Puberty Blocking Medications

Clinical Research Review:
Use in treatment for Gender Dysphoria

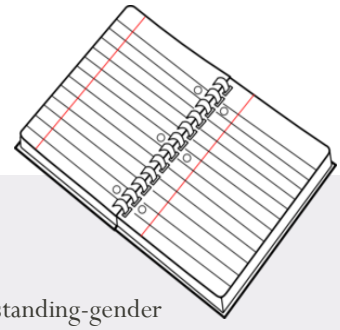
Also known as:
GnRH analogues

Puberty blockers are a medical treatment available to support the healthy development of transgender adolescents. By halting puberty, puberty blocking medications have been shown to reduce gender dysphoria (e.g., discomfort with sex characteristics) and promote mental health [1, 2, 3].

Photography provided by Lindsay Morris from ***You are You: A Photobook about Gender Unique Children***

Gender affirming medical care is considered medically necessary treatment for transgender individuals who experience physical dysphoria (i.e., distress associated with physical sex characteristics) [1, 2]. While not all individuals who experience a discrepancy between their gender identity and sex assigned at birth experience physical dysphoria, many do. Forms of gender affirming medical care include use of hormones and gender affirmation surgeries (e.g., "top" surgeries, "bottom" surgeries, facial feminization, and laser hair removal). Historically, transgender individuals were required to wait until age 18 to receive gender affirming medical care of any kind. Increasingly, transgender individuals are requesting care at earlier ages due to larger social shifts in visibility and acceptance that have resulted in earlier ages of "coming out." As a result, gender clinics specializing in the medical treatment of transgender individuals are offering cross-sex hormone therapy at younger ages (16-18 years old) [3, 4]. In addition, a number of doctors are now prescribing puberty blockers to adolescents with strong physical dysphoria that persists or emerges with the onset of puberty. Puberty blockers are prescribed after an assessment process with a multidisciplinary team and adolescents are tracked over time and provided with support during the transition period [5, 6].

The following report provides an overview of puberty blockers including how they work, how they are prescribed, and what research exists to support their use.



NOTES

Terms and Definitions:

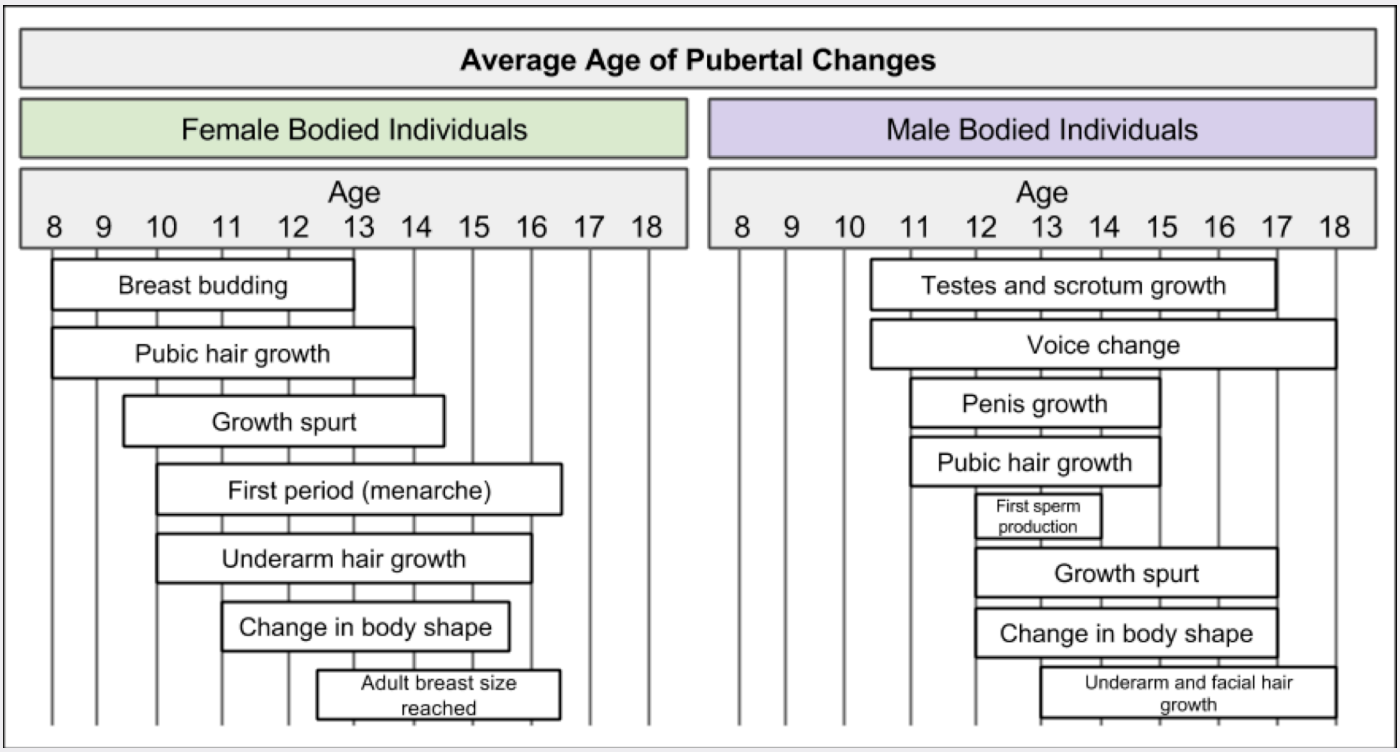
For more information on gender identity, terminology, and experiences commonly reported by transgender children and youth, please see: **Understanding Gender** genderspectrum.org/understanding-gender
Gender Identity Basics gaycenter.org/wellness/gender-identity

**Identity language used within the report references transgender children by their own stated gender identities (e.g., affirmed females/males). The terms "male bodied" and "female bodied" are used when relevant to discuss pubertal changes in the non-intersex population as identified by sex at birth. "Gender dysphoria" is used to reference distress associated with a discrepancy in gender identity and assigned sex/gender role while "physical dysphoria" is used to reference distress associated with physical sex characteristics.

