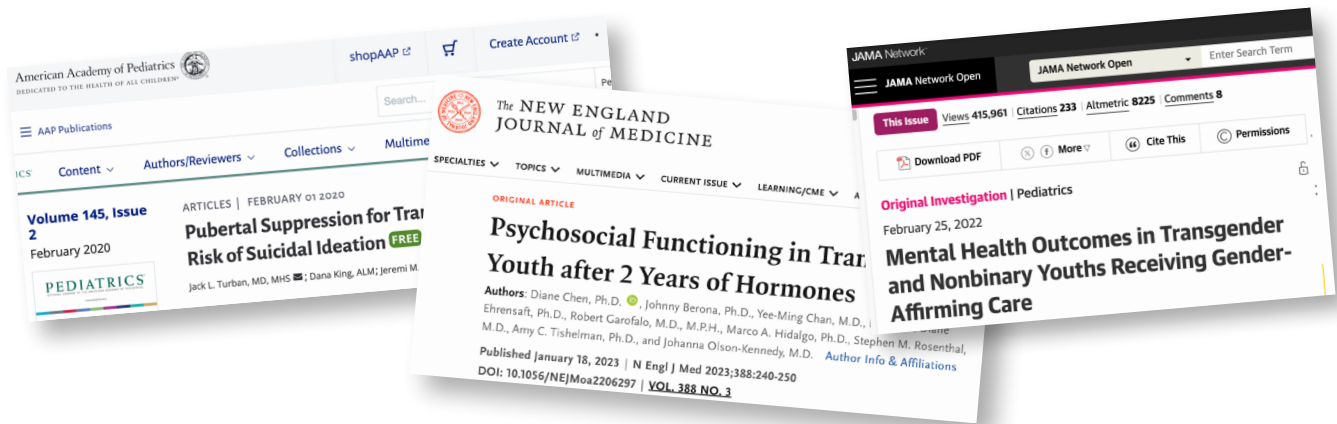




MAJOR PEDIATRIC GENDER STUDIES, MAJOR FLAWS



Research on pediatric gender medicine is highly politicized and rife with methodological limitations or outright malfeasance. It is for precisely this reason that the Cass Review of pediatric gender services in the United Kingdom concluded that the research base is of “poor quality.”

Many of the problems with the evidence base pertain to issues of **internal validity**, or how well a study justifies a cause-and-effect claim. Recurring problems include the absence of a control group, an inability to isolate the effect of hormonal treatment from concurrent psychotherapy, and unreliable survey data.

There are also concerns pertaining to **external validity**, or the generalizability of findings with small samples to some larger population. Much of the “evidence” on pediatric gender medicine comes from Europe, where the guardrails for accessing treatment are considerably higher than they are in the United States (e.g. patients must have a long history of dysphoria and must receive psychotherapy alongside hormonal treatment).

Moreover, a significant amount of the literature features data that predates a recent acceleration in the diagnosis and treatment of gender dysphoria.

Study #1: CHEN ET AL. (2023). PSYCHOSOCIAL FUNCTIONING IN TRANSGENDER YOUTH AFTER 2 YEARS OF HORMONES. *THE NEW ENGLAND JOURNAL OF MEDICINE*, 388(3), 240-250.

What it's used to show: Receipt of cross-sex hormones improves psychosocial functioning among minors.

Flaws:

- **Internal validity:** There is no comparison group. The researchers simply survey mental health through the course of treatment. Mental health naturally fluctuates, so without a comparison group it's impossible to infer whether these changes are related to the treatments.
- **Internal validity:** The “improvements” observed over two years are of dubious clinical significance.
- **Internal validity:** For reasons never explained, the researchers do not display a multitude of mental health measures that were collected for the study.

- **Internal validity:** The researchers gloss over the fact that 2 of 315 participants committed suicide.
- **External validity:** Benefits were limited to natal females, which raises the concern that benefits are attributable to the antidepressant effects of testosterone.
- **Internal validity:** The data is “winsorized,” a statistical technique in which extreme values are pulled toward the center. It’s unclear whether their results are sensitive to this decision.

Study #2: TURBAN ET AL. (2020). PUBERTAL SUPPRESSION FOR TRANSGENDER YOUTH AND RISK OF SUICIDAL IDEATION. *PEDIATRICS*, 145(2).

What it’s used to show: Children who received puberty blockers are less likely to experience suicidal ideation as adults.

