assess risk; for example, asking specifically about oral, anal, and genital sex in addition to any instrumentation will help inform counseling, safety recommendations, and screening.

In terms of pregnancy prevention, hormonal and surgical methods of contraception should be reviewed with all TGD youth, including those who are taking gender-affirming hormones, because these hormones do not adequately prevent unplanned pregnancies. (34)(35) Hormonal contraception methods may not be well tolerated and may trigger dysphoria, particularly if it leads to menstruation, vaginal bleeding, or cramping (eg, with the use of a cyclic oral contraceptive pill in a TGD youth with female anatomy that identifies as male). The specific hormone present may also lead to concerns or issues with compliance (eg, use of an estrogen-containing method in a TGD youth that identifies as male). Careful review of options, adverse effects, and expected menstrual patterns will help maximize satisfaction with care. For PPCPs who are not comfortable with contraceptive management options, partnership with a TGD-informed gynecologist or adolescent medicine specialist can facilitate timely access to care.

It is important to provide anticipatory guidance around methods of reducing sexually transmitted infections. External and internal condoms and dental dams should be discussed as barrier protection against sexually transmitted infection and pregnancy. In sexually active youth, laboratory and point-of-care testing for sexually transmitted infections, including gonorrhea, chlamydia, trichomonas, human immunodeficiency virus, and syphilis, should be conducted regularly based on individual risk factors. (36)(37)

Depending on the sexual practices of the patient, PPCPs should have a low threshold for additional screening tests (eg, herpes simplex virus, hepatitis A/B/C) (37)(38) and to start preexposure prophylaxis for human immunodeficiency virus prevention. (39)

Regardless of a TGD youth's affirmed gender, routine preventive screening examinations and tests (36) are conducted based on the patient's anatomy and biological sex. (10)(35) This should be carefully discussed and planned ahead of time with the youth and their family because accommodations may be necessary. For example, a TGD young adult who has a uterus would need gynecological care, including routine cervical cancer screening. Sedation for the procedure may be necessary to avoid emotional distress and reproductive anatomy dysphoria.

CREATING A WELCOMING CLINICAL ENVIRONMENT

In addition to striving for a nonjudgmental, gender-affirming interpersonal approach to care, the pediatric clinical environment itself can send an important message to patients and families attuned to gender concerns. PPCPs can promote a sense of safety and inclusion by visibly posting a rainbow flag, pink triangle, or other gender-inclusive symbol; identifying unisex bathrooms; exhibiting posters and brochures about TGD health concerns; and posting a public statement of nondiscrimination, including noncisgender options on registration forms and other materials (not just male or female) (40)(41)

Quality improvement initiatives and diversity training that addresses the unique needs of TGD youth and their families should be offered to all clinical and administrative staff. The patient-asserted name and pronouns should be used by staff and reflected in the medical record (prominently or confidentially) with the consent of the TGD youth. Some limitations may be imposed by factors such as safety concerns, billing systems, and the medical record system; staff should be sensitive to these limitations and discuss them proactively with the TGD patient. (41)

Careful consideration should be given when sensitive aspects of the physical examination are necessary because they can be very anxiety provoking for TGD youth. For example, some individuals may be uncomfortable changing into a gown or undergoing Tanner staging, breast examinations, or genitourinary examinations. Letting patients know what to expect in the examination ahead of time, and asking permission to proceed, can allow individuals the opportunity to express discomfort and give PPCPs the chance to inquire and address these concerns directly with the patient. If the patient declines any part of the examination, PPCPs should be comfortable deferring to a future date. Patients may appreciate an explanation of why the examination is important, and what to expect at the future visit. In some cases, patients or families may be able to articulate measures that can be taken to decrease anxiety and improve the experience in the future. (42)

MANAGEMENT OPTIONS

Management considerations range widely for TGD youth, and there is no single prescribed "path" or sequence of steps to gender affirmation. Rather, treatment planning depends on the specific indications and gender aspirations of the individual, the readiness of the individual and the parents to undertake a care plan, and the individual's developmental/pubertal stage.

PPCPs need to have some understanding of—if not expertise in—treatment options for gender dysphoria. At a minimum, PPCPs should be able to facilitate a basic discussion of management options and timely referral to other providers with expertise in this area if they are not comfortable or able to deliver comprehensive care themselves. National and state laws, as well as institutional policies, often dictate or direct care that can be provided to children and adolescents, including considerations regarding confidentiality and consent. PPCPs should be aware of these laws and policies. (6)

Various protocols are available to guide gender-affirmative care, including specific dosing recommendations for medications that can be administered in a primary or subspecialty care setting; most treatment plans are based on the World Professional Organization for Transgender Health Standards of Care (43) and the Endocrine Society guidelines. (44) This section briefly outlines several key management considerations relevant to the primary care setting. Importantly, no medication or other treatments are currently approved by the Food and Drug Administration (FDA) for the purposes of gender alteration and affirmation. There is ongoing research on the efficacy and safety of these medications, and this review article is not meant to encompass all aspects of medication use, controversies, or potential adverse effects; these can be found elsewhere. (44) Table 4 provides some general considerations that PPCPs should be familiar with as they counsel a TGD youth on potential next steps in gender management.