Disclaimer: *This publication is not able to provide medical care recommendations or advice specific to any one individual. If your child is expressing a strong desire for medical gender transition (e.g., hormones, puberty blockers) it is important to connect with supportive professionals. A number of organizations now exist to support transgender children and their families, including, but not limited to:*
Gender Spectrum, TransYouth Family Allies, Trans Youth Equality Foundation, TransActive, Gender Odyssey

What Changes During Puberty?

Puberty involves changes in body structures, body functions, and physical appearance. Differences between the sexes are often divided into primary and secondary sex characteristics. Primary sex characteristics include egg (ova) production in female bodied individuals and sperm production in male bodied individuals. These processes are referred to as primary because they are most closely linked to sexual reproduction. While females are born with eggs already produced, these eggs do not fully mature until menstruation begins. In contrast, males do not start producing sperm until they begin to ejaculate during puberty. Secondary sex characteristics include fat distribution, muscle mass, breast tissue, voice, body hair, height, and body frame. During puberty, both males and females also experience a growth spurt and change in bone density. Cognitive development (i.e., changes in the brain) also occurs during puberty. At the start of puberty, the connections between brain cells rapidly increase, particularly in the part of the brain that controls problem solving and planning. Several years after this burst in connections, connections that are not used are "pruned." A process called myelination also speeds up the communication between brain cells. Both pruning and myelination continue throughout the teen years to make the brain efficient and specialized. Most adolescents also experience an increase in sexual attraction and interest sex, sexuality, and dating, although not all individuals report these experiences (e.g., asexual identified youth).

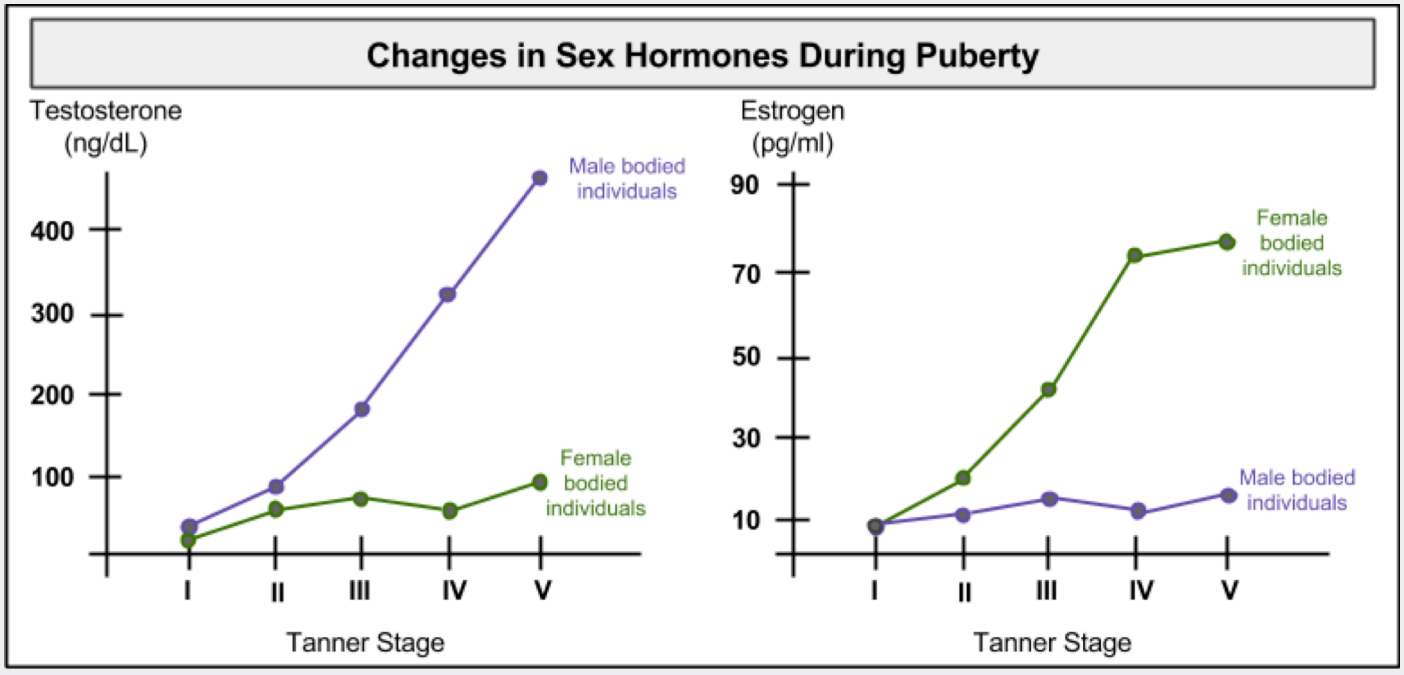


Tanner Staging:

Doctors often describe the changes associated with puberty using the Tanner staging system. Individuals at Tanner stage I are pre-pubertal, meaning they have not yet experienced any pubertal changes. Tanner stage II reflects the start of puberty while stage III and IV reflect continued pubertal changes. By Tanner stage V, sex characteristics have reached adult development. Tanner stages are typically assessed via examination of breast size, testicular volume and penis size, and pubic hair. Tanner stage also can be confirmed by a blood test that identifies the level of testosterone or estradiol circulating throughout the body.