Flaws:

- **Internal validity:** Data is taken from a 2015 survey that is completely unreliable. For example, most respondents who claimed they took blockers reported starting after age 18, which does not happen. Researchers claim they fix this problem by removing those people from the analysis, but it’s very unlikely that those were the only individuals providing incorrect answers.
- **Internal validity:** The researchers survey respondents who claim they received blockers going back to 1998. But with few exceptions, blockers didn’t become available as a treatment for gender dysphoria in the United States until the Endocrine Society endorsed them in 2009.
- **Internal validity:** Patients with the most severe mental health conditions would have been restricted from receiving blockers, so it’s likely that the group that received blockers had better mental health at baseline.
- **External validity:** The 2015 survey was not a random or representative sample, but one collected through advocacy organizations. Compared to the general population of gender-distressed youth, the population captured in this survey is more politically active and plausibly aware that their responses will be used for political advocacy.

Study #3: TORDOFF ET AL. (2022). MENTAL HEALTH OUTCOMES IN TRANSGENDER AND NONBINARY YOUTHS RECEIVING GENDER-AFFIRMING CARE. *JAMA NETWORK OPEN*, 5(2).

What it’s used to show: Receipt of blockers and hormones is associated with lower odds of suicidality and depression among minors.

Flaws:

- **Internal validity:** Mental health does not improve in the group that received blockers and hormones.

- **Internal validity:** The asserted evidence of benefit is that mental health deteriorates in the control group that sought but did not receive treatment. The implication is that the treatment group would have had the same experience in the absence of treatment. However, access to treatment isn't random but determined by mental fitness. It's plausible that the treatment group had a better mental health trajectory even in the absence of treatment.
- **Internal validity:** There is enormous attrition in the comparison group such that only six of the original 92 are included in the study at the end. This attrition reflects some combination of entering the treatment group (because their mental health was assessed as adequate) or leaving the gender clinic. The few who remained are not representative of the original control group.
- **External validity:** The follow-up from baseline (pre-treatment) was only one year.

Study #4: TURBAN ET AL. (2022). ACCESS TO GENDER-AFFIRMING HORMONES DURING ADOLESCENCE AND MENTAL HEALTH OUTCOMES AMONG TRANSGENDER ADULTS. *PLOS ONE*, 17(1).

What it's used to show: Receipt of gender-affirming hormones is associated with a lower incidence of suicidality.

Flaws:

- **Internal validity:** Data is taken from a 2015 survey that is completely unreliable. For example, most respondents who claimed they took blockers reported starting after age 18, which does not happen. Researchers claim they fix this problem by removing those people from the analysis, but it's very unlikely that those were the only individuals providing incorrect answers.
- **Internal validity:** An attempt to replicate the results of this study discovered glaring, basic errors in the analysis.
- **External validity:** The 2015 survey was not a random or representative sample, but one collected through advocacy organizations. Compared to the general population of gender distressed youth, the population captured in this survey is more politically active and plausibly aware that their responses will be used for political advocacy.
- **Internal validity:** Results suggest that those who received hormones engaged in less suicidal ideation over the past year. However, the results also show that those who claim to have received hormones before age 18 were far more likely than those who didn't to report a past-year suicide attempt requiring hospitalization. The authors make this finding disappear by setting a threshold of statistical significance which is highly unconventional in this type of research.
- **External validity:** The replication attempt of this study discovered that natal males who received hormones experienced a higher probability of planning, attempting, and being hospitalized for suicide. Benefits were limited to natal females, which raises the concern that benefits are attributable to the antidepressant effects of testosterone.

Study #5: DE VRIES ET AL., (2014). YOUNG ADULT PSYCHOLOGICAL OUTCOME AFTER PUBERTY SUPPRESSION AND GENDER REASSIGNMENT. *PEDIATRICS*, 134(4), 696-704.

What it's used to show: Behavioral and emotional problems and depressive symptoms decreased after the initiation of puberty blockers.

Flaws:

- **Internal validity:** Patients received traditional psychotherapy alongside puberty blockers. It is entirely unclear which treatments led to changes in mental health.
- **Internal validity:** There is no comparison group. The researchers simply survey minors about their mental health before and after starting puberty blockers. But mental health naturally fluctuates, so without a comparison group it's impossible to infer whether these changes are related to the initiation of puberty blockers.
- **External validity:** Participants were all from the Netherlands, where receipt of puberty blockers requires early-onset gender dysphoria that persists into adolescence. In many American clinics, puberty blockers are prescribed to kids with a more recent onset of gender distress.
- **External validity:** Participants received puberty blockers between 2000 and 2008, more than a decade before the exponential growth in the diagnosis and treatment of gender dysphoria among American adolescents. In other words, the minors who participated in this study were likely not as steered by social contagion, the dynamic in which minors become more likely to identify as transgender due to positive affirmation among peers, both in person and online.

Study #6: DE VRIES ET AL. (2011). PUBERTY SUPPRESSION IN ADOLESCENTS WITH GENDER IDENTITY DISORDER: A FOLLOW-UP STUDY. *J SEX MED*, 8(8), 2276-2283.