PUBERTAL SUPPRESSION

For many TGD children, pubertal onset in particular is accompanied by intense anxiety and distress. Gonadotropin-releasing

TABLE 4. **Framework for Pediatricians to Assess Patient Goals and Options for Gender-Affirmative Care**

	DEFINITIONS AND CONSIDERATIONS	TIMING
Social affirmation	Adopting gender-affirming name, pronoun, hairstyle, clothing, makeup, restroom use, etc • Involves no medications or other interventions	May occur any time in life when appropriate and safe
Legal affirmation	The process of making certain changes (name, gender marker) official on documents, such as birth certificate, identification, school forms	
Blocking puberty	Medications pause pubertal progression through suppression of sex steroid production • Gonadotropin-releasing hormone analogs (leuprolide, histrelin) • Considered safe and reversible, but limited research on long-term use • Can prevent permanent physical changes, future surgical or invasive interventions • Gives time for exploration and mobilization of necessary supports	Administered during puberty (Tanner stage 2-4), occasionally after puberty for menstrual suppression
Medical affirmation (gender-affirming hormones)	Sex steroids induce physical characteristic that affirm one's gender identity • "Masculinizing" hormone: testosterone • "Feminizing" hormone: estradiol Other medications: • Pro-androgenic progestins or contraceptives for menstrual suppression • Anti-androgens (spironolactone, finasteride) block testosterone, male pattern hair • Some effects are partially reversible (skin texture, muscle, and fat changes) • Others are irreversible (vocal and hair changes; breast development)	Can be given any time after onset of puberty, from early adolescence to adulthood
Surgical affirmation (gender-affirming surgery)	Surgical procedures alter physical appearance and function to better align one's appearance with gender identity • Variety of procedures, including chest alteration, genital alteration, facial feminization, and others • Considered irreversible	Usually considered in adults, but in adolescents on a case-by-case basis

hormone (GnRH) analogs are safe, reversible medications that pause pubertal development, thereby relieving the distress of pubertal development in an adolescent who is experiencing gender dysphoria. The medication can be initiated when patients reach Tanner stage 2 or at any subsequent point throughout puberty. The use of GnRH analogs allows the TGD adolescent and the family time to explore gender identity, access psychosocial supports, further refine treatment goals, and establish a longer-term treatment plan. Ultimately this intervention can prevent undesired, irreversible physical development and can allow avoidance of surgery that would otherwise be needed to revise such undesired development. (45)(46) Although GnRH analogs used in this manner lead to improved mental health outcomes, (47) the research on long-term risks is limited. (46) For many pediatric patients, use of GnRH analogs is the first step toward medical management of gender dysphoria.

GENDER AFFIRMATION

There are multiple factors that contribute to gender affirmation:

- *Social affirmation* includes reversible changes to one's gender expression, such as name or pronoun changes or changing one's clothing or appearance. These external changes can be critical for TGD youth: a recent longitudinal study suggests that early support and social acceptance of TGD identity is linked with decreased depression rates (similar to cisgender peers) and substantially reduced rates of anxiety. (24)

- *Legal affirmation* involves legally changing the name and gender identifier on all identification and legal documents.
- *Medical affirmation (gender-affirming hormones)* involves administration of sex steroids, primarily estradiol or testosterone, to induce feminine or masculine physical development, respectively. For some patients, including many TGD youth who identify as nonbinary, progestins and progestin agonists can provide benefit, including suppressing menses (contraceptive agents), suppressing endogenous androgens (spironolactone or finasteride), or augmenting feminization with estradiol. (35)(44) Medical affirmation may be done by PPCPs, with sufficient training and support available, or through consultation with trained gender specialists. (45)(48) When used longitudinally, gender-affirming hormones will eventually lead to both reversible and irreversible changes and will require intermittent serum monitoring to prevent subtherapeutic or supratherapeutic adverse effects. The use of gender-affirming hormones in TGD youth at serum levels physiologically concordant with the asserted gender seems to be safe, (49) with increasing evidence that supports its positive therapeutic impact. (50)(51)
- *Surgical affirmation (gender-affirming surgery)* involves irreversible procedures to achieve feminizing or masculinizing features related to hair distribution, chest contour, genitalia, facial features, etc. Current protocols typically reserve surgical affirmation for adults but allow for consideration in adolescence on a case-by-case basis depending on the potential benefit of the surgery to the individual's overall health and development. (52)(53) The PPCP can provide an important voice in this discussion (along with gender care specialists and mental health providers), facilitate referral to appropriate providers locally or elsewhere in the United States, and play a key role in presurgical and postsurgical planning, preparation, assessment, and follow-up.

FERTILITY AND FAMILY PLANNING

It is important to counsel all TGD youth and parents considering medical and surgical gender affirmation on the potential issues related to sexual function, fertility, and family planning. Gender-affirming hormones may impair erectile function and stop menses but do not necessarily prevent unintended pregnancy. (54) In addition, the effect of sustained GnRH analogs and gender-affirming hormones on fertility remains unknown (35); patients who start GnRH analogs early in puberty and transition directly to hormone therapy may experience a reduction or elimination of fertility. (44) Hormonal and surgical methods of contraception should be reviewed with all TGD youth, (34)(35) with careful consideration for menstrual pattern or absence depending on the method selected. TGD youth should be counseled about family planning and should be offered fertility preservation options early in treatment. (35)(55)(56) TGD individuals have options for achieving their desired family but report encountering many barriers to becoming a parent. (55) As reproductive technologies continue to evolve, it is likely that fertility preservation options for TGD individuals will expand (57); PPCPs should identify gynecologic and urologic collaborators in their region to support provision of all options.

AN ECOLOGICAL APPROACH: MENTAL HEALTH, FAMILY AND SCHOOL SUPPORT, AND PUBLIC POLICY

A youth's disclosure of his or her TGD identity, or "coming out," should occur when the patient deems to be ready, with appropriate support, and after consideration of any possible safety issues (ie, risk of interpersonal violence, homelessness, etc). Information related to gender and sexuality is considered confidential, as long as there is no apparent risk of harm, and it is never appropriate for a provider to openly disclose or "out" a patient's TGD status. (5)(28) The PPCP can act as a trusted adult for children and adolescents who are unsure of how to approach disclosure to family and friends. PPCPs can facilitate these important conversations with family, put supports in place, and brainstorm or provide safety plans for patients preparing to disclose their gender identity.