What Changes During Puberty? (cont.)

The timing of puberty varies across individuals. However, changes typically start with increases in testicular volume followed by pubic hair development and a growth spurt for male bodied individuals (age 10-16). Puberty typically starts earlier with pubic hair development and breast development for female bodied individuals (age 8-14). Sperm production (age 12-14) and menstruation (age 10-16.5) occur somewhat later. Without medical intervention, the vast majority of individuals who are transgender or gender non-conforming progress through the puberty typical of their birth sex. However, a small minority of individuals may experience puberty unusually early (precocious puberty) or late (delayed puberty). In addition, intersex conditions, or differences of sex development, are sometimes first identified when puberty does not progress as expected. These differences in sex development occur in approximately 1% of the population, but are not typically the cause of physical dysphoria or transgender identification. Within countries such as the US, the average age of puberty has been decreasing but the causes of this change are not fully understood. In addition, research suggests that, on average, African American individuals begin puberty at earlier ages than white individuals. Finally, genetics also plays a role. Research shows that individuals tend to progress through the stages of puberty at similar ages as biological siblings and parents.



The changes that occur during puberty are driven by changes in hormone production. Prior to puberty, male and female-bodied individuals have similar levels of testosterone (an androgen) and estradiol (an estrogen) hormones. During puberty, testosterone levels steadily increase in male-bodied individuals while estradiol levels steadily increase in female-bodied individuals. Testosterone also increases slightly in females and estradiol in males, although not nearly as much. In both sexes, this process is started by changes in the pattern of gonadotropin releasing hormone (GnRH) production in the hypothalamus (a region of the brain involved in the development and regulation of hormones). Depending on the amount and frequency of GnRH released, two additional hormones (luteinizing hormone, follicle-stimulating hormone) are secreted from the pituitary gland. These hormones then stimulate the testes or ovaries to produce testosterone or estradiol.

For More Information:

Puberty **American Academy of Pediatrics** healthychildren.org/English/ages-stages/gradeschool/puberty
Puberty 101 **Planned Parenthood** plannedparenthood.org/parents/puberty-101-for-parents
What are Intersex conditions? **Intersex Society of North America** isna.org/faq/what_is_intersex

Kuper, L.E. (2014) Puberty Blocking Medications: Clinical Research Review, IMPACT LGBT Health and Development Program

How Do Puberty Blocking Medications Work?

GnRH analogues (puberty blockers) are a synthetic form of the human body's GnRH hormone. When taken regularly GnRH analogues work by suppressing the secretion of luteinizing hormone and follicle-stimulating hormone. These are the two hormones that stimulate the testes to produce testosterone and the ovaries to produce estradiol. Testosterone and estradiol are responsible for the changes that occur during puberty. ***GnRH analogues can be taken in the form of injections monthly or every three months, or small implants that are placed under the skin for up to 12 months*** [4, 7]. Treatment of transgender adolescents with puberty blockers is fairly recent. As a result, they have not been approved by the US Food and Drug Administration (FDA) for use in this population. However, for approximately the past 30 years, these same medications have been successfully used to treat precocious puberty with few "side effects" identified. A number of studies have been conducted that have tracked these patients over time [7, 8, 9, 10, 11, 12]. Several small studies also have been conducted on transgender adolescents [4, 6]. Together, these studies provide information on the impact that puberty blockers have on development.

Impact on sex characteristics:

When started in the early stages of puberty (Tanner stages II-III), GnRH analogues prevent additional changes in primary and secondary sex characteristics. In some cases, GnRH analogues may be able to reverse initial pubertal changes if started shortly after their appearance. When started in middle to late puberty (Tanner stages III-IV), most of the existing changes will not reverse. However, the medication will prevent additional changes [4, 6, 7]. The first clinics to provide puberty blockers initially did so starting at age 12 [3]. Particularly for female-bodied individuals, irreversible pubertal changes may have already occurred by this age. As promising follow up data has started to accumulate, doctors have begun timing the initiation of puberty blockers to align with the start of puberty, which varies somewhat person to person [4].

GnRH analogues are a fully reversible intervention because once the medication is stopped, the biological changes of puberty resume as they would have if puberty blockers were not used to delay the process. In contrast, other aspects of gender affirming medical care are typically only partially reversible (i.e., cross sex hormones) or irreversible (i.e., "top" and "bottom" surgeries). For individuals who persist in their transgender identity, the use of puberty blockers often helps to prevent or reduce the number of surgeries or other procedures required to align one's physical body with their affirmed gender [4, 11, 12].

