



Do No Harm

North Dakota Senate

Senate Committee on Human Services

HB 1254

Daniel Weiss MD

Opening Statement

Chairwoman Lee and Members of the Committee:

My name is Dr. Daniel Weiss.

I am a board-certified internist and endocrinologist. I am also a senior fellow with the non-profit organization, [Do No Harm](http://donoharm.org). My commentary is mine alone and does not represent the views of any medical practice.

I believe my clinical experience is meaningful, in part, because I have provided hormonal treatments for persons with gender dysphoria in the past.

I do not do so now.

Why not? Because I discovered that most of these patients carried stories of traumatic childhoods and co-morbid depression. Their psychologic evaluation was inadequate before they were “cleared” for treatment. Furthermore, opposite sex treatment did not resolve any of their underlying psychologic issues.

I later learned that there is no good scientific or clinical evidence to support hormonal or surgical interventions for minors with gender dysphoria. Instead, there is increasing evidence to show that such treatments for gender dysphoria cause harm. I will briefly summarize key data in the medical literature.

The most-cited studies of hormonal treatment in minors report outcomes using the so-called Dutch protocol. I encourage you to review the references I have provided.

Multiple papers detail the many scientific flaws in the Dutch studies: There was no comparison group. The study subjects were highly selected. The study started with 111 children but only 55 were analyzed at its conclusion. Nonetheless, the small group of children showed no improvement in gender distress, anxiety, or anger after opposite sex hormone treatment. The researchers used an unvalidated measurement tool and manipulated its results. It is also little known that the series included, as a complication of surgery, a patient death. Independent researchers in the United Kingdom attempted to replicate the findings of the Dutch group, but, revealingly, were unsuccessful.

A paper published last year in the Endocrine Society's key journal summarized the evidence on hormonal interventions for "gender diverse adolescents" as sparse and of low quality. In the key authoritative endocrinology textbook, just published in 2023, the chapter on Transgender Healthcare, written by a WPATH member, states that "long-term prospective outcome studies of the effects of GAHT (gender affirming hormone therapy) of any type are lacking. What data that do exist are mostly retrospective and have numerous limitations."

And gender dysphoria resolves in the vast majority of children without any interventions.

I have touched on the lack of data showing benefit. So, what about harm? Many studies show that puberty blockers and opposite sex hormones damage bone health, cardiovascular health, and fertility. There is emerging evidence of increased rates of breast cancer and other adverse effects.

Those who state that puberty blockers are readily reversible and harmlessly "pause" puberty can cite no published data on the reversibility of these drugs in this setting. The FDA has not approved any drug for treatment of gender dysphoria.

How about suicide? The largest study documented 4 suicides out of 15,000 adolescents being treated for gender dysphoria in the United Kingdom. It is not known whether this rate is any different than that seen in adolescents undergoing mental health treatment who do not have gender dysphoria.

The best data suggest that hormonal and surgical interventions increase the risk of suicide. The Dutch study provided no data on suicide. In contrast, a long-term study of transgender persons in Sweden found a 19-fold overall higher suicide rate.

The rate was 40-fold higher in females and a 3-fold higher overall mortality, despite treatment with opposite sex hormones and surgery as compared to the control population. *In a study of over 8000 transgender person, two thirds of those who died by suicide were still receiving treatment at the gender dysphoria center.* In a New England Journal of Medicine article this year, suicide reportedly increased 45-fold with opposite sex hormonal therapy.

For more than a decade, long before opposite sex therapies became popular in the United States, European centers offered these treatments for gender confusion. Now, as increasing data show substantial harm, Finland, Sweden, France, and the United Kingdom have discouraged or terminated opposite sex treatments for minors. Instead, they advise supportive psychotherapy for minors with gender confusion.

Why have physicians and surgeons in the United States resisted the shift occurring among their European counterparts? I do not know the answer. However, I caution legislators to avoid all individual and institutional financial conflicts of interest while finalizing this bill.

In closing, it should be noted that strict international principles prohibit children from providing consent. This is because children cannot fully comprehend risk versus benefit. The United States is a signatory to the United Nations Convention on the Rights of the Child. The *Declaration of the Rights of the Child* states that “the child, by reason of his physical and mental immaturity, needs special safeguards and care.” These safeguards are uniquely important when it comes to an experimental medical intervention. The Declaration of Helsinki allows individual parents to consent to experimental treatment for their child. Usually, this choice is made in an extraordinary circumstance, to save that child’s life, and with the child’s assent. Experimental treatments to change gender appearance should not be an exception to these requirements.

Please help protect the children of North Dakota.

Thank you.