The treatment for gender dysphoria is affirmation, understanding, and support to prevent internalization and isolation. Multiple studies indicate that family acceptance of a TGD youth is critical to their short- and long-term well-being, with improved health outcomes well into adulthood. (58) Yet families often struggle to understand and accept their child's TGD identity because of their deep-set beliefs, fears, response to social pressure, and biases. (25) It is important to note that "acceptance" refers to the ability to recognize the youth's struggle and to provide unconditional love. There may be concerns, questions, and disagreements on the part of the parent and/or the youth that need to be acknowledged; this does not necessarily constitute rejection but is part of the process of acceptance and accommodation over time. (25)(59) A primary role of the PPCP is to facilitate these conversations and advocate for the TGD youth in making sure that dialogue occurs without causing harm.

Adolescents spend much of their time at school, and this environment may be particularly uncomfortable for TGD

adolescents. TGD youth report missing school due to feeling unsafe and/or being denied bathroom access and report being discouraged from participation in extracurricular activities. (31) They report increased experiences of verbal harassment, physical assault, and sexual abuse at school. (30) In a national study, only 6% of TGD youth said that their schools had policies to protect them based on gender identity. (31) In light of this, PPCPs can help adolescents and parents identify and access supportive adults in the school and can partner with schools to create a safe environment for TGD youth (eg, through support of antibullying policies and accommodations that affirm a child's asserted gender, such as use of asserted name and preferred bathroom use).

From a public health perspective, TGD individuals, compared with their cisgender peers, experience substantially higher lifelong rates of anxiety, depression, self-harm and suicidality, substance use, eating disorders, victimization, homelessness, and incarceration. (8)(10)(11)(19)(28)(30)(48)(60) Minority stress theory postulates that both explicit and implicit biases foster prejudice and discrimination against stigmatized minoritized groups, which, when combined with low social support and resources, leads to a physiologic stress response. When stress persists, it leads to anxiety, depression, and poor mental and physical health sequelae. (61) The experience of stigma and exclusion from a TGD identity can intersect with race, ethnicity, socioeconomic status, migrant status, and other marginalized identities to compound the experience of stress and sense of being different than others. (61)(62) This model may explain some of the extreme health disparities faced specifically by transgender women of color. (62) Leaders and policymakers need to understand the barriers faced by minoritized populations to promote population health through decisions that promote awareness and equity while reducing disparities in resources and opportunities. PPCPs can play an integral role in advocacy toward such change.

CONCLUSION

Our understanding of gender identity, including the medical and emotional needs of TGD youth and their families, is continually evolving. As our cultural understanding gains momentum, it can be challenging for PPCPs to keep up with new/changing terms, treatment options, and best practices. Historically, gaps in knowledge and training present unnecessary barriers to care for TGD individuals, particularly among children and adolescents. PPCPs have the potential to play an essential role in early identification and affirmation of gender-diverse youth. In delivering appropriate screening, anticipatory guidance, and supportive care to children and adolescents as they explore concepts of gender, sexuality, and gender identity, PPCPs can use the familiar pediatric framework of growth and development to support gender exploration and authentic gender assertion as a normative experience. This fosters early access to mental health, family support, and ongoing gender-affirming care that, ultimately, reduces the risk of gender dysphoria, isolation, and shame that many TGD youth unfortunately face. PPCPs can be strong allies for TGD patients and their families in the clinic, community, and beyond, providing the promise of both a medical home and a future that celebrates people for being true to themselves.

Evidence/Summary

Growing evidence reflects the value of using an ecological, gender-affirming approach to TGD youth in all settings, but especially in primary care. Supportive acceptance from a known PPCP can facilitate medical and psychosocial supports that will enable TGD youth to live their authentic gender experience at home, at school, and in their community.

- Based on strong recommendations B, C, and D, a pediatric gender-affirmative care model acknowledges an individual's unique gender experience within their developmental process. It naturally builds on the family-centered, strength-based focus of primary care pediatrics to foster positive development through open communication, empathy, and resiliency.
- Based on strong recommendations B and C, transgender and gender-diverse (TGD) youth may present to the clinical setting with heightened distress as they go through the physical and emotional changes of puberty. TGD youth may not explicitly identify gender concerns but might instead exhibit high-risk behaviors and social disengagement (eg, school failure, social isolation, substance use, self-harm, disordered eating, high-risk sexual behaviors).
- Based on strong recommendations C, D, and X, PPCPs play an essential role in identifying and normalizing gender diversity early so that family support and understanding can be established. This is achieved through routine gender screening and anticipatory guidance throughout childhood.
- Based on strong recommendations C, D, and X, early identification provides increased engagement and support, timely targeted planning and treatment options, and an increased likelihood that the TGD youth's ongoing development will be congruent with their asserted gender identity.
- Based on strong recommendations B, C, D, and X, there is growing understanding and research regarding best practice in gender care for children and adolescents. This knowledge base will continue to evolve, but current best practices support a gender-affirmative approach throughout childhood and adolescence. Approaches that force children to suppress rather than explore their authentic self, or that deny access to appropriate medical care and emotional supports, are detrimental to childhood health and well-being.