Other physical changes:

In addition to blocking the effects of puberty on primary and secondary sex characteristics, GnRH analogs also prevent other changes associated with puberty including growth spurts and increases in bone density. Adolescents continue to grow in height while on GnRH analogs, but this growth is not as fast as during puberty. With appropriate dosing and monitoring, youth who start cross-sex hormones following puberty blockers reach a final height in the range associated with their affirmed gender rather than their sex assigned at birth [4, 5]. Research also has shown that delays in bone density generally reverse after puberty is resumed or cross-sex hormones are administered. In addition, studies have consistently found that GnRH analogs do not impact body proportions or body mass index (e.g., weight in relation to height) [8, 9, 10]. Nonetheless, endocrinology treatment guidelines recommend regular testing of height (every 3 months), bone density, and bone age (every 6 months) [1]. While receiving GnRH analogs, hormone, glucose, and insulin levels are also monitored along with liver and renal function. This is to confirm that the GnRH analogs are being appropriately processed by the body and are not having any negative effects on other body systems [1].

Fertility Considerations:

If puberty blockers are taken for a period of time but then discontinued, they do not appear to impact future fertility (i.e., ability to conceive a child) [1, 8-12]. However, for transgender individuals who go on to take cross-sex hormones, future fertility may be extremely difficult if not impossible. Some transgender adults are able to conceive after discontinuing cross-sex hormone therapy for a period of at least several months (and remaining off of hormones for the course of the pregnancy, if carrying the child). Even in these cases, fertility may be difficult or not possible due to the prior effects of cross-sex hormones. Some transgender individuals choose to undergo procedures to harvest and store their sperm or eggs prior to starting cross-sex hormones. However, in both of these cases, individuals had already gone through the puberty associated with their birth sex. Individuals who go on puberty blockers during adolescence followed by cross sex hormones can stop hormone use during adulthood. These individuals would then experience many of the physical changes associated with the puberty of their birth sex (some of which would be irreversible such as facial hair growth). However, due to the lack of research in this area, it is not clear that going through this process would allow the individual to become fertile. It is important to factor this uncertainty regarding future fertility into the decision-making process. It may also be helpful to explore resources on alternate parenting options such as adoption [13, 14].

Use of Puberty Blocking Medication with Transgender Adolescents: Review of the Research Literature

In order to better understand the research conducted on transgender adolescents, it is helpful to know what research has been conducted on transgender adults receiving gender affirming procedures (such as hormones, "top" surgery, "bottom" surgery). First, it is important to note that as a group, **transgender individuals are diverse in their gender identities, gender expression, and desired physical appearance** [15, 16]. Many transgender-identified individuals do not experience physical dysphoria strong enough to seek gender affirming procedures. For those that do, ***research has consistently found that gender affirming procedures are effective at eliminating or significantly reducing physical dysphoria***. A recent meta-analysis combined data from 23 studies of clients receiving gender affirmation surgeries along with cross sex hormones [17]. Approximately 80% of these clients reported a decrease in gender dysphoria, improvement in sexual function, and an increase in quality of life. While a minority of adults receiving gender affirming procedures do report some dissatisfaction with surgical outcomes (e.g., difficulty with sexual intercourse, dissatisfaction with chest scarring) (7-13%), rates of regret are very low (about 1.5%) [18, 19, 20].

Just as with adults, **much variation exists in the gender related experiences of children and adolescents**. Many children and adolescents express cross-gender interests (e.g., enjoying toys and activities typically associated with the other sex). Some may also adopt cross-sex roles in pretend play and/or experiment with cross-sex clothing or dress up activities. Even among those children and adolescents who are consistently gender non-conforming in their interests and activities; research suggests that most will *not* go on to adopt a cross-sex identity that persists through adulthood [14, 15]. However, these gender nonconforming individuals may continue to prefer clothing, hairstyles, and nicknames that are typically associated with the other sex or are gender neutral. Some of these gender nonconforming individuals will affirm gender identities such as genderqueer or androgynous. In contrast, research suggests most adolescents who consistently assert a cross-sex identity in adolescence maintain this identity throughout adulthood [2, 21, 22]. These differences in gender-related trajectories were demonstrated in a small interview based study of adolescents who initially presented in childhood for evaluation at a specialized gender clinic in the Netherlands [23]. Steensma and colleagues found that, at the time interviewed (age 14 to 18), those who persisted in their cross-sex identity described this identity as stable by age 10. ***At the onset of puberty, physical dysphoria also intensified*** within this group, particularly in response to pubertal changes. ***Many also described a growing desire to live "full time" as their affirmed gender*** (e.g. most commonly by changing name/pronouns but also included growing out hair and/or changing clothing for affirmed females). In contrast, at the time of interview, those that did not persist in their cross-sex identity also did not report significant physical dysphoria or strong dislike of being referred to by their assigned sex. When reflecting on their childhood, these youth described being "boyish" girls or "girlish" boys who wished they were, or thought it would be easier to be, the other sex. In contrast, youth who affirmed a cross-sex identity described feeling as if they were truly this affirmed gender. It is important to note that in early childhood, youth from both groups reported not thinking much about gender or experiencing physical dysphoria. Further, during both early and middle childhood, youth from both groups described shared experiences of being gender non-conforming in their interests as well as desired clothing (particularly for those assigned female who had greater ability to dress as desired) [23].

