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Assessing the Effectiveness of Puberty Blockers in Gender-Affirming Care for Adolescents: A Systematic Review

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Abstract

Many claim that puberty suppression is an unsafe and unnecessary treatment for transgender adolescents to leverage support for limiting policies for gender-affirming care. This review establishes an overview of research on puberty blockers to evaluate the treatment's effectiveness and risks for gender dysphoric adolescents. Studies confirmed the necessity of puberty-blocking treatment after discovering that gender dysphoric individuals who do not receive treatment are significantly more likely to have suicidal ideation compared to individuals who have received treatment. Studies also found that puberty blockers are effective in reaching their desired functions as they lower the need for gender-affirming hormones, slow the development of secondary characteristics, and surpass their expected effective durations. Puberty blockers only posed a few serious risks to the individual's health, mainly a risk to bone health. However, most studies have not been able to define the severity of this risk to the individual's health. While more longitudinal research should be done to assess the severity of these risks, it is clear that banning access to this treatment is not the best approach forward. Understanding the implications of existing empirical data is crucial to preventing policies from further harming transgender adolescents by basing policies on misinformation or misinterpretations of existing research.

Introduction

In 2023, Tennessee State Law, SB1, banned the use of gender-affirming care to treat gender dysphoria for people under the age of 18 (Roberts, 2025). The only exception to the use of gender-affirming care (GAC) in Tennessee would be to treat a minor's congenital defect to help them conform to their sex assigned at birth (Roberts, 2025). Transgender minors, their parents, and healthcare providers challenged this policy under the 14th Amendment, claiming it violated the Equal Protection Clause due to sexual discrimination (Roberts, 2025). On June 18, 2025, in *U.S. vs Skrimetti*, the U.S. Supreme Court ruled that a state law banning access to puberty blockers and hormone therapy in Tennessee did not violate the 14th Amendment's Equal Protection Clause (Roberts, 2025). Since 2021, state policies limiting youth access to gender-affirming care have increased by more than fivefold (Dawson & Kates, 2025). As of June 2025, 27 states in the United States of America have enacted policies or laws to limit minor access to GAC (Dawson & Kates, 2024). Furthermore, 24 states impose felony or legal penalties on providers who refer patients for GAC (Dawson & Kates, 2025). Even though 30 accredited U.S. medical associations agree that GAC is a critical treatment and, when blocked, has life-threatening implications, an estimated 144,000 transgender adolescents over the age of 13 are denied treatment due to these state bans (Tanne, 2024).

Typical rationales behind banning GAC for transgender youth are that children are too young to make these decisions; that GAC is an irreversible, experimental, and unsafe treatment; and that gender dysphoria can be treated solely with less invasive medicine such as therapy (McNamara et al., 2022). Misrepresentation and misinformation of current GAC research have been an obstacle in finding the best approach toward treating transgender youth, especially regarding puberty blockers. In navigating what best practices are out there regarding puberty blockers for transgender youth, it is important to be aware of the misinformation circulating about GAC treatments and how it is limiting the implementation of innovative care.

While there is controversy over policies regarding GAC on transgender youth as a whole, this paper will more readily focus on hormonal GAC treatments such as puberty blockers. Puberty blockers slow the development of an individual's secondary sex characteristics by inhibiting the production of sex hormones such as testosterone and estrogen. In people assigned male at birth, treatment slows the growth of facial hair, body hair, and the penis, along with preventing the voice from deepening. For people assigned female at birth, treatment slows breast development and stops menstruation. Conversely, gender-affirming hormonal treatment helps an individual align their secondary sex characteristics to their desired gender by taking testosterone or estradiol. Puberty blockers are typically given as a shot every 2-3 months or as implants every 12 months (Pruthi, 2023). Research on puberty blockers for transgender youth is still understudied, which begs the question: What is the effectiveness of puberty blockers? How safe is it? What is its place in the approach to treating transgender youth?

The CASS review, recently published in April 2024, is a landmark peer-reviewed study on approaches to medical treatment for transgender youth. This systematic review emphasizes a more conservative approach, citing that there is not enough quality research about more invasive treatments such as puberty blockers (Cass, 2024). However, Professor Anne Alstott from the Yale School of Law and Dr. Meridithe McNamara from the Yale School of Medicine point out that the review omits key findings on

GAC due to its methodological flaws and misinterprets much of its data (McNamara et al., 2024). Furthermore, they discuss the repercussions of how the review's conclusions may be misrepresented in the media (McNamara et al., 2024). As the review leans toward a more conservative approach in medical care for transgender youth, many U.S. states may use it to support their bans on GAC, even though nowhere in the study does it suggest a ban on medical care for transgender youth is the best approach (McNamara et al., 2024). Although the review is controversial, it has serious implications for how GAC will be implemented around the world, and more specifically, policies on puberty blockers.