CASE FOLLOW-UP

Because Alex is uncomfortable talking about puberty, the PPCP affirms that puberty can be a sensitive topic for all children but that it is a critical period of physical, emotional, and cognitive change. The PPCP says, "Sometimes these changes may not feel right, and may make children scared or uncomfortable." Assurance is given to Alex that the clinic is a "safe space" where one can ask questions, raise concerns, or talk about anything that feels uncomfortable. The PPCP asks, "Do you have any questions or problems about your body?" Alex answers, "Kids at school sometimes tease me and say I am a boy, and sometimes I do feel more like a boy." Mom states, "Shouldn't Alex know her gender by now?" The PPCP responds, "Gender is complicated. While we often think kids have it figured out at a younger age, we now know that is not always the case. I am really glad we are talking about this because your mom and I are here to support you." Alex smiles as Mom states, "No matter what the gender, you are still Alex to me and I love Alex no matter what."

RESOURCES

Guidelines and Protocols

- World Professional Association for Transgender Health: http://www.wpath.org
- Endocrine Society: https://www.endocrine.org/guidelines-and-clinical-practice/clinical-practice-guidelines
- University of California San Francisco Center of Excellence for Transgender Health: http://transhealth.ucsf.edu/
- Fenway Health: http://fenwayhealth.org/care/medical/transgender-health/
- Human Rights Campaign & American Academy of Pediatrics - Supporting & Caring for Transgender Children: https://www.hrc.org/resources/supporting-caring-for-transgender-children
- Physicians for Reproductive Health, Adolescent Reproductive Sexual Health Education Project: https://prh.org/medical-education/

Hotlines for Youth

- GLBT National Youth Talkline (peer counseling, local resources): 800-246-PRIDE
- National GLB Youth Hotline: 800-347-TEEN
- The Trevor Project (suicide prevention, resources): 866-488-7386, http://www.thetrevorproject.org

General Education on LGBTQ Issues and Mental Health

- Gender Spectrum (resources, trainings for gender sensitivity): http://www.genderspectrum.org
- The Gender Book (book explaining complexities of gender, resources): http://www.thegenderbook.com
- National Alliance on Mental Health: https://www.nami.org/Find-Support/LGBTQ
- CDC Fact Sheet: http://www.cdc.gov/lgbthealth/youth.htm
- Gay, Lesbian & Straight Education Network (resources for educators): http://www.glsen.org

Family Resources

- The Family Acceptance Project: https://familyproject.sfsu.edu
- Parents, Families & Friends of Lesbians and Gays (PFLAG): http://community.pflag.org
- The Parents Project: http://www.theparentsproject.com
- Gender Spectrum (includes resources for schools): http://www.genderspectrum.org

References for this article are at http://pedsinreview.aappublications.org/content/41/9/437.

Trans Teen Shares Her Story

EDITOR'S NOTE
Jazz Jennings is an adolescent who at a young age identified herself as a female after being "assigned" as a male at birth. Jazz and her mother, Jeanette, advocate for LGBTQ (lesbian, gay, bisexual, transgender, queer/questioning) rights. Their commentary is a powerful statement on the serious consequences that result from ignoring the issues facing youth with transgender dysphoria.

Jazz: I've always known I was a girl. My heart and soul are female. I just happen to have been born with male genitalia. From the time I could express myself, I acted like a stereotypical girl and told my parents that I was a girl.

At first they thought it was a phase, but the harder I pushed, the more they listened. They never forced me to be someone I wasn't and let me transition into the girl I knew I was at the age of 5, but I was one of the lucky ones. There are so many kids who hide who they are or aren't accepted by their parents.

Jeanette: When my daughter Jazz was first diagnosed with gender identity disorder, now called gender dysphoria, at the age of 3, my husband and I were broken-hearted. We knew that her journey in life was going to be filled with hardship, but instead of trying to change her to comply with societal norms, we embraced her for who she was and promised her a life filled with unconditional love and acceptance.

Jazz endured bigotry, discrimination, and bullying, but her biggest fear was that she would look like her dad one day. She'd have nightmares about growing a beard and a mustache. We educated ourselves and learned that because Jazz was still young, it would be possible to delay puberty and avoid having her body betray her. Fifty percent of transgender youth attempt suicide before they are age 21, and we were determined that she wouldn't be another statistic. In our eyes, hormone treatment was a life or death situation. We wanted a live daughter, not a dead son.

Jazz: The puberty blockers and cross-sex hormones did save my life. If my parents had waited, it would have been too late. It's impossible to erase all of the secondary male characteristics that accompany male puberty. I have friends who transitioned after puberty. They have Adam's apples that need to be shaved and have full beards that will need to be removed with painful electrolysis and laser treatments. Many of them self-harm, have attempted suicide, and end up hospitalized. It's devastating for them.

They all wish that they could have stopped male puberty like I did. The same holds true for my guy friends. All of them have had or will need double mastectomies, and they wanted to die when their menstrual cycles began.

Jeanette: I have committed my life to helping transgender youth. Their voices need to be heard when they are young. The signs are often there, and, therefore, it's up to the adults to be in tune with them and listen to what they have to say. In addition, those adults need to take action and put their child's needs and wants ahead of their own egos.

Education is the key. There's so much information on the internet and in the media. There's no excuse for those who look the other way. Early professional intervention is mandatory so that these children can lead happy, productive lives. As Jazz would say, "They are just kids, and all kids deserve to be happy."