Participants from this previous study who persisted in their cross-sex identity were part of a **larger cohort of 111 adolescents who were the first to receive puberty blockers between 2000 and 2008 at the Amsterdam gender identity clinic in the Netherlands** [24]. During this time, 29 adolescents between the ages of 16 and 18 also were prescribed cross-sex hormones but had progressed too far into puberty for blockers. Neither puberty blockers nor cross sex hormones was deemed to be appropriate for an additional 56 adolescents (29%). deVries and colleagues reported on outcome data for the first 70 of these adolescents to receive puberty blockers. These adolescents were assessed just before start of puberty suppression and again just before the start of cross-sex hormone therapy (an average of 2 years later). All but one of these adolescents socially transitioned during the assessment process (e.g., change in pronouns and name across settings), and all 70 adolescents continued with cross-sex hormone therapy. Between these time points, ***general functioning improved while depression, behavioral, and emotional difficulties decreased*** (ratings of anxiety and anger remained similar). However, approximately one third of these adolescents and their families required ongoing counseling to address co-occurring social, emotional, and relational concerns such as oppositional behavior, depression, and family conflict. The average assessment period of 6 to 12 months was often prolonged in these cases [25].

Use of Puberty Blocking Medication with Transgender Adolescents: Review of the Research Literature (cont.)

In an additional follow up study, 55 of these 70 adolescents were re-assessed in early adulthood, an average of 6 years after this initial start of puberty blockers, 4 years after starting cross-sex hormones, and 1.5 years since gender affirmation surgery (vaginoplasty or mastectomy and hysterectomy) [25]. Based on results from standardized measures, the authors concluded that this process of medical gender transition is successful at both eliminating gender dysphoria and reducing emotional distress. The authors also noted that no participants experienced regrets about transitioning, few reported experiences of victimization (11%), many regarded their social transition as "easy" (71%), and all reported being fairly to very satisfied with outcomes.

In a separate cohort study of 109 adolescents evaluated at a gender identity clinic in Toronto Canada [26], puberty blocking was recommended to a slightly lower percent of children presenting with their families for evaluation (60.6%). Although follow-up data is not yet available for this cohort, those recommended for puberty suppression reported more severe physical dysphoria and cross-sex identification, less self-reported emotional, behavioral, and academic distress, and were less likely to be in institutional care (e.g., foster care). In a study reporting on data from an adolescent gender clinic ***in Boston, MA, adolescents generally presented for care later than in Toronto or Amsterdam clinics*** [6]. This was likely due to the lack of insurance coverage available for gender affirming procedures in the US. Within the Boston cohort, 69.6% of those eligible had already reached tanner stage 4 or 5 and were prescribed cross-sex hormones. In contrast, only 19.6% were at tanner stage 2 or 3 and were prescribed puberty blockers. Consistent with findings from the Netherlands, very few, if any, adolescents expressed regrets regarding puberty blocking medication or subsequent cross-sex hormone use.

Several studies have also examined the outcomes of adolescents receiving cross-sex hormones between the ages of 16 and 18. Most of these adolescents also obtained gender affirming surgeries in early adulthood. Outcomes of these adolescents appeared similar to, if not better than, the outcomes of transgender individuals who transitioned in adulthood, with none expressing regret [22, 27]. For both adolescents and adults, favorable surgical outcomes (e.g., lack of complications), acceptance within interpersonal relationships, and earlier age of treatment have been linked with greater satisfaction and overall adjustment [18, 19, 20]. Despite the overwhelming helpfulness of gender affirming procedures as a whole, many countries such as the US have not historically covered them under either public or private insurance, making cost and lack of access significant barriers in attempting to obtain care [28]. However, with changes such as the Affordable Care Act, these policies are changing. Consulting the websites of transgender related legal organizations is recommended for the most up to date information.

As reflected in the research literature, ***this multidisciplinary approach has been successful at identifying adolescents appropriate for puberty blocking intervention and providing support during this process***. Nonetheless, treatment recommendations remain unclear in a variety of cases, demonstrating the need for additional treatment and outcomes-based research. For example, adolescents assigned male at birth present to clinics at a similar rate to those assigned female but are less likely to be identified by therapists and physicians as candidates for puberty suppression [26]. Researchers have noted that this could be due to differences in the level of social support present, but the impact of this trend on youth's experiences of gender dysphoria is unknown. Similarly, the decision regarding if and when to provide puberty blockers to adolescents with significant co-occurring mental health concerns (e.g., autism, severe self-harm/suicidality), unsupportive environments (e.g., parents unwilling to consent their child or youth to receive treatment), and/or later onset gender dysphoria is not well established and may vary clinic to clinic [3, 26].

A note on research methods and gender clinic locations:

Treatment protocols for transgender adolescents originated in the Netherlands and other parts of Eastern Europe (e.g., Sweden). These countries cover gender-related care under universal healthcare systems and have tended to possess social views that are more accepting of gender and sexual minorities. As a result, much of the research previously reviewed has come from clinics in these countries [3, 21-25, 27]. Within the past several decades, a handful of gender clinics specializing in adolescents have opened in the US (e.g., in Boston, San Francisco, New York City, Los Angeles, Chicago). These clinics have generally modeled their treatment protocols after existing clinics in Europe. Although detailed outcome data are not yet available, the specialists who run these clinics have reported similarly positive outcomes using these protocols [4, 6, 26]. Combined with increases in provider awareness and knowledge, the number of these specialized clinics and providers continues to grow in the United States (see **Gender Expansive Youth Resources**) as well as globally.