Daniel Weiss MD

Key References:

Lack of efficacy

de Vries A. L. *et al.* Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. *J. Sexual Medicine* 2011; 8: 2276-2283.

“Dutch Study.” There was no change in anxiety, depression or gender distress following GnRH therapy (puberty blockers) and opposite sex therapy in children. There was no comparator control group, and all received psychologic support.

de Vries A.L. *et al.* Young adult psychological outcome after puberty suppression and gender reassignment. *Pediatrics* 2014; 134: 696-704.

“Dutch Study.” A non-validated assessment tool was used to assess dysphoria, there was no control group, and the 55 patients were tested in such a way that improvements in scores would be seen even without treatment. There was one post-surgical death. Only 55 of the original 111 children were included in the analysis.

Carmichael P. *et al.* Short-term outcomes of pubertal suppression in a selected cohort of 12- to 15-year-old young people with persistent gender dysphoria in the UK. *PLOS One* 2021; 16 (2) *These researchers could not confirm any of the claims of DeVries et al in young people treated with the Dutch protocol in the U.K.*

Kaltiala R, *et al.* Adolescent development and psychosocial functioning after starting cross-sex hormones for gender dysphoria. *Nord J Psychiatry.* 2020;74(3):213-219.

This retrospective chart review showed no improvement in psychiatric status in 52 adolescents after opposite sex hormone treatments.

Abbruzzese E. *et al.* The Myth of “Reliable Research” in Pediatric Gender Medicine: A critical evaluation of the Dutch Studies—and research that has followed, *Journal of Sex & Marital Therapy.* January 2023.

This paper is a comprehensive and critical review of De Vries’ studies identifying the many flaws and biases in the methodology.

Levine S. *et al.* Reconsidering informed consent for trans-identified children, adolescents, and young adults. *J. Sex and Marital Therapy* 2022; 48: 706-727.

This paper describes the challenges in providing full and proper informed consent to children with gender dysphoria and their parents in light of the flaws in the Dutch protocol and limitations in our knowledge base.

O’Connell MA, *et al.* Approach to the Patient: Pharmacological Management of Trans and Gender-Diverse Adolescents. *J Clin Endocrinol Metab.* 2022;107(1):241-

257. This review stresses the need for improvement in the “evidence base” emphasizing that the “evidence relating to hormonal therapies in youth is low” and that “data on wellbeing in transgender persons is sparse”.

Levine SB, et. al. What are we doing to these children? Response to Drescher, Clayton, and Balon commentaries on Levine et. al. 2022. *J Sex and Marital Therapy* 2023; 49:115-125. *In a response to comments, the authors discuss the benefits of psychotherapeutic interventions and the frequent conflicts of interest of those clinicians who solely promote hormonal and surgical interventions.*

Deutsch, MB. Transgender Healthcare. p 1752-1757 in Degroot’s *Endocrinology. Basic science and clinical practice*. 8th edition. 2023.

In this authoritative textbook on endocrinology, Dr. Madeline Deutsch, a member of the World Professional Association for Transgender Health (WPATH) writes that “long-term prospective outcome studies of the effects of GAHT (gender affirming hormone therapy) of any type are lacking. What data that do exist are mostly retrospective and have numerous limitations.”

Role of psychotherapy or non-intervention

Ristori J, Steensma TD. Gender dysphoria in childhood. *Int Rev Psychiatry*. 2016;28(1):13-20. *85% of children with gender dysphoria show spontaneous resolution of their symptoms and distress without any intervention.*

Clayton, A. Gender-affirming treatment of gender dysphoria in youth: a perfect storm environment for the placebo effect—the implications for research and clinical practice. *Arch Sex Behavior* Nov. 2022.

This paper provides an overview of the poor data in support of opposite sex hormone treatment, of the harms caused by opposite sex treatment and improvement in response to placebo. For perspective, it describes historical treatments which once were popular, but eventually proved harmful to children.

Costa R. et. al. Psychological support, puberty suppression, and psychosocial functioning in adolescents with gender dysphoria. *J Sex Med* 2015; 12: 2206-2214.

This UK study found that psychological support alone lead to significant improvement in psychological function in adolescents with gender dysphoria, mean age of 15.5.

Psychiatric co-morbidities in youth with gender dysphoria

Becerra-Culquie TA et. al. Mental health of transgender and gender nonconforming youth compared with their peers. *Pediatrics* 2018; 141: e20173845.

Over 60 % of transgender adolescents were diagnosed with depression, autism spectrum disorders, psychoses, substance abuse, anxiety or eating disorders.