Jeanette Jennings, Jazz Jennings

NOTE: *Jazz Jennings is a 15-year-old transgender girl who socially transitioned when she was 5. She's been an advocate for trans youth since she was first interviewed*

AUTHOR DISCLOSURE Mrs. Jennings has disclosed no financial relationships relevant to this article. This commentary does contain a discussion of an unapproved/investigative use of a commercial product/device.

by Barbara Walters at the age of 6. She is the coauthor of the children's picture book, "I Am Jazz," about her early life. Jazz was named one of "The 25 Most Influential Teens" in 2014 and 2015 by Time *magazine.*

Jeanette Jennings is a proud mom of four who has been married 22 years to her husband Greg. Her youngest, 15-year-old daughter Jazz, is transgender. In 2007, the family started sharing their story publicly and created the TransKids Purple Rainbow Foundation. She and Jazz speak all over the country at schools, universities, medical conferences, and symposiums.

Jazz, Jeanette, and their family are the subjects of the TLC docuseries "I Am Jazz."

Parent Resources from the AAP at HealthyChildren.org

- English only: https://www.healthychildren.org/English/ages-stages/gradeschool/Pages/Gender-Non-Conforming-Transgender-Children.aspx

Definitions: Accepted terminology can evolve rapidly, so it may not always be possible to know every single term. However, exerting some effort to be familiar with basic concepts and frequently used terms demonstrates genuine respect for Transgender and Gender Diverse people and is an important aspect of building trust with your patients. The National LGBTQIA+ Health Education Center maintains an up-to-date list of terminology for Healthcare teams. It is useful to skim this periodically to update your basic working knowledge. If patients use a term with which you are unfamiliar, it is ok to be open about your gap in knowledge, but it is important that you not rely on patients exclusively for your education. Make a note and look it up!

LGBTQIA+ Glossary of Terms for Health Care Teams » LGBTQIA+ Health Education Center

Outdated Terminology should not be used, **UNLESS** a patient specifically indicates that they prefer a particular term. Remember, patients are the authority on their own identities. It is the healthcare team's job to help patients feel comfortable and safe in our clinics, so that effective partnership that supports the patient's health can be achieved. The following terms are generally considered outdated:

- Transsexual
- Transgenders / Transgendered
- "Preferred" Pronouns
- FTM and MTF
- Sex reassignment surgery
- Cross sex hormone therapy
- Gender Non-Conforming

Development of Gender Identity – These commonly cited milestones are based on research with cisgender children and may not capture the full range of healthy variation among human beings. Recognize that even young children are beginning to understand concepts of gender and are able to communicate their internal experiences to others.

- **2 years:** Children become conscious of physical differences between boys and girls.
- **3 years**: Most children will easily label themselves as either a boy or a girl
- **4-5 years**: Most children have a stable sense of their gender identity.

Health Inequities among TGD youth are well documented in the medical literature. It is important to recognize that differences in health outcomes correlate strongly with the frequency of discriminatory experiences both within the healthcare system and broader society. Current evidence supports that unconditional acceptance and affirmation fosters healthy development among TGD youth.

Mental Health

- Higher rates of depression and more than twice as likely to have SI
- Higher rates of eating disorders
- Experience significantly higher rates of bullying and physical violence
- Stigmatization and parental rejection are common—often leading to psychological distress, low self-esteem, and homelessness; which all increase rates of risky behavior.

Sexual Health

- More likely to have intercourse before age 13, with > 4 partners, and less likely to use protection.
- HIV rates for bisexual and/or gay men and trans feminine youth are increasing among 13 to 24 year olds.

Drug Use

- Higher rates of tobacco, alcohol, marijuana, cocaine, ecstasy, methamphetamine, heroin use
- People who are denied safe alternatives for gender affirming healthcare may resort to unsafe practices, such as injecting liquid silicone, share needles, or using hormones form unreliable sources.

Adverse Experiences (in adults, as reported in the 2015 US Transgender Survey)

- 10% experienced violence from an immediate family member
- 8% experience homelessness before 18, 13% lived in foster care before 18
- 54% verbally harassed in school and 24% physically assaulted
- 33% reported at least 1 negative experience with a clinician
- 23% avoid seeking medical care due to fear of mistreatment
- 40% report a suicide attempt in their lifetime (9x the general population)
    - Increases with increase in discriminatory experiences

Office Visits

Making a LGBTQ friendly office- Create an accepting environment

- Questionnaires and intake forms should not assume patient/parent(s) are cisgender/heterosexual
- Ensure all staff use inclusive terms (i.e. using “partner” instead of “girlfriend”)
- Create a confidential environment: inform caregiver and patient that information will not be shared without consent, unless there is a concern for safety (abuse, SI/HI)
- Use appropriate names and pronouns - mirror language of the patient
- Acknowledge and apologize for mistakes. Don’t dwell on it, but DO commit to learning..
- Safety signals, such as a lapel pin with a Pride flag or your pronouns, can show that TGD youth are expected in your clinic and can trust that their healthcare needs will be met.
- When cisgender people include pronouns in their signature block, it shows allyship and signals safety.

Health Care

- It can be helpful to ask patients if they are willing to share their gender story with you
    - Listening without judgment helps build trust
- Pertinent history:
    - Social support system (family and friends)
    - Affirming practices that may prompt further screening questions (tucking, binding, etc.)
    - Mental health diagnoses
    - Prior use of puberty blockers or hormone therapy
- Obtain an appropriate comprehensive and nonjudgmental psychosocial history.
- Referrals to consider:
    - Behavioral Health is always appropriate for affirming support.
        - WPATH SOC8 stresses the importance of BH involvement for all youth considering medical interventions, especially irreversible ones.
    - Endocrinology/ Adolescent Medicine
        - Referral is appropriate for children with diagnosis of gender dysphoria requesting puberty blockers or GAHT.
        - Tricare covers GAHT if meeting readiness criteria outlined in the Endocrine Society Guidelines, typically not before age 14. Requires informed consent of all custodial parents and assent of the child.
- CDC recommends assessing all teens for STI risk and following STI testing based on sexual behaviors. Never presume sexual behaviors based on gender identity or sexual orientation.
- If an individual has a body part or organ which meets criteria for cancer screening, screening should be completed regardless of history of treatment with GAHT

Specifics for Transgender Care

A diagnosis of Gender Dysphoria is currently required to document the medical necessity of (and thus insurance coverage for) gender affirming healthcare services. There is a push to step away from using this diagnosis due to the historic stigmatization of categorizing transgender identities as mental health disorders. ICD11 includes the diagnosis of "gender incongruence" which recognizes that not all TGD people experience "dysphoria". There will likely be further evolution in the future of how gender affirming healthcare services are coded and billed.