Current research on puberty suppression does not exactly coincide with the CASS Review's conclusions or the consensus of mainstream media. A main concern is the lack of research on the long-term effects of puberty blockers. While the long-term effects of puberty suppression for adolescents are understudied, the existing research on puberty suppression reports few serious complications, the main one concerning bone health (Rew et al., 2020). However, the severity of these risks is unclear (Rew et al., 2020). On the other hand, existing research has found that puberty blockers have several positive, even life-saving implications (Rew et al., 2020). Positive implications of puberty suppression include decreased suicide, a more positive mental health status, and prevention of more invasive treatments in the long term, such as surgeries (Rew et al., 2020). While there is concrete evidence that puberty blockers have positive implications, research fails to evaluate the severity of the risks puberty blockers pose to adolescents.

This systematic review aims to establish an overview of the existing literature and research on the effectiveness and risks of puberty blockers in gender-affirming care for adolescents. A total of 7 studies were gathered for this review to provide a comprehensive overview of puberty blockers used for GAC in transgender adolescents.

Methodology

To investigate the effectiveness of puberty blocker use in gender-affirming care for transgender adolescents, the following research questions were proposed:

RQ1: What popular methods are used to research puberty blockers?

RQ2: What evidence is there to support the effectiveness of puberty blockers?

RQ3: What potential risks do puberty blockers pose and how should puberty blockers be integrated into treatment plans to best support these individuals?

These questions provided a framework to define the inclusion and exclusion criteria. The inclusion and exclusion criteria were defined to keep studies included in this review relevant to our RQs. The following inclusion criteria were defined as follows:

- Only studies published after 2010
- If multiple papers cited the same source, only the most cited paper was included

The exclusion criteria were defined as follows:

- Papers written in languages other than English
- Studies not targeted toward the adolescent age bracket (ages 10 to 18)

Only studies published after 2010 were included, so only the newest and most relevant research studies were included. Studies not targeted toward the adolescent age bracket were excluded to keep the review as specific as it could be.

Once these criteria were defined, a set of key search terms was devised to find eligible studies for this systematic review. The keywords used were: “hormone therapy transgender youth”, “puberty blockers transgender youth”, “GnRHa youth”, and “endocrine treatment transgender youth”. The search term “youth” was also substituted with the search term “adolescent”. Google Scholar and the UCSB Library Database were used to establish an initial pool of studies. After reviewing these studies with the inclusion and exclusion criteria, the pool was narrowed and the final studies were grouped into the following categories:

Effectiveness of Puberty Blockers

Studies included in this category focused on how functional puberty blockers are and any positive implications of puberty blockers. While other topics concerning puberty blocking may be included in the study, they were not the main focus.

Risks of Puberty Blockers

This category included studies assessing the risks that puberty blockers pose for adolescents and their severity. While other qualities of puberty blockers may have been evaluated, the study was mainly concerned about the risks and negative effects of puberty blockers.

Results

A table was created to better understand the effectiveness of puberty blockers, their possible risks, and the best way to integrate them into GAC for adolescents, including research studies and their findings. The studies in Table 1 were arranged by the study’s focus and then sorted by methodology. The first four studies focused on research that evaluated the effectiveness of puberty blockers. The last three studies focused on research that assessed the risks of puberty blockers, and one study examined the side effects of gender-affirming hormonal treatments as well. Five of the seven studies used retrospective chart reviews as their methodology; however, cross-sectional surveys and physical examinations were also conducted. All studies used some statistical test to interpret the significance of their results and all findings on the table were statistically significant in their respective studies. Please refer to Table 1 at the end of the results section.

