COMMENTARY

Time to Hit Pause on 'Pausing' Puberty in Gender-Dysphoric Youth

William Malone, MD

September 17, 2021

Teens are identifying as transgender in record numbers. In 2017, 3-4 in 100 teens in the United States reported that they are or may be transgender. A more recent 2021 study suggests that the rate of transgender identification among America's youth may be as high as 9 in 100. All of the major gender centers in the world have reported a several-thousand-percent increase in youth presenting with gender distress.

How do we reconcile these numbers with 2013 data reporting the prevalence of adult gender dysphoria to be a rare 2-14 in 100,000? Reflection is warranted because many US medical societies support providing youth who have transgender identification (over 1 million children and adolescents, using the latest estimates) with access to powerful endocrine interventions.

GnRH analogues (colloquially known as "puberty blockers") are now available at Tanner stage 2 of puberty — a threshold crossed by females as young as 8-9 years old. Cross-sex hormones and surgeries follow, and mastectomies are now available to children as young as 13. Genital-altering surgeries, as well as the removal of the ovaries, uterus, and testes, can be obtained as soon as a patient turns 18.

What's driving this massive increase in trans-identified youth? What are the risks, benefits, and uncertainties associated with hormonal and surgical interventions? Do such interventions improve the long-term psychological health of gender-dysphoric youth? How many will regret the irreversible changes made to their bodies during what may have been a temporary phase in their development?

We don't know the answers to these questions, but we need to figure them out before offering such interventions. Frontline clinicians — especially those working with youth — will not be able to remain on the sidelines of this issue for much longer. Each clinician considering writing a prescription for puberty blockers or cross-sex hormones, or generating a referral for surgery, will need to answer for themselves: *Just because I can, does it mean I should?*

What's Contributing to the Rapid Rise of Gender-Dysphoric Youth?

The etiology of the rapid rise of transgender identifications in young people is vigorously debated. Proponents of hormonal and surgical interventions for youth argue that the several-thousand-percent increase in the numbers of youth seeking gender reassignment is a reflection of more social acceptance of transgender identities, allowing more young people to "come out." But closer examination of this claim reveals several inconsistencies.

Because adolescent and young adult females now account for 6-8 in 10 of the presenting cases (previously, prepubertal males were more common), one would expect a commensurate increase in the rate of transgender identification in older females. This has not occurred. In addition, more than three quarters of currently presenting cases have significant mental health problems or suffer from neurocognitive comorbidities such as autism spectrum disorder or attention-deficit/hyperactivity disorder — a much higher burden of mental health comorbidities than the historical cohort with gender dysphoria.

There is legitimate concern that these comorbid mental health conditions, as well as the influence of social groups and online immersion into transgender topics, may be playing a role in the rapidly growing rate of transgender identification among these particularly vulnerable youth.

The initial study positing the theory that social influence is playing a role in the increased incidence of "late" or adolescent-onset (vs childhood-onset) transgender-identified youth was harshly attacked by proponents of medical transitioning of youth, despite the fact that the study utilized similar methods used in other areas of health research. The study underwent an unprecedented second peer review and emerged with largely unchanged conclusions.

Since the study's publication, a number of mental health clinicians working directly with gender-distressed youth have corroborated a rapid onset of transgender identification among teens with previously gender-normative childhoods.

Pioneers in Gender Dysphoria Treatment Are Changing Course

Several European countries that were pioneers in pediatric medical transition are now reversing course toward far more caution after their own evidence evaluations failed to show that medically transitioning gender-distressed youth improves mental health outcomes. In Sweden, following Karolinska Hospital's announcement that it will no longer transition people under 18 outside of strictly regulated clinical trials, a number of other pediatric gender clinics followed suit and made the same decision.

In the UK, Keira Bell — a young woman who was treated with "affirmative" hormonal and surgical interventions before detransitioning — brought a challenge against the national gender clinic. Her landmark case and the UK High Court's original judgement against the clinic have highlighted the urgency to reassess treatment approaches for the increasingly varied presentations of gender dysphoria in young people. As this article went to press, the UK's national gender clinic won its appeal against Keira Bell, meaning that doctors there will once again be able to decide whether their patients under 16 can properly consent to puberty blockers. Keira Bell said she is disappointed with this decision and will be seeking permission to appeal to the Supreme Court. She said the medical service had become "politicized," and added: "A global conversation has begun and has been shaped by this case. It has shone a light into the dark corners of a medical scandal that is harming children and harmed me. There is more to be done."