Use of Puberty Blocking Medication with Transgender Adolescents: Summary of Clinical Protocol

Medical care for transgender adolescents is provided by a multidisciplinary team. This team typically includes both medical doctors (most commonly those specializing in pediatric endocrinology or adolescent medicine) as well as psychologists or social workers (i.e., individuals with a doctoral degree in clinical or counseling psychology or a masters degree in social work). Medical doctors are responsible for collecting information on medical history and performing medical exams. Doctors are also responsible for prescribing puberty blocking medication and monitoring its biological effects. Counselors or therapists collect information regarding the adolescent's social, emotional, and academic functioning as well as a detailed history of the adolescent's gender identity, expression, and personal experiences with physical dysphoria. In order to help gain the perspective of all of those involved, counselors will commonly meet with the family together as well as the adolescent and parents alone. Counselors or therapists may also use standardized assessments to help identify potential areas of concern. Standardized assessments refer to self and parent report forms that provide scores that can be compared to scores averaged from a dataset that contains a large number of responses from similarly aged adolescents. In certain cases, additional testing related to academic and/or general reasoning ability may be recommended [1-6]. For families that do not live nearby a clinic able to provide puberty blocking medication, this process is often coordinated with local pediatricians and therapists or counselors.

Typically a multidisciplinary team helps guide decisions regarding whether or not to recommend hormone blockers. Several criteria guide the recommendation:

a) Consistent gender dysphoria, often beginning in childhood (e.g., cross-sex identity that results in distress or impairment in functioning). This is typically documented via the diagnosis of Gender Dysphoria according to the Diagnostic and Statistical manual of Mental Disorders (DSM 5).
b) Presence of physical dysphoria and an increase in dysphoria related to pubertal changes.
c) Lack of major mental health concerns that interfere with the ability to assess gender dysphoria.
d) Adequate social support and knowledge of how puberty blockers work, including their impact on fertility and social relationships.

NOTE: Consent to treatment is required from both the adolescent and parent (or legal guardian)

Professional guidelines include: ***World Professional Association of Transgender Health (WPATH) Standards of Care, Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline, and the Center of Excellence for Transgender Health's Primary Care Protocol***

Once puberty blockers are started, adolescents are seen for follow up care every 3 to 6 months. Adolescents and their families also are strongly encouraged to participate in regular counseling, either at the clinic or with an outside provider who consults with the clinic. Counseling may cover a range of topics including, but not limited to, gender identity development, coping with gender dysphoria, coming out and transition, managing negative responses from others, disclosure and dating, and maintaining a healthy lifestyle (as obesity and smoking can increase risks associated with gender affirming procedures). Counselors also can help parents advocate for appropriate school and extracurricular accommodations and provide support and guidance during the process of social transition (e.g., change in name, pronoun, clothing, and hairstyle). In addition, family therapy techniques can help families improve communication, resolve conflicts, and assist parents in setting age-appropriate limits and responsibilities [1-6]. Counselors or therapists with expertize in working with transgender children can also provide support in situations where the use of puberty blockers does not appear to be a good fit or when children must wait until they are older to be eligible but are experiencing distress.

Regular meetings with all members of the multidisciplinary team assists in the monitoring of each adolescent's gender identity development, physical dysphoria, and overall functioning. By age 16 hormones are typically introduced, assuming that puberty blockers were helpful at reducing gender dysphoria and that cross-sex hormones are desired. Typically, hormone levels are then gradually increased every 6 months for about 2 years until adult levels are reached. Follow up care continues throughout this process and into adulthood although the frequency of visits may decrease over time [1-6, 26].

Kuper, L.E. (2014) Puberty Blocking Medications: Clinical Research Review, IMPACT LGBT Health and Development Program

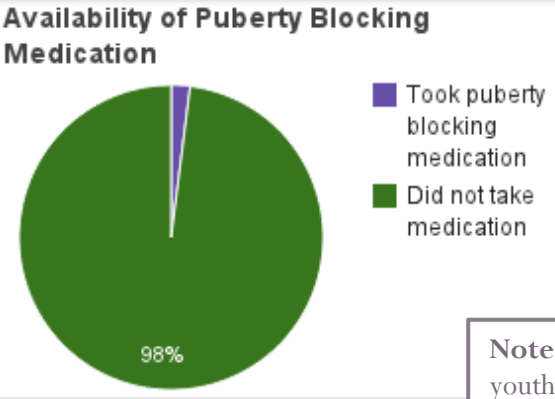
Why not wait to see if gender dysphoria resolves during or after puberty?

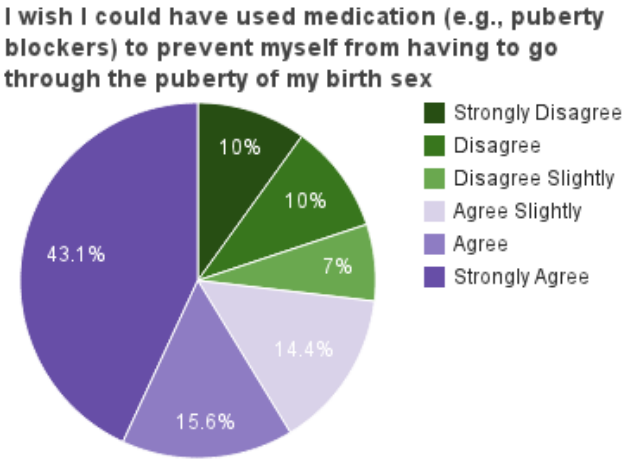
Some doctors and clinicians have expressed concerns regarding providing gender-related medical interventions to adolescents because this is a time when identity development is typically taking place. They worry that these adolescents' gender identities or physical dysphoria may change during or following puberty. For many gender non-conforming, gender fluid, or gender diverse children, puberty blocking treatment is indeed not necessary or appropriate [14, 16]. However, doctors and clinicians specializing in the care of transgender adolescents point out that there is no evidence that the changes associated with puberty are helpful at resolving strong and consistent physical dysphoria. In contrast, preliminary research suggests that ***when strong and consistent physical dysphoria is present, delaying treatment is linked to higher rates of depression, anxiety, eating disorders, and sucidality***. These mental health difficulties also can negatively impact social and academic functioning and distract from identity development in other areas [3, 4, 5, 14].