Effectiveness of Puberty Blockers

In the study conducted by Jensen et al. (2019), the charts of 85 patients were reviewed to see if GnRH agonists like leuprolide or histrelin produced their desired effect to ease the transition to gender-affirming hormones. After comparing the gender-affirming hormonal treatment plans of patients who went through GnRHa treatment versus patients who were never on GnRHa, Jensen et al. (2019) found that in both the female-affirming and male-affirming populations, GnRHa treatment correlated with lower doses of gender-affirming hormones. Additionally, female-affirming individuals who were not on GnRHa treatment often needed to take spironolactone in addition to estrogen to achieve their desired transition (Jensen et al., 2019). In the male-identifying subjects, 55% of the patients who took GnRHa experienced side effects during their testosterone treatment, while 76% of patients who did not take GnRHa experienced side effects during testosterone treatment. The female-identifying subjects had no significant difference in the frequency of side effects. Overall, the researchers concluded that GnRHa treatments effectively reach the desired effects of easing the transition to gender-affirming hormones by lowering the dosage an individual would need. The researchers also emphasized that while there was a decreased frequency of side effects in the male-affirming population, the severity of side effects was not evaluated. Jensen et al. (2019) found that the most common cause of stopping GnRHa treatment was lapses in insurance coverage, not risks to health or side effects.

Meija-Otero et al. (2020) is another study that supports the trend that puberty blockers are effective in reaching their desired effects. Meija-Otero et al. (2020) was conducted to determine whether GnRHa effectively suppresses the hypothalamic-pituitary-gonadal (HPG) axis in adolescents. Meija-Otero et al. (2020) did this by comparing the blood levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone/estradiol between 30 transgender patients and 30 central precocious puberty (CPP) patients before and during treatment. In the male-affirming population, researchers found that FSH, LH, and testosterone levels were more similar to males with CPP than assigned males at birth (AMAB). In the female-affirming population, levels of FSH and LH were also more similar to females with CPP than assigned females at birth (AFAB); however, estradiol levels were higher in AFAB. When comparing leuprolide to histrelin, researchers found that FSH levels were lower in histrelin patients (Meija-Otero et al., 2020).

Tulchinskaya et al. (2023) found results that complement the findings of Jensen et al. (2019), suggesting GnRHa treatment effectively reaches its desired effects. Similar to Jensen et al. (2019), Tulchinskaya et al. (2023) used a retrospective chart review; however, they evaluated the effective duration of histrelin implants to see if it correlates with the FDA's recommendation of one year. Tulchinskaya et al. (2023) reviewed 48 patients and found that the mean duration of effective treatment was longer than the FDA's approved one year. Effective treatment lasted on average for 641 days with a range from 264 to 1310 days (Tulchinskaya et al., 2023). This study shows that puberty blockers are effective in reaching their desired effects and some puberty blockers have exceeded expectations..

Alternatively to the last three studies, Turban et al. (2020) use a cross-sectional survey to evaluate patient satisfaction with puberty-blocking treatment, in particular, the individual's mental health after GnRHa treatment. Turban et al. (2020) surveyed 619 18 to 36-year-olds who went through puberty-blocking treatment in their adolescence. Only 16.9% of this sample reported that they ever

wanted puberty suppression treatment, however, of those individuals, only 2.5% ever received treatment. After comparing individuals who received GnRHa treatment to those who did not, those who received treatment had significantly lower odds of suicidal ideation.

Risks of Puberty Blockers

As many studies on puberty blockers lack research over extended periods, the long-term impacts of GnRHa treatment are unknown. However, the following three studies list some preliminary research on short-term impacts that implicate potential long-term effects and their severity.

Shulmeister et al. (2022) conducted a study using a retrospective chart review to evaluate GnRHa's impact on height velocity (HV) and growth in 55 transgender (TGD) patients. Shulmeister et al. (2022) found that TGD patients and non-TGD patients had similar height velocities and growth if treatment started towards the beginning of puberty or at a prepubescent age. However, if GnRHa was started later in puberty, TGD patients had significantly lower height velocities compared to their non-TGD patients (Shulmeister et al., 2022). The authors mention that their studies did not incorporate the HV or bone density after gender-affirming hormones were initiated. Vlot et al. (2017) fill in this gap by assessing bone mineral apparent density and bone turnover after puberty-blocking and cross-sex hormone treatment. Vlot et al. (2017) used a retrospective chart review to assess 56 TGD adolescents. After puberty-blocking treatment, P1NP and 1CTP levels decreased indicating a decrease in BT, however, BMAD levels were unchanged. After 24 months of CSHT, a decrease in BT was seen in all populations except older male-affirming patients. The BMAD levels saw a significant increase after 24 months in all populations. The authors note that the severity of these effects on the individuals' health needs to be further evaluated.

