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Chair Roegner, Vice Chair Antani, Ranking member Smith, and members of the Government Oversight Committee, thank you for the opportunity to testify in favor of House Bill 68, otherwise known as the SAFE Act.

There is a growing body of evidence that the use of Puberty Blockers and Cross-Sex Hormones are not safe for use in gender transformation and are not fully reversible. The use of these medications can affect bone, brain development, sterility, and a host of chronic illnesses such as metabolic disorders (ie. Diabetes) and Cardiac diseases.

Puberty Blockers like Lupron® (leuporelin) are beneficial in the treatment of precocious puberty and certain types of cancers that are responsive to sex hormones. In the treatment of precocious puberty, the puberty blocker is used to inhibit the surge of sex hormones that occurs at the time of puberty. In precocious puberty the hormone surge begins at an age too young for puberty development which can result in the child having secondary sex traits at an early age (around 8 or 9 years of age), this can be traumatic enough at this age but, more importantly, their bone growth will stop as it does in puberty that occurs at the normal age. This means the child will be of shorter stature than they would have been if they had developed during the normal age range. When used in a youth experiencing gender dysphoria the medication is used on a physically healthy child at a time when their bodies are supposed to develop into adulthood. When an adolescent is prevented from experiencing the hormonal and physical changes of the body during puberty the body does not develop in a normal manner leading to long term, many times permanent, disability.

The brain continues to develop well into adulthood. Part of the brain's development is mediated by the sex hormones. Throughout adolescence, there are changes in the structure and function of the brain. Differences in the brains of female and male suggest a relationship to puberty and the hormones released at that time. The gonadal steroid hormones estrogen and testosterone, as well as their weaker adrenal counterparts, influence the physical appearance of the body. They also affect the brain and behavior. Some of the changes in the brain occur before we are born and continue through adolescence and into early adulthood. Gray matter development initially increases during childhood and reaches its peak in adolescence and declines steadily in adulthood. White matter development occurs between childhood and adolescence, with this increase slowing and stabilizing into adulthood. This increase differs between the sexes across adolescence.¹ The brain has a wide distribution of receptors for hormones like estrogen and testosterone, which allows these sex steroids to affect a multitude of brain circuits, influencing how, where, and when brain cells communicate². It is clear brain development could be adversely affected by use of puberty blockers and cross-sex hormones.

Bone development is also affected by the use of puberty blockers. As a result of the use of puberty blockers, bone density goes down. The addition of cross-sex hormones has been shown to build bone density but not to the level it should be. The Cleveland Clinic and the Mayo Clinic, both centers perform transgender procedures acknowledge the risk of lower bone mineral density.

Puberty cannot simply be paused and started back again later without permanent consequences. Concerns are growing among some medical professionals about the consequences of these drugs used to block puberty. These concerns are fueling government reviews in Europe prompting a push for more research and leading some prominent specialists to reconsider at what age to prescribe and for how long. England's National Health Service proposed restricting use of the drugs to research settings only. Sweden and Finland have also placed limits on their use. More than ten thousand adverse event reports have been filed with the FDA concerning the use of puberty blockers including: brittle bones, faulty joints, osteopenia, osteoporosis, pain, hip replacement, depression, and anxiety. The New York Times published an article about emerging evidence of potential harm from using puberty blockers from a review of scientific papers and interviews with more than 50 doctors and academic experts around the world. Dr. Sandeep Khosla, who leads the bone research lab at the Mayo Clinic, states "There is going to be a price paid" for using these drugs.

Cross-sex hormone therapy also carries long term consequences including, sterility, increased risk of cardiovascular disease, increased risk of breast and uterine cancers, mood swings and psychosis.³ In a study published in The Lancet there has been an increased mortality risk in transgender people using hormone treatment, regardless of treatment type. This increased mortality risk did not decrease over time. The cause-specific mortality risk because of lung cancer, cardiovascular disease, HIV-related disease, and suicide gives no indication to a specific effect of hormone treatment.⁴

Another study published in Medscape states that transgender individuals are twice as likely to die early as the general population.⁵

Sex Hormones carry adverse effects in any individual who receives them.

Testosterone: Problems with heart, brain, liver, endocrine and mental health systems, enlarged breasts, small testicles, infertility, high blood pressure, bone growth problems, addiction, aggressive and violent behavior, blood clots, high cholesterol, polycythemia, weight gain.

Estrogen: Higher chance of developing liver tumors or cancer, glucose intolerance, high blood pressure, above normal levels of calcium in blood, blood clots.

In consideration of the possibility of long-term consequences of these therapies for youth who have gender dysphoria, it seems prudent to rely on mental health therapy for pediatric and adolescent patients.