And the UK National Health Service (NHS) has already commissioned an independent systematic review of data, which concluded that the evidence of benefit of hormonal interventions in gender dysphoric youth is of very low certainty and must be carefully weighed against the risks. An independent taskforce has also been convened to reassess the country's approach to treating gender dysphoric youth.

Finland has arguably undertaken the biggest change of all. An early adopter of pediatric medical transition, researchers there noticed that adolescents who had mental health struggles at baseline failed to improve after transition. The Finnish national Gender Identity Development services issued new treatment guidelines in 2020 stating that psychotherapy, rather than gender reassignment, should be the first line of treatment for gender-dysphoric youth.

The leadership of America's medical societies have been slower to respond. Last month, the Society for Evidence-Based Gender Medicine applied to share information about youth gender transitions at the yearly meeting of the American Academy of Pediatrics (AAP). The application was denied without explanation, despite the fact that 80% of rank-and-file pediatricians who voted on AAP resolutions days earlier endorsed a resolution calling for a reassessment of the evidence and more caution regarding gender transitions of minors.

The AAP leadership apparently ignored the resounding support for this resolution, but the clear message from that vote is that frontline pediatricians do not agree with the "one size fits all" approach of automatically affirming gender-distressed youth as transgender and proceeding to gender reassignment.

What We Know and Don't Know

There is now growing evidence that the "gender-affirming" model, based on the unproven assumption that gender reassignment is the best way to help gender-distressed youth, is not living up to its promise. This should not be surprising. Despite more than 50 years of experience with mature adult gender transitions, there is a lack of convincing evidence that transitions improve the psychological functioning of those with gender dysphoria, and studies on regret have been plagued by high dropout rates that prevent meaningful conclusions for practitioners and patients alike. Pediatric transitions are a much more recent phenomenon, with little to no quality data to guide decision-making.

We are witnessing a growing number of vocal regretters who underwent gender reassignment as teens and young adults under "gender-affirming" care protocols in recent years. A review of stories on the subreddit r/detrans, which counts over 20,000 members (not all are detransitioners, as the forum is open to those fully detransitioned, partially detransitioned, desisted [those who identified as transgender for a period of time in their youth but no longer do], and questioning their transition) is flush with first-hand accounts of regret and should be mandatory reading for any clinician who is considering becoming a prescriber of gender-affirmative care.

Here is a brief outline of what we know — and more importantly, what we don't know — about the practice of medically transitioning minors.

- Most cases of early childhood-onset gender dysphoria self-resolve. Eleven out of 11 studies that followed the
 trajectory of gender-variant youth show that the most common outcome is natural resolution of gender dysphoria
 around or after puberty. Among those diagnosed as having gender identity disorder, 67% no longer met the
 diagnostic criteria as adults; among those subthreshold for diagnosis, 93% were not gender dysphoric as adults.
 Gender dysphoria in childhood is a far better predictor of future homosexuality than of future trans identity.
- The future trajectory of people whose transgender identity emerged during or after puberty is entirely unknown. No one has studied future trajectories of patients whose transgender identity emerged for the first time after the onset of puberty a previously rare but now increasingly common presentation. Growing numbers of young detransitioners and desisters are precisely from this demographic, suggesting that a transgender identity that emerges in adolescence may not be durable.
- Social transition does not improve mental health outcomes. Recent studies show that while socially transitioned children can thrive in the short term, they do not fare any better than their non–socially transitioned dysphoric peers. It appears that peer relations, not the social transition status, predict mental health in gender-dysphoric children. We don't yet know the long-term trajectories of socially transitioned minors, but emerging evidence suggests that they may be more likely to persist with gender-related distress rather than outgrow it, as previously observed. This in turn necessitates decades of invasive and risky medical interventions. In fact, the Dutch researchers who pioneered the protocol used to medically transition minors (see Box) explicitly and strongly discouraged social transition of children and early adolescents.