Schagen et al. (2016) conducted physical examinations every 3 months for 119 patients on GnRHa treatment to measure the development of secondary sex characteristics, height, hormone levels, body mass, and fat percentage. Schagen et al. (2016) found that puberty blockers were effective in their desired effects as 43 of 49 female-affirming patients had a significant decrease in testicular volume and one in every four male-affirming patients saw complete breast regression. Schagen et al. (2016) found there were no significant abnormalities in any of the patients in their levels of creatinine, sex steroids, liver enzymes, and gonadotropins. However, they also found that for both boys and girls, the height standard deviation score and lean body mass percentage decreased while their fat percentage increased.

Table 1: Summary of Findings on Puberty Blocker Use for Gender-Affirming Care						
Study	Method	Sample Size	Type of Treatment(s)	Focus	Years Data Extrapolated	Summary
(Jensen et al., 2019)	retrospective chart review	85	GnRHa, leuprolide, histerlin	effectiveness of PB	2016 - 2018	- assessed if the use of puberty blockers improved gender-affirming hormone treatment for individuals - patients who used GnRHa used lower doses of gender-affirming hormones than patients who did not use GnRHa treatments - frequency and side effects of gender-affirming hormones were the same whether the patient used GnRHa or not, the severity of side effects was not evaluated - strong evidence that side effects caused by puberty blockers largely reflect changes one commonly experiences during puberty - most common cause for ceasing GnRHa treatment was lapses in insurance coverage - concerns about changes in liver enzymes or hematocrit emphasize the importance of patient monitoring during treatment
(Meija-Otero et al., 2020)	retrospective chart review	60	GnRHa	effectiveness of PB	2021-2021	- compare the blood levels of secondary sex characteristic hormones during GnRHa treatment to blood levels of patients with central precocious puberty - treatment resulted in luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone levels similar to males with CPP than transgender patients assigned male at birth (AMAB) - estradiol levels were higher in patients assigned female at birth (AFAB), suppression of LH and FSH was similar to females with CPP compared to patients AFAB - FSH levels were lower in patients treated with histrelin
(Tulchinskaya et al., 2023)	Retrospective chart review	48	histerlin	effectiveness of PB	2013 - 2022	- assess the effectiveness of histrelin implants for puberty suppression compared to FDA's approved use of one year - mean duration of effectiveness for 641 days (range: 264 to 1310) - degree of puberty suppression after first year of treatment was satisfactory for families and patients
(Turban et al., 2020)	cross-sectional survey	619	GnRHa	effectiveness of PB	2020-2020	- assessing mental health benefits of GnRHa treatment - 16.9% reported they ever wanted pubertal suppression - of that 16.9%, 2.5% received pubertal suppression - those who received pubertal suppression had lower odds of suicidal ideation than those who did not receive treatment
(Schulmeister et al., 2022)	retrospective chart review	55	GnRHa	risk of PB	2022-2022	- compared height velocity and growth (HV) of patients who received GnRHa versus patients who did not - when controlled for age, there was not a significant difference in HV for patients with GnRHa treatment and their non-treatment counterparts - TGD youth who start GnRHa later in puberty have a lower HV to their non-treatment counterparts
(Vlot et al., 2017)	Retrospective Chart Review	56	GnRHa, 17-β estradiol, Sustanon, MSD	risk of PB	2016-2016	- assess bone turnover (BT) and bone mineral apparent density (BMAD) after puberty-blocking and cross-sex hormone treatment (CSHT) - a decrease of P1NP and 1CTP indicating a decrease in BT but unchanged levels of BMAD - 24 months after CSHT P1NP and 1CTP decreased in all groups except older transmen, BMAD increased
(Schagen et al., 2016)	physical examination, dual X-ray absorptiometry	116	GnRHa, triptorelin	risk of PB	2016-2016	- assess efficacy and safety of GnRHa treatment - decrease in testicular volume in 43 of 49 M-to-F patients - one in four of F-to-M patients complete breast development regression - no abnormalities in levels of gonadotropins, sex steroids, liver enzymes or creatinine - for both boys and girls height SD score and lean body mass percentage decreased, fat percentage increased

Table 1 summarizes the seven studies collected for this systematic review categorizing them by methodology, sample size, type of treatment used, years data was extrapolated, and a summary of the study's findings.

