



Do No Harm

Protecting Ohio's Most Vulnerable Residents from Gender Ideology: Evidence in Support of HB 68

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The New England Journal of Medicine [published a short letter](#) which claims that prescription opioids rarely lead to addiction.ⁱ The letter was [“heavily” and “uncritically”](#) cited to justify the prescription practices that followed suit.ⁱⁱ

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Countless public health “experts” who had advised against large gatherings due to concerns over COVID-19 transmission suddenly change their tune and say that such gatherings are permissible under the pretense of racial justice.

These milestone moments in public health demonstrate that experts can be disastrously wrong, and that “science” sometimes serves politics rather than vice versa. A sobering and honest look at the state of evidence on pediatric gender medicine reveals that past is prologue. The politicization of scientific discourse and inquiry has rendered the U.S. a dangerously extreme outlier in its approach toward the medical transition of children.

Advocates for the status quo would have you believe that their position is “evidence-based” and grounded in science. However, in my position as director of research at the nonprofit organization Do No Harm, I have thoroughly reviewed this scientific evidence and found it lacking or its results misused by advocates.

Tellingly, no major national medical organization seems inclined to explain why the European countries that have conducted systematic reviews of the safety and efficacy of puberty blockers and cross-sex hormones are urging caution and restricting access to irreversible medical interventions before the age of majority. As the British Medical Journal notes, American standards of care are “consensus-based”, but they are not evidence-based.ⁱⁱⁱ

The justification for American standards of care relies on obfuscation of whether surgery is performed on children. Additionally, American standards operate in deference to assertions that puberty blockers are “completely reversible”, that cross-sex hormones are “partially reversible,” that receipt of puberty blockers and cross-sex hormones improves mental health outcomes, that receipt prevents suicide, and that children simply “know who

they are” and are well-positioned to consent to irreversible medical interventions. Allow me to explain why these positions are unjustified and why other countries and states are making different determinations about the balance of benefit and harm.

Claim: No Ohio hospital performs “gender affirming” surgery on patients under the age of 18

[Wexner Medical Center](#)^{iv} and the [Cleveland Clinic](#)^v both state that they use WPATH guidelines for surgery. [WPATH Standards of Care Version 8](#) clearly state that certain surgeries are permissible before 18.^{vi} Regarding vaginoplasty- “studies suggest there may be a benefit for some adolescents to having these procedures performed before the age of 18.” Plus, were it true that surgery is not performed under the age of 18, nobody should be concerned about legislation to restrict it.

Claim: Puberty blockers are totally reversible

There is no-long term data to evaluate the safety of pubertal suppression in children with gender dysphoria.

Within the last 3 years Finland, Sweden, and the UK conducted systematic reviews of the evidence, and all concluded that a lack of evidence and suspected side effects amount to a need for great caution.

- The Cass review in the UK determined that the evidence base for puberty blockers- including long term health impacts- is “very low.” Studies are “[small, uncontrolled observational studies, which are subject to bias and confounding, and all the results are of very low certainty.](#)”^{vii}
- Finland’s revised guidelines for “gender-affirming care” cited concerns about potential impacts on [brain maturity](#) as a reason to restrict the use of puberty blockers.^{viii}
- A systematic review conducted in Sweden concluded that the use of puberty blockers is “experimental” and that [the risks outweigh the benefits.](#)^{ix}

In addition,

- The Norwegian Healthcare Investigation Board said there is [insufficient evidence](#) for the use of puberty blockers to treat GD in young people.^x
- [The French National Academy](#) advised “*taking into account the side effects such as the impact on growth, bone weakening, risk of sterility, emotional and intellectual consequences and, for girls, menopause-like symptoms... the greatest caution*” is needed in administering puberty blockers and cross-sex hormones to children.^{xi}
- In 2022 the [FDA issued a warning](#) that gonadotropin-releasing hormone agonists can cause brain swelling and vision loss.^{xii}
- “[Concerns have been raised that hormonal suppression of puberty may permanently alter neurodevelopment](#)”^{xiii}
- “[GnRH-analogs may have irreversible effects on sexual function.](#)”^{xiv}