Gender Dysphoria (DSM-V TR criteria): 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, lasting at least 6 months and manifested by at least 2 of the following:

- 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)

· In order to meet criteria for the diagnosis, the condition must be associated with clinically significant distress **OR** impairment in social, occupational, or other important areas of functioning. Self-reported distress is sufficient.
· Diagnosis of 'Gender Dysphoria' is currently required for TRICARE coverage of gender affirming treatments (Active Duty and dependents)
· Once begun, GnRH agonists (puberty blockers) or GAHT can always be stopped if the youth determines that another path will be more authentic. The goal of treatment is authenticity and supporting the overall wellness of the individual.

Active Duty Personnel – DoD Instruction allows for open service by transgender personnel, access to affirming healthcare services (GAHT and Surgery), and provides an administrative process by which a SM may request to transition to a different gender marker in the DEERS system. If questions arise, good resources for information include:

· Transgender Health Medical Evaluation Unit (THMEU) in San Antonio (usaf.jbsa.59-mdw.mbx.59-mdw-thmeu-mmdt@health.mil - POC Lt Col Joshua Smalley)

· NCR Transgender Health Program (dha.bethesda.j-11.mbx.transgender-health-program-ncr@health.mil - POC LTC Noelle Larson or Dr Brandy Hellman)

· Navy Medical Forces Atlantic or Pacific Transgender Care Teams (located at Portsmouth and San Diego - usn.hampton-roads.navhospporsva.list.nmcp-transgendercareteam@health.mil)

Military Instructions

- Executive Order (14004) Enabling All Qualified Americans To Serve Their Country in Uniform
  - https://www.federalregister.gov/documents/2021/01/28/2021-02034/enabling-all-qualified-americans-to-serve-their-country-in-uniform
- DoD Instruction 1300.28 – "In-Service Transition for Transgender Servicemembers" (Effective as of Apr 30, 2021)
  - https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/130028p.pdf
- Action Memo: "Health Care for Transgender Service Members – Guidance for Service Members Who Identify as Non-Binary"
- Army Directive 2021-22 – "Army Service by Transgender Persons with Gender Dysphoria"
  - https://armypubs.army.mil/epubs/DR_pubs/DR_a/ARN32878-ARMY_DIR_2021-22-000-WEB-1.pdf
- Air Force guidance:
  - Multiple resources on the AF Portal, search "Air Force Transgender Policy"
  - DAFPM2021-36-01
- Interim Guidance for Service of Transgender Navy Personnel
  - https://www.mynavyhr.navy.mil/Portals/55/Messages/NAVADMIN/NAV2021/NAV21112.txt?ver=LuE9Glp3b43jo7YX8pHFDg%3d%3d
- Marine Corps Guidance:
  - https://www.marines.mil/DesktopModules/ArticleCS/Print.aspx?PortalId=1&ModuleId=542&Article=2604406

Resources for Providers

- World Professional Association for Transgender Health. (2022). Standards of Care for the Health of Transgender and Gender Diverse People [8th Version].
  - https://www.wpath.org/publications/soc
- Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline
  - Hembree, WC., et al. Endocrine Treatment of Gender Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017, 102 (11): 3869-3903.
  - CORRIGENDUM FOR "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline"
- VHA Self-Paced Training Modules for Practitioners
  - https://www.train.org/main/search?query=VHA%20transgender%20and%20gender%2 0diverse
  - https://www.lgbtqiahealtheducation.org/collection/trans-pediatric-care-toolkit/

Gender Diverse Youth Quiz

1. Define the following terms:

a. Assigned Sex:

Refers to the sex that is assigned to an infant, most often based on the infant's anatomical and other biological characteristics. Commonly abbreviated as AFAB (assigned female at birth) or AMAB (assigned male at birth).

b. Gender Identity:

A person's inner sense of being a girl/woman/female, boy/man/male, another gender, or having no gender.

c. Gender Expression:

The way a person may communicate their gender to the world through mannerisms, clothing, speech, behavior, etc. Gender expression varies depending on culture, context, and historical period.

d. Sexual Orientation

How a person characterizes their emotional and sexual attraction to others.

e. Transgender:

May describes a person whose gender identity does not correspond to the sex they were assigned at birth, based on traditional expectations. For example, a person assigned female sex at birth who identifies as a man; or a person assigned male sex at birth who identifies as a woman. Transgender can also include people with gender identities outside the girl/woman and boy/man gender binary structure; for example, people who are gender fluid or non-binary. Sometimes abbreviated as trans.

f. Cisgender:

A person whose gender identity is consistent with their sex assigned at birth; for example, a person assigned female sex at birth whose gender identity is woman/female. The term cisgender comes from the Latin prefix cis, meaning "on the same side of."

g. Non-binary:

Describes a person whose gender identity falls outside of the gender binary structure of girl/woman and boy/man. Sometimes abbreviated as NB or enby.

h. Ally:

A person who actively supports the rights of a marginalized community even though that person is not a member of that community; for example, a heterosexual person who campaigns for the rights of gay people.