Kozłowska, K. et. al. Australian children and adolescents with gender dysphoria: clinical presentations and challenges experienced by a multidisciplinary team and gender service. *Human Systems: Therapy, Culture and Attachments* 2021; 1: 70-95

88% of these youth had comorbid mental health diagnoses and other indicators of psychological distress and adverse childhood events. 19% had a history of sexual abuse. 54% were bullied. What is the best approach to treating these youth?

Devor, H. Transexualism, dissociation and child abuse: an initial discussion based on nonclinical data. *J Psychology and Human Sexuality* 1994; 6: 49-72.

In depth interviews disclosed that sixty percent of the natal females disclosed one or more types of child abuse; more than 50% of that abuse was sexual.

Harm

Mortality:

Dhejne C, et al. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. *PLoS One*. 2011;6(2):e16885.

This long-term study found an overall 19-fold higher suicide rate (40 fold in female to male) and a 3-fold higher overall mortality in 324 transgender persons at 11 years after full transition, compared to the control population.

de Blok CJM. et al. Mortality trends over five decades in adult transgender people receiving hormone treatment: a report from the Amsterdam cohort of gender dysphoria. *The Lancet Diabetes & Endocrinology*. 2021;9(10):663-670.

This study documented increased rates of mortality in all persons receiving opposite sex hormone therapy.

Bone:

Biggs M. Revisiting the effect of GnRH analogue treatment on bone mineral density in young adolescents with gender dysphoria. *J Pediatr Endocrinol Metab*. Jul 27, 2021;34(7):937-939. *Children treated with puberty blockers showed a marked reduction in bone density in those treated with GnRH analogues (puberty blockers); this change would be expected to increase the risk of fractures.*

Cardiovascular:

Nota NM, et al. Occurrence of Acute Cardiovascular Events in Transgender Individuals Receiving Hormone Therapy. *Circulation*. 2019;139(11):1461-1462.

This study found increased rates of heart attacks, strokes, and blood clots in those treated with opposite sex hormone therapy.

Getahun D. et. al. Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons: A Cohort Study. *Ann Intern Med*. Aug 21, 2018;169(4):205-213.

This study documents increased rates of blood clots as well as strokes and heart attacks in males given opposite sex hormone treatment.

Fertility:

Baram S, et al. Fertility preservation for transgender adolescents and young adults: a systematic review. *Hum Reprod Update*. Nov 5, 2019;25(6):694-716.

The authors raise concerns that opposite sex hormone therapies cause infertility, but offer no solutions to this problem.

Cancer:

de Blok, et. al. Breast cancer risk in transgender people receiving hormone treatment: nationwide cohort study in the Netherlands. *BMJ* 2019; 365: 11652.

Males given opposite sex hormones experience a 46-fold increase in the occurrence of breast cancer.

Gurralla RR, et. al. The impact of exogenous testosterone on breast cancer risk in transmasculine individuals. *Ann Plastic Surg* 2023; 90: 96-105.

Breast cancer occurred 20 yrs earlier than expected in this population of females even though most had mastectomies before the diagnosis. Despite mastectomy, they retained some breast tissue.

Wang, JC et. al. Factors associated with unsatisfactory Pap tests among sexually active trans masculine adults. *LGBT Health* 2023;

Those females who had received 1 year or more of testosterone were three and half times more likely to have an unsatisfactory Pap test, making early detection of cervical cancer much more difficult.

Breastfeeding:

Gribble, K. *et al.* Breastfeeding grief after chest masculinisation mastectomy and detransition: a case report with lessons about unanticipated harm. *Frontiers in Global Women's Health* 2023; Feb.

This case report describes the challenges faced by a woman who detransitions and who grieves over being unable to breastfeed her infant. Detransition is discussed and the importance of including in the informed consents before mastectomy the inability to breastfeed.

Brain:

Schneider MA, *et. al.* Brain maturation, cognition, voice pattern in a gender dysphoria case under pubertal suppression. *Frontiers in Human Neuroscience* Nov 2017; 11. *This patient showed an abnormal failure to increase brain white matter. In addition the patient experienced a reduction in IQ and memory during 22 months of puberty blockers.*

Post-surgical complications

Van der Sluis WB, *et. al.* Genital gender-affirming surgery for transgender women. *Best Practice and Research Clinical Obstetrics and Gynecology* Dec 2022.

The surgical procedures of vulvoplasty and vaginoplasty typically require 5 day hospital stay. The authors describe the risk of severe complications, the possibility of repeat surgeries and the fact that there is no accepted validated questionnaire to assess postoperative satisfaction.

Ortengren, C. *et. al.* Urethral outcomes in metoidioplasty and phalloplasty gender affirming surgery and vaginectomy: a systematic review. *Translational Andrology and Urology* 2022; 11: 1762-1770.