A national systematic review of the evidence on puberty blockers has never been conducted in the United States. Commentary in *Child and Adolescent Mental Health* rightly concludes that [“The clear signals emerging from the various reviews of the available evidence of the use of puberty blockers for GD youth are that there is very low certainty of the benefits of puberty blockers, an unknown risk of harm and there is need for more rigorous research.”](#)^{xv}

Claim: Cross-sex hormones are “safe” and “partially reversible”

Without randomized controlled trials there is [uncertainty](#) about the long-term safety of cross-sex hormones.^{xvi} It is known that [treatment can cause permanent infertility](#). In addition, [a review of the literature](#) on the effects of cross-sex hormones on cardiovascular and skeletal health concludes: “Current limited evidence from non-randomized studies suggests that transgender women taking GAHT have increased risks of myocardial infarction, ischemic stroke and VTE.”^{xvii} The Mayo Clinic also flags weight gain and type 2 diabetes among potential complications of [masculinizing](#)^{xviii} and [feminizing](#)^{xix} hormone therapy.

Claim: Restricting puberty blockers and cross-sex hormones will lead to an increase in suicide

The study seminal to the assertion that mental health considerations necessitate child access to medical transition is a 2020 study called [“pubertal suppression for transgender youth and risk of suicidal ideation.”](#)^{xx} The study claims that transgender individuals who wanted puberty blockers and received them experience a lower level of suicidal ideation than individuals who wanted blockers but did not receive them. The study features technical mistakes and limitations that warrant great skepticism.

- Data comes from the 2015 U.S. Transgender Survey. It appears that most respondents who claim to have taken puberty blockers misunderstood the questions they were being asked and confused puberty blockers with cross-sex hormones. The authors attempt to mitigate this by excluding from analysis those who claim to have initiated puberty blockers at 18 or later, [but there is no way to correct for the fact that the same confusion was almost certainly relevant to a question that asks whether respondents ever wanted puberty blockers.](#)^{xxi}
- The respondents in the sample were recruited online by politically aligned organizations. The sample of “trans,” “genderqueer” and “nonbinary” individuals is not representative of that population and did not include detransitioners.
- Issues in identifying who received puberty blockers and the appropriate comparison group are further compounded by a mistaken assertion about when American doctors started using GnRHa as treatment for gender dysphoria. Consequently, the [“subsample included older respondents who, in fact, had no opportunity to obtain these drugs and so cannot be used for comparison.”](#)^{xxii}
- By the admission of the authors of the original study “reverse causation cannot be ruled out: it is plausible that those without suicidal ideation had better mental

health when seeking care and thus were more likely to be considered eligible for pubertal suppression.”

- The original study assessed nine areas of mental health distress including six measures of suicidality. Only one of the nine mental health measures (lifetime suicidal ideation) was significantly correlated with uptake of puberty blockers. Items can be correlated with one another for any number of reasons, including random chance. That only 1 of 9 measures was significantly correlated with (imprecisely estimated) access to puberty blockers amounts to weak descriptive evidence to support the hypothesized link between access to blockers and suicidality or suicide.
- Commentary in the Archives of Sexual Behavior rightfully concludes that the study [“contributed nothing to our knowledge of the effects of suppressing puberty in adolescents.”](#)^{xxiii}

[Another study](#) foundational to the purported mental health benefit of medical transition was published by the same lead author utilizing the same dataset but examined the correlation between reported uptake of cross-sex hormones and suicidal behaviors.^{xxiv} The dataset is so flawed that it probably conveys no useful information. However, if one accepts that the dataset is sufficiently reliable, it does provide some notable insights that the study attempts to bury. For one, the study combines results for both sexes, but analysis by Dr. Michael Biggs found that [“Males who took estrogen are more likely to plan suicide, to attempt suicide, and to require hospitalization for a suicide attempt.”](#)^{xxv} Notably, [testosterone has an antidepressant effect](#), so it’s plausible that the more favorable finding among natal females isn’t due to greater concordance with gender identity.