2. In what ways does an affirming home environment benefit transgender youth?

The treatment for gender dysphoria is affirmation, understanding, and support to prevent marginalization and isolation. Multiple studies indicate that family acceptance of a TGD youth is critical to their short- and long-term well-being, with improved health outcomes well into adulthood. ''LGBTQ youth who reported having at least one LGTBQ-affirming space had 35% reduced offs of reporting a suicide attempt'' (Trevor Project)

3. List 3 ways you can make your clinic more welcoming and inclusive for transgender youth.

Intake forms should not assume cisgender or heterosexuality of the patient or caregivers, use appropriate pronouns and terms, create a confidential environment (with the exception for safety concerns), display signals to convey acceptance and allyship (i.e. pins), use pronouns in signature block, teach screeners and other staff to use inclusive language and practices with all patients.

4. What are 2 benefits of GnRH agonist therapy for transgender youth?

- Pubertal suppression can expand the diagnostic phase, giving the patient more time to explore options and to live in the experienced gender before making a decision to proceed with gender-affirming sex hormone treatments and/or surgery
- The experience of progressing through puberty is an undesirable condition for the GD/gender-incongruent individual and may seriously interfere with healthy psychological functioning and well-being

- Physical outcome is improved compared with initiating physical transition after puberty has been completed (can prevent the irreversible development of undesirable secondary sex characteristics)
- Pubertal suppression is recommended in early or mid-puberty. Other options are available for adolescents in later pubertal stages to stop menses or mitigate the appearance of facial/body hair when desired.

5. Should GnRH agonists be considered in prepubertal children?

No.

Tanner stage 2 is the optimal time to start pubertal suppression. Adolescents with GD/gender incongruence should experience the first changes of their endogenous puberty, because the emotional reaction to the first physical changes has diagnostic value in establishing the persistence of gender incongruence.

6. Are pubertal suppressive effects of GnRH agonists reversible?

Yes.

If, after further exploration with behavioral health, an individual discovers that medical transition is not the right path for them, they may choose to discontinue pubertal suppression. In children with precocious puberty, spontaneous pubertal development has been shown to resume after patients discontinue taking GnRH analogs. Pubertal suppression treatment in early puberty will limit the growth of the penis and scrotum. This may have implications for future options for gender affirming surgery. The primary risks of pubertal suppression in GD/gender-incongruent adolescents may include adverse effects on bone mineralization (which can theoretically be reversed with sex hormone treatment), compromised fertility if the person subsequently is treated with sex hormones, and unknown effects on brain development.

7. When is it appropriate to consider GAHT in a transgender adolescent?

After a multidisciplinary team of medical and mental health providers confirm the persistence of GD/ gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years.

Adolescents are eligible for subsequent sex hormone treatment if:
1. A qualified MHP has confirmed:
•the persistence of gender dysphoria,
•any coexisting psychological, medical, or social problems that could interfere with treatment (*e.g.*, that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start sex hormone treatment,
•the adolescent has sufficient mental capacity (which most adolescents have by age 16 years) to estimate the consequences of this (partly) irreversible treatment, weigh the benefits and risks, and give informed consent to this (partly) irreversible treatment,
2. And the adolescent:
•has been informed of the (irreversible) effects and side effects of treatment (including potential loss of fertility and options to preserve fertility),
•has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,
3. And a pediatric endocrinologist or other clinician experienced in pubertal induction:
•agrees with the indication for sex hormone treatment,
•has confirmed that there are no medical contraindications to sex hormone treatment.

8. What term is used for therapy that attempts to change the gender identity of a child? Why is this intervention harmful to transgender children?

"Reparative" or "conversion" psychotherapy describes a range of dangerous and discredited practices that attempt to change a person's sexual orientation or gender identity or expression. This practice undermines trust in the medical field/ medical professionals, ignores individuals lived experiences, and places patients (especially minors) at an increased risk for depression, anxiety, drug use, homelessness, and suicide.

Such practices have been rejected by every mainstream medical and mental health organization for decades, but due to continuing discrimination and societal bias against LGBTQ people, some practitioners continue to conduct conversion therapy.

https://www.hrc.org/resources/the-lies-and-dangers-of-reparative-therapy

Gender Diverse Youth Cases

Case 1: You are on an overnight call on the Pediatric Ward of your hospital. The ER calls you to evaluate a 16 year old transgender girl who was assigned male sex at birth and goes by the name Samantha. She is complaining of abdominal pain. As you arrive, you overhear the nurse refer to the patient using he/him pronouns and with her "dead name", John. How might you address this situation with the ER staff?

1. Politely correct the nurse (i.e. "her name is Samantha"). You might recommend to the staff to acknowledge the mistake directly with the patient and use the proper name and pronouns moving forward.

How might you address the patient to help rebuild trust and provide compassionate, patient-centered care?

1. Create a confidential environment: inform caregiver and patient that information will not be shared without consent, unless there is a concern for safety
2. Use appropriate names and pronouns - mirror language of the patient
3. Acknowledge, briefly apologize for mistakes, and most importantly. correct them moving forward.
4. Consider displaying safety signals

Case 2: In your clinic rotation you see a 13 year old assigned female sex at birth. During the psychosocial evaluation of the patient without parents in the room, the patient tells you that they identify as male but parents do not know and the patient is very interested in receiving gender affirming care. How might you proceed?