In addition, ***it is more difficult to align the body with one's affirmed gender once physical changes in secondary sex characteristics occur***, especially for male-bodied individuals. Changes in facial structure, facial hair, Adams apple, and voice will not reverse with hormone treatment once puberty is complete, which can make it very difficult for some affirmed females to have their gender correctly identified and respected. In addition, the medical procedures associated with altering these features are often expensive, painful, and time consuming (e.g., electrolysis, facial feminization). For both affirmed males and females, puberty blockers followed by cross-sex hormones helps to prevent the need for "top" surgery and produces a final height and body frame more in line with affirmed gender. These outcomes cannot be accomplished by only using cross-sex hormones. Additionally, while research suggests that rates of post-surgical regret are generally very low, those who do experience regret were more likely to have received care at older age. Regrets also appear to be more common among those who experience complications during surgery as well as those who experience difficulty "passing" as their affirmed gender, most likely due to higher rates of experiencing discrimination and violence [18, 19, 20, 28]

In light of the irreversible changes that occur during puberty, specialists who work with transgender adolescents emphasize that "wait and see" approaches are <u>not</u> neutral responses to persistent gender dysphoria. That being said, in a minority of cases, adolescents and/or families may initially express unrealistically high expectations for puberty blockers. It is important to note that while extremely helpful in many cases, co-occurring mental health difficulties may persist even after treatment. Transgender individuals also are likely to continue to face unique adjustment-related challenges throughout adolescence and adulthood (e.g., navigating social stigma, managing disclosure). For these reasons, providers also emphasize the importance of building and maintaining supportive social and professional networks for the adolescent as well as their family [3, 4, 5, 6]

Research data on puberty blocking medication use in a recent sample of transgender and gender nonconforming youth and young adults





Note: Sample size of 1,956 transgender and gender nonconforming youth and young adults (age 14-30 years old) from the United States. Data collected online in the spring of 2014.

Cost and Insurance Coverage

Depending on the type of puberty blocking medication prescribed (e.g., injections vs. implants), costs typically range from $15,500 to $24,000 per year, not including other medical treatment such as exams and blood work. While many transgender individuals are able to access cross-sex hormones via insurance coverage or sliding scale clinics, these options are not as readily available for puberty blocking medication. Recent changes in healthcare policy and transgender healthcare advocacy efforts are helping to change this (for example, the Affordable Care Act, nondiscrimination policies). In addition, some parents have reported success at obtaining coverage for their transgender adolescents via petitioning insurance companies. Professional guidelines, along with the recommendation of the adolescent's providers, can be used to argue for the medical necessity of puberty blocking medication.

Kuper, L.E. (2014) Puberty Blocking Medications: Clinical Research Review, IMPACT LGBT Health and Development Program