In another indication that decisions around data analysis were self-serving, Dr. Jay Greene observes that the [“study finds that 16- and 17-year-olds who received hormones were more than twice as likely to report a ‘past-year suicide attempt requiring inpatient hospitalization,’ but that finding fails to achieve statistical significance by setting the standard for significance higher than is conventional. Only by adopting a standard for statistical significance that is different from the one more commonly used in empirical research does the study avoid concluding that this significant harm from hormone therapy exists.”](#)^{xxvi}

Attempts to understand a link between child access to hormonal treatment and suicide are hampered by a lack of observation over long time horizons. Stories of regret and detransition among individuals who received hormone treatment for years raise the specter that short-term observation provides insufficient understanding of long-term impacts on suicidality and suicide. [A 30-year Swedish follow-up study](#) found that the suicide rate was 19 times higher among transitioned adults compared to cis-gender adults.^{xxvii} Worryingly, differences in all-cause mortality sharply diverged after the ten-year mark.

The chief psychiatrist at Finland’s largest gender clinic said that it was “irresponsible” and [“purposeful disinformation”](#) to assert that denial of these medical interventions will culminate in a greater number of suicides.^{xxviii}

Claim: Receipt of puberty blockers and cross-sex hormones leads to improved mental health

There have not been any randomized controlled trials to test the link between mental health and receipt of hormonal treatment. Consequently, the studies that examine mental health outcomes are descriptive studies limited by their inability to determine whether outcomes among those who initiate medical transition represent an improvement over what would have occurred without transition. Individuals mired in the worst mental health crises theoretically face higher obstacles to receiving hormonal or surgical treatment. It's no surprise then that descriptive studies might observe a positive correlation between mental health and receipt of these interventions. These observations are not a substitute for causal evidence, which can only be ascertained through randomized controlled trials.

One of the most important studies in support of this claim was published earlier this year in the [New England Journal of Medicine](#).^{xxix} The researchers observe that self-reported measures of mental health improve in the two years following initiation of cross-sex hormones by the narrowest of margins. Notably, there is no improvement among the group of children who initiated puberty blockers early in puberty. Whether these outcomes represent improvement over what would have occurred in the absence of hormonal intervention is impossible to determine.

While the U.S. medical community has handled questions surrounding transition and mental health as settled science, European countries that engage with the evidence reach different conclusions. The Cass Review characterizes the certainty of the evidence on mental health and medical transition as “very low.” A pediatric endocrinologist at Sweden’s largest gender clinic meanwhile warned that puberty blockers “[can affect mental health in an unintended, undesirable way](#).”^{xxx}

Claim: Children know their gender identity from a very young age

Central to debates over pediatric gender medicine are whether children who express gender dysphoria are experiencing temporary distress or whether it is a permanent feature of their identity. Past studies collectively indicate that [about 4 in 5 children who experience dysphoria will later desist in such feelings](#).^{xxxi} Many of the studies were conducted decades ago and long precede the recent [meteoric growth](#) in the proportion of youths who identify as transgender or gender-nonconforming.^{xxxii} The 4 in 5 estimate is likely an undercount of current reality.

Standards of care in the United States lack the guardrails needed to prevent medical transition in children who would otherwise desist in their dysphoria. [The American Academy of Pediatrics denounces “watchful waiting”](#) as outdated and instead encourages affirmation of all expressions of dysphoria.^{xxxiii} This approach puts kids on the fast track toward social and medical transition, and indeed the Cass Review states that the “affirmative model” that “originated in the USA” amounts to insufficient safeguarding. The director of the pediatric gender clinic at Boston Children’s Hospital admits that puberty blockers are given out “[like candy](#).”^{xxxiv} Whistleblowers have revealed instances in which puberty blockers were prescribed [after a single doctor’s visit](#).^{xxxv}

CONCLUSION

European countries that have confronted the evidence (or lack thereof) on the safety and efficacy of medical transition in kids are skeptical or altogether dismissive of the prospect that benefits outweigh harms. Major medical organizations in the United States should conduct their own systematic reviews of safety and efficacy. Alternatively, they should explain why they disagree with the conclusions made in the U.K., Sweden, or Finland, which amount to certainty of harm and poor evidence of benefit. Unless or until such reviews or explanations are offered, Ohio should follow the lead of European nations and the 15+ states that have curtailed access to these experimental treatments by enacting House Bill 68.