1. Take a good history from the patient (HEADSSS, are they willing to share their gender story, have they expressed these feelings to anyone else, are they presenting as male in any domains of their life-such as school or other social environments)
2. Ask whether the patient feels comfortable discussing this with their parents
    1. Assess for safety at home, school
    2. Any parental disagreement regarding the patient's gender identity?
    3. Offer support to help guide the conversation between the patient and their parents
3. Referrals
    1. Behavioral health support is always an appropriate first step.
    2. Adolescent medicine/ endocrinology, depending on patient goals. May be helpful for gathering accurate information about options, even if not ready to pursue any specific treatment. Good to set appropriate expectations, i.e. there might be a further evaluation process, might not receive GAHT at the first visit, if that is their ultimate goal.

Through further discussion with the family, you learn they are about to PCS to a state prohibiting gender affirming care for minors. What additional factors would you consider? Who could you refer to for help?

Through further discussion with the family, you learn they are about to PCS to a state prohibiting gender affirming care for minors. What additional factors would you consider? Who could you refer to for help?

There is no perfect solution, and the landscape is evolving. It is important to ensure the patient and family know that you are an ally and will try to get them set up for appropriate care.

1. Could EFMP enrollment for adolescent or endocrinology follow-up be helpful?
2. Reach out to adolescent medicine colleagues to help troubleshoot (virtual visits)
3. https://www.lgbtmap.org/equality-maps (The Movement Advancement Project (MAP) tracks over 50 different LGBTQ-related laws and policies)

Case 3: You see a 17 year old transgender male for a well check in clinic. He and his family just moved to the area and he is not established with adolescent medicine or endocrinology. He is currently coming up on 6 months of receiving testosterone injections (and has plenty of medication). What are things you need to do during this appointment in addition to routine adolescent care? *Hint- be sure to review Endocrine Society's Gender Dysphoria/ Incongruence CPGs*

- HEADSSS
- Ask about physical changes so far, if they continue to be wanted, and if there are any adverse reactions
- Ensure safe practice of binding.
- Screenings: Endocrine Society Guidelines
    - Monitor signs of virilization and adverse reactions (every 3 months for the first year, then bi-annually or annually after)
    - Every 3-6 months
        - Obtain height, weight, sitting height, blood pressure, Tanner stage
        - Transgender Males: Measure serum testosterone every 3 months until they are ''normal male values''
    - Every 6-12 months
        - In transgender males: Hgb/Hct (every 3 months for the first year, and every 6-12 months after), lipids, 25-OH Vit D
        - In transgender females: prolactin, estradiol, 25OH vit D
    - Every 1-2 years
        - BMD using DXA (should be monitored until age of 25-30 years, or until peak bone mass has been reached)
        - Bone age on Xray of left hand

Provide referrals: adolescent/ endocrinology/ behavioral health

Table 9. Baseline and Follow-up Protocol During Induction of Puberty

Every 3–6 mo
•Anthropometry: height, weight, sitting height, blood pressure, Tanner stages
Every 6–12 mo
•In transgender males: hemoglobin/hematocrit, lipids, testosterone, 25OH vitamin D
•In transgender females: prolactin, estradiol, 25OH vitamin D
Every 1–2 y
•BMD using DXA
•Bone age on X-ray of the left hand (if clinically indicated)
BMD should be monitored into adulthood (until the age of 25–30 y or until peak bone mass has been reached).
For recommendations on monitoring once pubertal induction has been completed, see Tables 14 and 15.

Adapted from Hembree *et al.* (118).

Abbreviation: DXA, dual-energy X-ray absorptiometry.

Table 14. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Male

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of virilization and for development of adverse reactions.
2. Measure serum testosterone every 3 mo until levels are in the normal physiologic male range:[a]
a. For testosterone enanthate/cypionate injections, the testosterone level should be measured midway between injections. The target level is 400–700 ng/dL to 400 ng/dL. Alternatively, measure peak and trough levels to ensure levels remain in the normal male range.
b. For parenteral testosterone undecanoate, testosterone should be measured just before the following injection. If the level is <400 ng/dL, adjust dosing interval.
c. For transdermal testosterone, the testosterone level can be measured no sooner than after 1 wk of daily application (at least 2 h after application).
3. Measure hematocrit or hemoglobin at baseline and every 3 mo for the first year and then one to two times a year. Monitor weight, blood pressure, and lipids at regular intervals.
4. Screening for osteoporosis should be conducted in those who stop testosterone treatment, are not compliant with hormone therapy, or who develop risks for bone loss.
5. If cervical tissue is present, monitoring as recommended by the American College of Obstetricians and Gynecologists.
6. Ovariectomy can be considered after completion of hormone transition.
7. Conduct sub- and periareolar annual breast examinations if mastectomy performed. If mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society.

a Adapted from Lapauw *et al.* (154) and Ott *et al.* (159).

The patient's father was not able to attend many of his prior appointments and asks you to review some of the risks associated with testosterone therapy. What do you tell them?

Chart below

Table 10. Medical Risks Associated With Sex Hormone Therapy

Transgender female: estrogen
Very high risk of adverse outcomes:
•Thromboembolic disease
Moderate risk of adverse outcomes:
•Macroprolactinoma
•Breast cancer
•Coronary artery disease
•Cerebrovascular disease
•Cholelithiasis
•Hypertriglyceridemia
Transgender male: testosterone
Very high risk of adverse outcomes:
•Erythrocytosis (hematocrit > 50%)
Moderate risk of adverse outcomes:
•Severe liver dysfunction (transaminases > threefold upper limit of normal)
•Coronary artery disease
•Cerebrovascular disease
•Hypertension
•Breast or uterine cancer