Discussion

The first research question was asked to assess the common research methods in evaluating puberty blockers. Five of the seven studies used retrospective chart reviews on patients who received puberty-blocking treatment over an extended period to evaluate the effects of puberty blockers on adolescents. Using a baseline from the patient's initial assessment, researchers could compare hormone and blood levels to determine the statistical significance of the puberty blocker treatment. Other methods, like physical examination, were used to evaluate the effectiveness of puberty blockers and methods like a cross-sectional survey were used to evaluate the mental health implications of puberty-blocking use. While retrospective chart reviews seem to be the most widely used approach for puberty-blocking research, they lack longitudinal reliability. Moving forward, researchers should be checking the health of these patients on these treatments over years, even decades at a time. Right now, this may not be as feasible as a retrospective study, but at some point, research should be conducted over extended periods to provide more clarity on the severity of the risks puberty blockers pose.

The second research question was asked to evaluate the evidence to support the effectiveness of puberty blockers. Jensen et al. (2019), Tulchinskaya et al. (2023), and Meija-Otero et al. (2020) showed that GnRHa treatment was effective in reaching the patient's desired degree of pubertal suppression. Jensen et al. (2019) showed that the use of GnRHa treatment helped patients use lower doses of gender-affirming hormones and in the male-affirming population, less frequent side effects. Meija-Otero et al. (2020) showed that on average GnRHa treatment gets patients to hormone sex levels similar to CPP counterparts. Tulchinskaya et al. (2023) demonstrated how some puberty-blocking treatments exceed expectations, as GnRHa treatment had an effective duration longer than the FDA-approved period. While

these studies showed that puberty blockers are effective in producing the desired physical effects, Turban et al. (2020) showed that gender dysphoric adolescents who receive puberty-blocking treatment have lower suicide rates and increased mental health. The results of these studies show that there is ample evidence to prove that puberty blockers are effective in achieving their desired function and have positive implications for gender dysphoria patients.

The third research question was asked to investigate the severity of the risks of puberty blockers and offer a way that puberty blockers can be integrated into GAC to best support the individuals who need them. Schagen et al. (2016) study showed that GnRHa treatment did not cause any abnormalities in levels of creatinine, sex steroids, liver enzymes, and gonadotropins. However, Shulmeister et al. (2022), Vlot et al. (2017), and Schagen et al. (2016) report that puberty blockers cause decreases in height velocity and bone density. However, Vlot et al. (2017) point out the severity and the impact of these effects on the individual have not been studied. Moreover, Shulmeister et al. (2022) failed to consider that most adolescents undergoing puberty blockers follow up this treatment with gender-affirming hormonal therapies. Shulmeister et al. (2022) note that gender-affirming endocrine treatment has been shown to reverse effects on bone deficits caused by puberty-blocking. Currently, research supports that puberty blockers are an effective adjunct to gender-affirming hormones instead of a monotherapy. If anything, the risks found in this review emphasize the importance of thorough discussion with the patients on the potential risks and benefits and constant patient health monitoring throughout treatment.

Although this systematic review has provided a valuable overview of existing studies on puberty blockers in adolescents, it has its limitations. The main limitation of this review is that puberty-blocking treatment has only been in practice since the 90s and has only become more popularized in the last decade. While the conclusions made from existing research studies on puberty blockers show that puberty blockers pose risks to bone health, the severity is unknown. What is known is that puberty blockers are effective in completing their desired function of suppressing the development of secondary sex characteristics and easing the transition into gender-affirming treatments such as lowering hormone dosages. Puberty blockers have also been statistically proven to have positive effects on an individual's mental health such as decreasing suicide ideation in these patients. Most patients who stop puberty-blocking treatment do not stop due to health risks, but stop due to lapses in their insurance coverage (Tulchinskaya et al., 2023). Most adolescents are experiencing health deficits due to a lack of access to GAC rather than the risks the treatment presents. Current research has proven that a lack of access to treatment for gender dysphoric patients poses life-threatening risks as these individuals are significantly more likely to have suicidal thoughts (Turban et al., 2020). After reviewing these seven studies, it is clear that banning access to puberty blockers does not help gender dysphoric adolescents. However, more research needs to be done to determine possible lower-age limits for GnRHa treatment and GnRHa's long-term effects on bone health to better advise the patient and their family when making decisions in their treatment plans. Hopefully, this review can provide more information regarding the best approaches to implementing puberty blockers into GAC for adolescents and combat the misinformation spread about these treatments.

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