ⁱ Porter, J. & Jick, H. (1980). *N Engl J Med* 10;302(2):123

ⁱⁱ Leung, P., Macdonald, E. Stanbrook, M., Dhalla, I., & Juurlink, D. (2017). *N Engl J Med*; 376:2194-2195

ⁱⁱⁱ *BMJ* 2023;380:p382

^{iv} The Ohio State University Wexner Medical Center. Feminization surgery. <https://wexnermedical.osu.edu/gender-affirming-care/surgery-options/feminization-surgery>

^v Cleveland Clinic. Gender affirming surgical services. <https://my.clevelandclinic.org/about/community/lgbt-health/transgender-surgical-services#treatments-procedures-tab>

^{vi} Coleman et al. (2022). Standards of Care for the Health of Transgender and Gender Diverse People, Version 8, *International Journal of Transgender Health*, 23:sup1, S1-S259.

^{vii} NICE. (2020). Evidence review: Gonadotrophin releasing hormone analogues for children and adolescents with gender dysphoria. <https://cass.independent-review.uk/nice-evidence-reviews/>

^{viii} https://segm.org/sites/default/files/Finnish_Guidelines_2020_Minors_Unofficial%20Translation_0.pdf

^{ix} <https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/kunskapsstod/2022-3-7799.pdf>

^x *BMJ* 2023;380:p697

^{xi} https://segm.org/sites/default/files/English%20Translation_22.2.25-Communique-PCRA-19-Medecine-et-transidentite-genre.pdf

^{xii} FDA. Risk of pseudotumor cerebri added to labeling for gonadotropin-releasing hormone agonists. <https://www.fda.gov/media/159663/download>

^{xiii} Jorgensen, S., Hunter, P., Regenstreif, L., Sinai, J. & Malone, W. (2022). Puberty blockers for gender dysphoric youth: A lack of sound science. *Journal of the American College of Clinical Pharmacy*, 5(9), 1005-1007.

^{xiv} Ibid

^{xv} Clayton, A., Malone, W., Clarke, P., Mason, J. & D'Angelo, R. (2021). Commentary: The signal and the noise

^{xvi} <https://www.nhs.uk/conditions/gender-dysphoria/treatment/>

^{xvii} Swe, N.C., Ahmed, S., Eid, M., Poretsky, L., Gianos, E., & Cusano, N. (2022). *Metabol Open*, 13.

^{xviii} Mayo Clinic. Masculinizing hormone therapy. <https://www.mayoclinic.org/tests-procedures/masculinizing-hormone-therapy/about/pac-20385099>

^{xix} Mayo Clinic. Feminizing hormone therapy. <https://www.mayoclinic.org/tests-procedures/feminizing-hormone-therapy/about/pac-20385096>

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- ^{xxi} Biggs, M. (2020). Puberty Blockers and Suicidality in Adolescents Suffering from Gender Dysphoria. *Arch Sex Behav* 49(7):2227-2229.
- ^{xxii} Ibid
- ^{xxiii} Ibid
- ^{xxiv} Turban, J., King, D., Kobe, J., Reisner, S. & Keuroghlian, A. (2022). Access to gender-affirming hormones during adolescence and mental health outcomes among transgender adults. *PLOS One*, 12;17(1)
- ^{xxv} <https://journals.plos.org/plosone/article/comment?id=10.1371/annotation/dcc6a58e-592a-49d4-9b65-ff65df2aa8f6>
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