What it's used to show: Mental health improves among minors as they receive a course of treatment that entails puberty blockers, cross sex hormones, and surgery.

Flaws:

- **Internal validity:** Patients received traditional psychotherapy alongside puberty blockers. It is entirely unclear which treatments led to changes in mental health.
- **Internal validity:** There is no comparison group. The researchers simply survey minors about their mental health before and after starting puberty blockers. But mental health naturally fluctuates, so without a comparison group it's impossible to infer whether these changes are related to the initiation of puberty blockers.
- **Internal validity:** Patients selected for treatment were those with the best mental health.
- **External validity:** Participants were all from the Netherlands, where receipt of puberty blockers requires early-onset gender dysphoria that persists into adolescence. In many American states, puberty blockers are prescribed without such a long observation period.

- **External validity:** Data comes from 2000–2008, more than a decade before the exponential growth in the diagnosis and treatment of gender dysphoria among American adolescents. In other words, the minors who participated in this study were likely not as steered by social contagion.
- **Internal validity:** The researchers captured several measures of mental health. Nearly half of those measured showed no statistically significant improvements. Improvements in the minors that did improve were very modest.
- **Internal validity:** The sample consists of the first 70 children on puberty blockers approved for cross-sex hormones. Their timelier approval would have been based in part on better mental health and raises the possibility that their mental health would have improved even in the absence of hormonal intervention.”

Study #7: COSTA ET AL. (2015). PSYCHOLOGICAL SUPPORT, PUBERTY SUPPRESSION, AND PSYCHOSOCIAL FUNCTIONING IN ADOLESCENTS WITH GENDER DYSPHORIA. *J SEX MED*, 12(11), 2206-2214.

What it's used to show: Daily life for minors (sometimes referred to as “global functioning”) improves after initiation of puberty blockers.

Flaws:

- **Internal validity:** Patients received psychotherapy as part of their treatment. So not only is it unclear to what extent changes in mental health result from the treatment, it's unclear what the treatment itself is.
- **External validity:** Data comes from 2010–2014, before the meteoric growth in the diagnosis and treatment of gender dysphoria among American adolescents. In other words, they were probably not steered by social contagion.
- **External validity:** Participants were from the United Kingdom. There, unlike here, access to so-called “gender-affirming care” requires early-onset gender dysphoria that persists into adolescence.
- **Internal validity:** One group received “immediate” puberty blockers, and one group was “delayed” until after the study if their psychosocial issues were more profound. The “immediate group” experienced the same rate of improvement in global functioning in the first six months when they only received psychotherapy as in the following 12 months when they received both psychotherapy and puberty blockers. In other words, the improvements appear to be because of psychotherapy, not blockers.
- **Internal validity:** The “immediate group” that received blockers during the trial period ended up with global functioning scores that were not statistically significantly different from the “delayed” group, who never received blockers during the study.

Study #8: GREEN ET AL. (2022). ASSOCIATION OF GENDER-AFFIRMING HORMONE THERAPY WITH DEPRESSION, THOUGHTS OF SUICIDE, AND ATTEMPTED SUICIDE AMONG TRANSGENDER AND NONBINARY YOUTH. *JOURNAL OF ADOLESCENT HEALTH*, 70(4), 643-649.

What it's used to show: Receipt of gender-affirming hormones is associated with lower odds of recent depression.

Flaws:

- **Internal validity:** The study provides a snapshot measure of mental health among those who received cross-sex hormones compared to those who wished to receive them but did not. Patients with the most severe mental health conditions would have been restricted from receiving hormones, so it's likely that the group that received them had better mental health at baseline.
- **Internal validity:** The researchers do not clarify how long respondents have been in receipt of cross-sex hormones.

Study #9: KUPER ET AL. (2020). BODY DISSATISFACTION AND MENTAL HEALTH OUTCOMES OF YOUTH ON GENDER-AFFIRMING HORMONE THERAPY. *PEDIATRICS*, 145(4).

What it's used to show: Receipt of blockers and hormones is associated with improvements in body dissatisfaction, depression, and anxiety.

Flaws:

- **Internal validity:** There is no comparison group. The researchers simply survey mental health before and after starting puberty blockers and/or cross sex hormones. Mental health naturally fluctuates, so without a comparison group it's impossible to infer whether these changes are related to the treatment.
- **Internal validity:** Measures of "body dissatisfaction" improve for the group that only receives puberty blockers. But blockers only prevent puberty from progressing and do not reverse it. That this group experiences improvement is suggestive of a placebo effect.
- **External validity:** The follow-up from baseline (pre-treatment) was, on average, only 15 months.
- **Internal validity:** Changes in depressive symptoms were measured by self-report and by clinicians. While there is improvement in the self-report measure, the clinician report does not change from baseline to follow-up. It's plausible that patients seek to validate the efficacy of the treatments and consciously or unconsciously misrepresent their true feelings.