- Nearly 100% of children who begin puberty blockers will proceed to cross-sex hormones and surgeries. The two main studies that have evaluated the effects of puberty blockers on mental health found no improvements or improvements of marginal clinical significance. Both studies are also at critical risk of bias due to the absence of control groups. Four additional studies looking at the mental health effects of puberty blockers were plagued by design limitations and also failed to show any convincing positive effects on psychological health. However, one effect of puberty blockers has been consistently replicated: At least four studies show that virtually all of the children who start puberty blockers proceed to cross-sex hormones. This suggests that rather than being a pause button, puberty blockers may serve as the "gas pedal" for gender transition.
- Most of the long-term health risks are largely unknown. No long-term studies exist of patients who underwent medical transition as teens or young adults. Therefore, our ability to assess risks vs benefits is limited. Puberty blockers have been demonstrated to significantly impair bone health, and it is not clear whether this will result in future osteoporosis. Cross-sex hormones are associated with roughly 3-5 times the risk for heart attacks and strokes, though long-term studies are of insufficient quality for accurate risk assessments. Other risks associated with these endocrine interventions will come to light as the practice continues to scale and as young people spend years and decades on these interventions. The risks to fertility are largely unknown, but it is almost certain that if puberty blockers are given at the early stages of puberty and followed by cross-sex hormones, sterility will result.
- The medical pathway of "affirmative care" rests on a single Dutch study that is not applicable to the current populations of gender-dysphoric youth. Most of the youth presenting for care today would have been explicitly disqualified by the original Dutch protocol, as most have significant mental health comorbidities and post-puberty onset of trans identities. This fact has been recognized by the principal investigators of the Dutch protocol itself, who have recently begun to sound the alarm about the potential misapplication of their protocol and who suggest that psychotherapy rather than gender reassignment is more appropriate for many of the currently presenting cases.

On Suicidality

The urgency to put gender-dysphoric youth through gender reassignment despite the dearth of evidence appears to stem from the notion that if we don't intervene medically and in short order, these youth will commit suicide. However, studies using quality data reveal a markedly different reality.

While gender-dysphoric youth do have elevated rates of suicidality, it's not uniquely high. In fact, it's roughly similar to the rate of suicidality found in populations of youth referred for other mental health conditions. Quality long-term studies that explored whether transition leads to reduced suicidality have not been able to demonstrate a reduction.

Medicine has a pattern of enthusiastically embracing unproven medical interventions, only to find out years or decades later that the harms from those interventions outweigh the benefits. We owe it to our patients to be transparent about the limits of our knowledge and the fact that the "affirmative care" pathway is largely irreversible.

When the benefits of an intervention have not been shown to outweigh the risks, medical ethics dictate that such interventions should not occur outside of clinical trials. We must not conflate medical care for gender-dysphoric youth with experimental and risky interventions that are based on low-quality evidence. It's time to hit pause on gender transitions for youth.

A Brief History of the Dutch Protocol

Before the mid-1990s, medical transition was primarily reserved for mature adults. However, noting the "never-disappearing masculine appearance" of many adult male transitioners, a team of Dutch researchers hypothesized that it might be appropriate to provide early intervention to a carefully selected group of adolescents before the irreversible physical changes of puberty occur.

To differentiate the majority of gender-dysphoric children who would outgrow their cross-sex identification by adulthood from the few who would probably not have resolution and would wish to transition later in life, the Dutch gender clinic designed a rigorous screening protocol, with multidisciplinary teams closely following prospective candidates for several years.

To qualify for early intervention, the adolescents had to have had persistent and severe cross-sex identification from early childhood (cases of adolescent-onset trans identity were disqualified); the distress had to worsen during puberty; and the adolescents had to be free from any other significant mental health conditions. For qualifying adolescents, puberty blockers were initiated no earlier than 12 years of age, cross-sex hormones at 16, and surgeries upon turning 18. Ongoing psychotherapy was provided through the entire assessment and intervention period.

The Dutch team published the final results of their research in 2014. The authors reported that at the average age of 21 (approximately 1.5 years post-surgery), the young people were free from gender dysphoria and functioning well. Despite a postsurgical death from infection, several new diagnoses of metabolic illness, and multiple dropouts, the Western world enthusiastically embraced the early-intervention model. Concerningly, the only attempt to replicate the Dutch protocol outside of the Netherlands failed to show any psychological improvements, and to date, no long-term outcome data are available for the cohort of the 55 treated Dutch adolescents.

These progressively irreversible interventions form the basis of the "Dutch Protocol." Currently, this protocol is being scaled in ways it was never designed for. For example, it strongly discouraged childhood social transition and did not transition adolescents with postpubertal onset of transgender identity or those with significant mental health comorbidities. Yet, treating such cases with the interventions outlined in the Dutch protocol is now common, and the age of eligibility for hormonal and surgical interventions has progressively lowered, with children as young as 8 now eligible to begin puberty blockers.

William Malone, MD, is an assistant professor of endocrinology practicing in Southern Idaho and an advisor to the Society for Evidence-Based Gender Medicine.

Follow Medscape on Facebook, Twitter, Instagram, and YouTube

Credits:

Lead Image: Medscape Illustration/Getty Images

Medscape Diabetes © 2021 WebMD, LLC

Any views expressed above are the author's own and do not necessarily reflect the views of WebMD or Medscape.

Cite this: William Malone. Time to Hit Pause on 'Pausing' Puberty in Gender-Dysphoric Youth - Medscape - Sep 17, 2021.