The authors review reports of surgical outcomes including the ability to urinate while standing after surgery. Of those reporting this result, 25% of patients were unable to urinate while standing. Up to 63% had complications including urethral strictures and infections. No description was provided of patient satisfaction after surgery.

Kamal K, *et.al.* Addressing the physical and mental impacts of postsurgical scarring among transgender and gender diverse people. *LGBT Health* 2023

The authors describe the “dearth of peer-reviewed research” on the “repercussions” of postsurgical scarring and the lack of coverage by insurance for “scar treatment”.

Potter, E. *et. al.* Patient reported symptoms and adverse outcomes seen in Canada's first vaginoplasty postoperative care clinic *Neurourol Urodyn* 2023; 42: 523-529

Pain, bleeding, sexual dysfunction, and urinary symptoms were common (> 50%) in this series of 80 biologic males who had undergone surgery to create a vagina.

Wang, AMQ, et. al. Outcomes following gender affirming phalloplasty: a systematic review and meta-analysis. *Sexual Medicine Reviews* 2022; 10: 499-512.

The authors describe a 76% complication rate after attempts to create a penis in biologic females. Goals of surgery include being able to urinate with standing, having sensation, and aesthetics, i.e being similar in appearance to biologic male genitalia. The objective the authors considered did not include having a penis that can function for intromission. Only 6% of those centers reporting results aesthetic results.

Suicide risk

Wiepjes CM, et. al. Trends in suicide death risk in transgender people; results from the Amsterdam Cohort of Gender Dysphoria study (1972-2017). *Act Psychiatr Scand* 2020; 141: 486-491.

This long-term study of 8263 transgender adults, (mean age of 25 at first visit to gender dysphoria center) showed that suicide deaths occur during every stage of gender transitioning. There were 49 suicides out of 8263 persons with average follow-up of 7.5 years. This number is a rate of 40/100,000 which may be compared to 11/100,000 in the general population. Two thirds of those who died by suicide were still receiving treatment at the gender dysphoria center. The average age at the time of suicide was 41. This study provided no additional psychiatric information.

Biggs, M. Suicide by clinic-referred transgender adolescents in the United Kingdom. *Arch Sexual Behavior* 2021; 51: 685-90.

In this study, of the Gender identity Development Service in the UK, 4 patients committed suicide out of 15,000. This rate was 5.5 times higher than the overall adolescent population without psychiatric diagnoses. The study reached no conclusion as to the best approach to prevent these suicides.

Chen, D. et. al. Psychosocial functioning in transgender youth after 2 years of hormones. *N Engl J Med* 2023; 388: 240-250.

There was no control group in this study of children, aged 12-20 (mean age 16) treated with opposite sex hormones over 2 years in 4 US transgender clinics. Psychiatric care was not described. The biologic males showed no improvement in depression, anxiety, or life satisfaction. There were no reports of adverse physical events but 2 children, on treatment, committed suicide during this short-term study.

The rate of suicide in this group translates into a 45-fold higher rate than the CDC reported suicide rates for those of comparable age in the general population.

Regret and Detransition

Littman L. Individuals treated for gender dysphoria with medical and/or surgical transition who subsequently detransitioned: a survey of 100 detransitioners. Arch. Sex Behavior. 2021; 50: 3353-3369.

This study recruited subjects with gender dysphoria and offered them a 115-question anonymous survey on several social media sites. The response showed that 48% of the natal females had trauma within 1 year before onset of gender dysphoria. 55% felt they did not receive adequate evaluation from a doctor or mental health professional before opposite sex therapy. Only 24% let their clinician know they had chosen to detransition. In 23%, the desire to “transition” was a response to difficulty in accepting themselves as gay, lesbian, or bisexual. Gender dysphoria started on average at age 11 and transition occurred on average at age 22. On average, detransition occurred 4 years later.

Roberts CM, et. al. Continuation of gender-affirming hormones among transgender adolescents and adults. J Clin Endocrinol Metab 2022; 107: e3937-e3943.

This study used the US Military Healthcare System database to determine the adherence rates for opposite sex hormone treatment in 952 persons with a mean age 19. 66% of this cohort were natal females. Over 4 years, 36% of the natal females discontinued treatment. Of those who started opposite sex treatment below the age of 18, 26% discontinued within 4 years.

Ethics

https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-50/subpart-D/section_50.52

Code of federal regulations relating to institutional review board requirements for clinical investigations involving children. There must be an anticipated benefit that is as favorable as other available treatments and there must be assent of the children and permission of the parents or guardians.

Declaration of Helsinki (1964) BMJ 313, 1448-1449, 1996