CITED RESEARCH

[1] Hembree, W. C., Cohen-Kettenis, P., Delemarre-van de Waal, H. A., Gooren, L. J., Meyer III, W. J., Spack, N. P., ... & Montori, V. M. (2009). Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. *Journal of Clinical Endocrinology & Metabolism*, *94*(9), 3132-3154.
[2] Coleman, E., Bockting, W., Botzer, M., Cohen-Kettenis, P.,... & Zucker, K. (2012). Standards of care for the health of transsexual, transgender, and gender-nonconforming people, version 7.*International Journal of Transgenderism*, *13*(4), 165-232.
[3] Cohen-Kettenis, P. T., Delemarre-van de Waal, H. A., & Gooren, L. J. (2008). The treatment of adolescent transsexuals: Changing insights. *The Journal of Sexual Medicine*, *5*(8), 1892-1897.
[4] Olson, J., Forbes, C., & Belzer, M. (2011). Management of the transgender adolescent. *Archives of Pediatrics & Adolescent Medicine*, *165*(2), 171-176.
[5] Delemarre-van de Waal, H. A. (2014). Early medical intervention in adolescents with gender dysphoria. In *Gender Dysphoria and Disorders of Sex Development* (pp. 193-203). Springer US.
[6] Spack, N. P., Edwards-Leeper, L., Feldman, H. A., Leibowitz, S., Mandel, F., Diamond, D. A., & Vance, S. R. (2012). Children and adolescents with gender identity disorder referred to a pediatric medical center. *Pediatrics*, *129*(3), 418-425.
[7] Mul, D., & Hughes, I. A. (2008). The use of GnRH agonists in precocious puberty. *European Journal of Endocrinology*, *159*(suppl 1), S3-S8.
[8] Heger, S., Partsch, C. J., & Sippell, W. G. (1999). Long-term outcome after depot gonadotropin-releasing hormone agonist treatment of central precocious puberty: Final height, body proportions, body composition, bone mineral density, and reproductive function. *Journal of Clinical Endocrinology & Metabolism*, *84*(12), 4583-4590.
[9] van der Sluis, I. M., Boot, A. M., Krenning, E. P., Drop, S. L., & de Muinck Keizer-Schrama, S. M. (2002). Longitudinal follow-up of bone density and body composition in children with precocious or early puberty before, during and after cessation of GnRH agonist therapy. *Journal of Clinical Endocrinology & Metabolism*, *87*(2), 506-512.
[10] Pasquino, A. M., Pucarelli, I., Accardo, F., Demiraj, V., Segni, M., & Di Nardo, R. (2008). Long-term observation of 87 girls with idiopathic central precocious puberty treated with gonadotropin-releasing hormone analogs: impact on adult height, body mass index, bone mineral content, and reproductive function. *Journal of Clinical Endocrinology & Metabolism*, *93*(1), 190-195.
[11] Bertelloni, S., & Mul, D. (2008). Treatment of central precocious puberty by GnRH analogs: long-term outcome in men. *Asian Journal of Andrology*, *10*(4), 525-534.
[12] Tanaka, T., Niimi, H., Matsuo, N., Fujieda, K., Tachibana, K., Ohyama, K., ... & Kugu, K. (2005). Results of long-term follow-up after treatment of central precocious puberty with leuprorelin acetate: evaluation of effectiveness of treatment and recovery of gonadal function. The TAP-144-SR Japanese Study Group on Central Precocious Puberty. *Journal of Clinical Endocrinology & Metabolism*, *90*(3), 1371-1376.
[13] De Sutter, P. (2007). Reproduction and fertility issues for transpeople. *Principles of transgender medicine and surgery*, 209-222.
[14] Brill, S., & Pepper, R. (2013). *The transgender child: A handbook for families and professionals*. Cleis Press.
[15] Lev, A. I. (2004). Transgender emergence. *Binghamton, NY: Haworth Press*.
[16] Kuper, L. E., Nussbaum, R., & Mustanski, B. (2012). Exploring the diversity of gender and sexual orientation identities in an online sample of transgender individuals. *Journal of sex research*, *49*(2-3), 244-254.
[17] Murad, M. H., Elamin, M. B., Garcia, M. Z., Mullan, R. J., Murad, A., Erwin, P. J., & Montori, V. M. (2010). Hormonal therapy and sex reassignment: a systematic review and meta-analysis of quality of life and psychosocial outcomes. *Clinical Endocrinology*, *72*(2), 214-231.
[18] Smith, Y. L., Van Goozen, S. H., Kuiper, A. J., & Cohen-Kettenis, P. T. (2005). Sex reassignment: Outcomes and predictors of treatment for adolescent and adult transsexuals. *Psychological Medicine*, *35*(1), 89-99.
[19] Lawrence, A. A. (2003). Factors associated with satisfaction or regret following male-to-female sex reassignment surgery. *Archives of Sexual Behavior*, *32*(4), 299-315.
[20] De Cuypere, G., Elaut, E., Heylens, G., Van Maele, G., Selvaggi, G., T'Sjoen, G., ... & Monstrey, S. (2006). Long-term follow-up: Psychosocial outcome of Belgian transsexuals after sex reassignment surgery. *Sexologies*, *15*(2), 126-133.
[21] Delemarre-van de Waal, H. A., & Cohen-Kettenis, P. T. (2006). Clinical management of gender identity disorder in adolescents: A protocol on psychological and paediatric endocrinology aspects. *European Journal of Endocrinology*, *155*(suppl 1), S131-S137.

[22] Smith, Y. L., van Goozen, S. H., & Cohen-Kettenis, P. T. (2001). Adolescents with gender identity disorder who were accepted or rejected for sex reassignment surgery: A prospective follow-up study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *40*(4), 472-481.
[23] Steensma, T. D., Biemond, R., de Boer, F., & Cohen-Kettenis, P. T. (2011). Desisting and persisting gender dysphoria after childhood: A qualitative follow-up study. *Clinical Child Psychology and Psychiatry*, *16*(4), 499-516.
[24] de Vries, A. L., Steensma, T. D., Doreleijers, T. A., & Cohen-Kettenis, P. T. (2011). Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. *The Journal of Sexual Medicine*, *8*(8), 2276-2283.
[25] de Vries, A. L., McGuire, JK, Steensma, T. D., Wagenaar, E. C., Doreleijers, T. A., & Cohen-Kettenis, P. T. (2014). Young adult psychological outcome after puberty suppression and gender reassignment. *Pediatrics, 134*(4), 1-9.
[26] Zucker, K. J., Bradley, S. J., Owen-Anderson, A., Singh, D., Blanchard, R., & Bain, J. (2010). Puberty-blocking hormonal therapy for adolescents with gender identity disorder: A descriptive clinical study. *Journal of Gay & Lesbian Mental Health*, *15*(1), 58-82.
[27] Cohen-Kettenis, P. T., & van Goozen, S. H. (1997). Sex reassignment of adolescent transsexuals: A follow-up study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*(2), 263-271.
[28] Grant, J. M., Mottet, L. A., Tanis, J., Herman, J. L., Harrison, J., & Keisling, M. (2010). National Transgender Discrimination Survey Report on health and health care. *National Center for Transgender Equality and National Gay and Lesbian Task Force. Washington, DC*, 1-23.

IMPACT
The LGBT Health and Development Program
@Northwestern University

AUTHOR INFORMATION
Laura Kuper, MA
lakuper@gmail.com
Research website: aboutLGBTQ.org

REVIEWED AND EDITED BY
Lisa Simons, MD
Ann & Robert H. Lurie Children's Hospital of Chicago
Jae A. Puckett, PhD
Brian Mustanski, PhD
IMPACT LGBT Health and Development Program

PHOTOGRAPHY PROVIDED BY
Lindsay Morris
lindsaycmorris.com