1. The role of puberty in the developing adolescent brain., Authors: Sarah-Jayne Blakemore, Stephanie Burnett, Ronald E Dahl, Human Brain Mapping/ Volume 31, Issue 6 p.926-933, <https://doi.org/10.1002/hbm.21052>
2. Sex Hormones and the Brain, Author: Kayt Sukel, published 8/2/2019, Dana Foundation
3. Study: Effects of Puberty blockers can last a lifetime, Author: Mary Jackson, World, December 18,2020
4. Bone Development in Transgender Adolescents Treated With GnRH Analogues and Subsequent Gender-Affirming Hormones, Authors: Sebastian E Schagen, Femke M Wouters, Peggy T Cohen-Kettenis, Louis J Gooren and Sabine E Hannema, J Clin Endocrinol Metab 2020 Dec; 105(12): e4252-e4263 Published online 2020 Sep 10 doi:10.1210/clinem/dgaa604 PMID: 32909025
5. Gender-Affirming Hormone Treatment Decreases Bone Turnover in Transwomen and Older Transmen, Authors: Mariska C Vlot, Chantal M Wiepjes, Renate T de Jongh, Gut T'Sjoen, Annemieke C Heijboer, and Martin den Heijer; J Bone Miner Res. 2019 Oct; 34(10): 1862-1872, published online 2019 Aug 19. Doi: 10.1002/jbmr.3762, PMID: 31099910
6. Bone Mass in Young Adulthood Following Gonadotropin-Releasing Hormone Analog Treatment and Cross-Sex Hormone Treatment in Adolescents With Gender Dysphoria, Authors: Daniel Klink, Martine Caris, Annemieke Heijboer, Michael van Trotsenburg, and Joost Rotteveel, J Clin Endocrinol Metab, February 2015, 100(2):E270-E275, doi: 10.1210/jc.2014-2439
7. Revisiting the effect of GnRH analogue treatment on bone mineral density in young adolescents with gender dysphoria, Michael Biggs, <https://doi.org/10.1515/jpem-2021-0180>
8. Gender-Affirming Hormone Treatment Decreases Bone Turnover in Transwomen and Older Transmen, Mariska C Vlot, Chantal M Wiepjes, Renate T de Johngh, Guy T'Sjoen, Annemieke C Heijboer, Martin den Heijer, DOI: 10.1002/jbmr.3762, PMID: PMC6852079
9. Pubertal blockers for transgender and gender-diverse youth, Mayo Clinic Staff, Mayo Clinic
10. Managing skeletal issues in transgender and gender-nonconforming individuals, Mayo Clinic
11. What Are Puberty Blockers? Cleveland Clinic, published 01/10/2022/ Pediatrics
12. Behavioral and neurobiological effects of GnRH agonist treatment in mice—potential implications for puberty suppression in transgender individuals, Christopher Anacker, Ezra Sydnor, Briana K. Chen, Christina C LaGamma, Josephine C McGowan, Alessia Mastrodonato, Holly C Hunsberger, Ryan Shores, Rushell S. Dixon, Bruce S. McEwen, William Byne, Heino F. L. Meyer-Bahlburg, Walter Bockting, Anke A Ehrhardt and Chrisine a Denny., Nature, published online 12 September 2020
13. Hormone therapy for transgender patients, Cecile A. Unger, Transl Androl Urol 2016 Dec; 5(6): 877-884, doi: 10.21037/tau.2016, PMID: 28078219
14. Mortality trends over five decades in adult transgender people receiving hormone treatment: a report from the Amsterdam cohort of gender dysphoria, Christel JM de Blok MD, Chantal M Wiepjes, Daan M van Velzen, Annemieke S Staphorsius, Nienke M Nota , Louis JG Gooren, Published September 02, 2021, DOI: [https://doi.org/10.1016/S2213-8587\(21\)00185-6](https://doi.org/10.1016/S2213-8587(21)00185-6), The Lancet
15. Puberty blockers do not alleviate negative thoughts in children with gender dysphoria, finds study, BMJ 2021; 372 doi: <https://doi.org/10.1136/bmj.n356> BMJ 2021; 372:n356
16. Puberty blockers for gender dysphoric youth: A lack of sound science, Sarah C. J. Jorgensen, Patrick K. Hunter, Lori Regenstreif, Joanne Sinai, William J. Malone, <https://doi.org/10.1002/jac5.1691>

17. Drug used to halt puberty in children may cause lasting health problems, Christina Jewett, Kaiser Health News Feb. 2, 2017
18. FDA Drug Safety Communication: Ongoing Safety Review of GnRH Agonists and possible increased risk of diabetes and certain cardiovascular diseases.
19. Growing body of evidence disputes claims that puberty blockers are safe, reversible, Laura Duggan, November 14, 2022
20. Transgender Individuals Twice as Likely to Die Early as General Population, Becky McCall, September 07, 2021, Medscape
21. When transgender Kids Transition, Medical Risks are Both Known and Unknown, Priyanka Boghani (<https://www.pbs.org/wgbh/frontline/person/priyanka-boghani/>)
22. Long-term effects and significant adverse drug reactions (ADRs) associated with the use of a gonadotropin-releasing hormone analogs (GnRHa) for central precocious puberty: a brief review of literature, Vincenzo De Sanctis, Ashraf T Soliman, Salvatore De Maio, Nada Soliman, heba Elsedfy, Acta Biomed 2019; 90(3):345-359 doi: 10.23750/abm.v90i3.8736, PMID: 31580327
23. Use of Puberty Blockers: (Lupron) GnRH analoge, MayoClinic.org
24. Gender affirming medical care of Transgender youth, Caroline Salas-Humara, MD; Gina M Sequeira, MD; National Library of Medicine, PMC8496167
25. New York Times: The Paused Puberty, but is there a cost?; Megan Twohey and Christina Jewett, 11/14/2022
26. New York Times: What are puberty blockers? Zena Wilson, 05/11/2021
27. STAT, Drug used to halt puberty in children may cause lasting health problems., Christina Jewett, Kaiser Health News, 02/02/2017
28. American College of Cardiology, Hormone Therapy for Gender Dysphoria ay raise cardiovascular risks. 02/23/2023, Katie Glenn