Study #10: ALLEN ET AL. (2019). WELL-BEING AND SUICIDALITY AMONG TRANSGENDER YOUTH AFTER GENDER-AFFIRMING HORMONES. *CLINICAL PRACTICE IN PEDIATRIC PSYCHOLOGY*, 7(3), 302-311.

What it's used to show: Levels of suicidality decrease, while general well-being increases, among adolescents diagnosed with gender dysphoria after receiving hormone treatments.

Flaws:

- **Internal validity:** There is no comparison group. The researchers simply survey mental health before and after starting hormone therapy. Mental health naturally fluctuates, so without a comparison group it's impossible to infer whether these changes are related to the initiation of hormone therapy.
- **External validity:** Short follow-up (participants answered surveys, on average, after only 349 days of treatment).

Study #11: ACHILLE ET AL. (2020). LONGITUDINAL IMPACT OF GENDER-AFFIRMING ENDOCRINE INTERVENTION ON THE MENTAL HEALTH AND WELL-BEING OF TRANSGENDER YOUTHS: PRELIMINARY RESULTS. *INTERNATIONAL JOURNAL OF PEDIATRIC ENDOCRINOLOGY*, 2020:8.

What it's used to show: Receipt of puberty blockers and hormones is associated with reduced depression.

Flaws:

- **Internal validity:** The change in "quality of life" survey scores was not statistically significant
- **Internal validity:** Among natal females, changes in depression were not statistically significant.
- **External validity:** There is a big change in depression scores between the time before starting treatment and when participants are initially surveyed after starting treatment. However, changes largely level off between the second check and a later check, suggesting that the initial euphoria associated with receiving treatment wanes over time (a fact that highlights why the short time horizons in other studies are so problematic).

Study #12: VAN DER MIESEN ET AL. (2020). PSYCHOLOGICAL FUNCTIONING IN TRANSGENDER ADOLESCENTS BEFORE AND AFTER GENDER-AFFIRMATIVE CARE COMPARED WITH CISGENDER GENERAL POPULATION PEERS. *THE JOURNAL OF ADOLESCENT HEALTH*, 66(6), 699-704.

What it's used to show: Kids who receive puberty blockers have better psychological measures compared to kids referred to the clinic who haven't yet started blockers.

Flaws:

- **Internal validity:** Patients received psychotherapy as part of their treatment. It's not possible to disentangle the effect of the blockers from the effect of psychotherapy.
- **External validity:** The sample comes from the Netherlands. There, unlike here, receipt of hormone therapy requires early-onset gender dysphoria that persists into adolescence.

- **Internal validity:** The Dutch Protocol requires clinicians to rule out severe psychological comorbidities before beginning treatment. So the overall better psychological functioning of the group that received blockers compared to the referral group that hopes to receive treatment reflects, at least in part, that the former group was well enough to receive treatment.
- **Internal validity:** The study provides results from one snapshot in time. It's not clear whether the group that received blockers improved from before treatment.

Study #13: KALTIALA ET AL. (2020). ADOLESCENT DEVELOPMENT AND PSYCHOSOCIAL FUNCTIONING AFTER STARTING CROSS-SEX HORMONES FOR GENDER DYSPHORIA. *NORDIC JOURNAL OF PSYCHIATRY*, 74(3), 213-219.

What it's used to show: Patient need for psychiatric treatment for depression, anxiety, and suicidality decreases after initiation of cross-sex hormones.

Flaws:

- **Internal validity:** There is no comparison group. The researchers simply survey mental health before and after starting hormone therapy. Mental health naturally fluctuates, so without a comparison group it's impossible to infer whether these changes are related to the initiation of hormone therapy.
- **External validity:** The sample comes from Finland. There, unlike here, receipt of hormone therapy requires early-onset gender dysphoria that persists into adolescence.
- **External validity:** "The follow-up period was approximately only a year, which inhibits drawing conclusions on long-term outcomes."

Study #14: DE LARA ET AL. (2020). PSYCHOSOCIAL ASSESSMENT IN TRANSGENDER ADOLESCENTS. *ANALES DE PEDIATRIA*, 93(1), 41-48.

What it's used to show: Levels of depression, anxiety, and dysphoria decrease after initiating cross-sex hormones.

Flaws:

- **External validity:** Participants were required to have an "absence of psychiatric comorbidity that could affect the experience of gender dysphoria" and must demonstrate ability to understand the risks and benefits associated with hormone therapy. These requirements are not observed by the "affirmative model" used in the United States.
- **External validity:** Short follow-up (participants answered surveys only one year after starting hormone treatment).

ENDNOTES

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