

Article

Politics Aside, Healthcare Considerations Motivate More Caution before Medical Intervention for Trans-Identifying Youth

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Abstract: The 2022 article “Legislation restricting gender-affirming care for transgender youth: Politics eclipse healthcare” by K. L. Kraschel et al. implies that attempts in the United States to restrict medical interventions for gender dysphoria are due to political motivations. Although there are likely some whose stance on these interventions is based upon politics, there are sound medical reasons, independent of politics, for advocating for more cautious medical intervention protocols. Neglecting mention of these reasons obscures the fact that medical intervention outcomes are difficult to predict and that serious risks and irreversible consequences are present. In other countries, following extensive evidence review, supportive alternatives to medical intervention are being prioritized instead. Here, several claims of Kraschel et al. regarding the state of medical intervention healthcare are compared to the research evidence and shown to fall short. Healthcare issues alone justify challenging current United States medical treatment protocols.

Keywords: gender dysphoria; medical intervention

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Introduction

The article “Legislation restricting gender-affirming care for transgender youth: Politics eclipse healthcare” by Kraschel et al. (2022)¹ claims that attempts to restrict medical interventions for gender dysphoria in the United States are due to political motivations and have no basis in healthcare concerns. Kraschel et al.’s argument that proposing restrictions on these interventions is a political issue rests on the claims that there are “evidence-based clinical guidelines” for current US practices (with the implication that the

¹ Kraschel, K. L., Chen, A., Turban, J. L., & Cohen, I. G. (2022). Legislation restricting gender-affirming care for transgender youth: Politics eclipse healthcare. *Cell Reports Medicine*, 3(8), 100719. [link to this article](#).

medical interventions are well supported by evidence), that the medical interventions are not dangerous, and that these interventions have been shown to be beneficial. If all of these (including the implications) were true, then one might argue that objections to these medical treatments are in conflict with healthcare priorities. As shown below, when compared to the medical evidence, the last two assertions can be shown to be not true, and the first, regarding the evidence base, is misleading. Although politics may and likely does motivate some policies, the (state of the) research evidence behind these treatments, on its own, leads to serious healthcare concerns about these medical interventions. Some related claims² have been rebutted³ previously.

Evidence-Based Clinical Guidelines

Kraschel et al. accurately claim that the two following guidelines set out treatment protocols:⁴

A series of evidence-based clinical guidelines set out the treatment for gender dysphoria, in particular the Endocrine Society Clinical Practice Guideline for Endocrine Treatment of gender-dysphoric/gender-incongruent persons and the World Professional Association for Transgender Health [WPATH] Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People.

This statement does not mean there is reliable evidence behind the treatments. The Endocrine Society itself has rigorously evaluated the evidence behind its own recommendations, and found almost all of the supporting evidence to be low quality, very low quality, or ungraded.⁵ Only three of the 28 recommendations were supported by moderate quality evidence: confirm diagnosis, counsel regarding fertility preservation, and evaluate and address other medical conditions that might be exacerbated by hormonal treatment. Another six recommendations were “ungraded good practice statements,” i.e., with evidence “either unavailable or not systematically appraised.” The evidence behind the remaining 19 treatment recommendations was found to be low or very low quality GRADE,⁶ meaning that the true effect may be (for low quality) or is likely to be (for very low quality) substantially different from the estimate of the effect. Thus the Endocrine Society itself found the evidence base for its recommended treatments to be inadequate for estimating outcomes.

The inability of a low quality study to estimate outcomes in a reliable way is highlighted by the fact that the only statement the Endocrine Society Guidelines offer as evidence for the mental health benefits of puberty blockers (Gonadotrophin releasing hormone analogs, denoted as GnRH analogs or GnRHAs) is “Treating GD[gender

² Park, B. C., Das, R. K., & Drolet, B. C. Increasing criminalization of gender-affirming care for transgender youths—a politically motivated crisis. *JAMA Pediatrics*, 175(12), 1205–1206. [link to this article](#).

³ Hunter, P. K. (2021). Political issues surrounding gender-affirming care for transgender youth. *JAMA Pediatrics*, 176(3), 322–323. [link to this article](#).

⁴ Kraschel et al., op. cit., p. 1.

⁵ Hembree, W. C., Cohen-Kettenis, P. T., Gooren, L., Hannema, S. E., Meyer, W. J., Murad, M., ... T'Sjoen, G. G. (2017). Endocrine treatment of gender-dysphoric/gender-incongruent persons: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism*, 102(11), 3869–3903. [link to this article](#).

⁶ In systematic reviews of evidence, the quality or certainty GRADE reflects confidence that the estimates of the effect are correct; see Balshem, H., Helfand, M., Schünemann, H. J., Oxman, A. D., Kunz, R., Brozek, J., ... Guyatt, G. H. (2011). GRADE guidelines: 3. Rating the quality of evidence. *Journal of Clinical Epidemiology*, 64(4), 401–406. [link to this article](#).

dysphoric]/gender-incongruent adolescents entering puberty with GnRH analogs has been shown to improve psychological functioning in several domains (86).” The referenced study (86),⁷ however, failed replication.⁸

The weakness of the evidence base is further reflected in the Endocrine Society guideline statement: “In the future, we need more rigorous evaluations of the effectiveness and safety of endocrine and surgical protocols. Specifically, endocrine treatment protocols for GD/gender incongruence should include the careful assessment of the following: (1) the effects of prolonged delay of puberty in adolescents on bone health, gonadal function, and the brain (including effects on cognitive, emotional, social, and sexual development); ... (4) the risks and benefits of gender-affirming hormone treatment in older transgender people.”⁹ These are significant uncertainties, especially given that every young person receiving treatment is expected to become one of the older people affected by (4).

The other “evidence-based” guideline mentioned is the WPATH SOC7, “Standards of Care.”¹⁰ However, the WPATH SOC7 are not evidence based¹¹ nor standards of care, but rather practice guidelines, which can be biased.¹² In fact, in a formal guideline review,¹³ five out of six reviewers did not recommend use of WPATH SOC7 as guidelines; the last reviewer recommended use only if modified. The reviewers observed: “Some extracted statements might have been intended as recommendations or standards, but many were flexible, disconnected from evidence and could not be used by individuals or services to benchmark practice.” After the appearance of Kraschel et al.,¹⁴ WPATH released new recommendations (WPATH SOC 8),¹⁵ which also have significant shortcomings, for example, “the strength of evidence presented to justify a recommendation was ‘at odds with what their own systematic reviewers found.’”¹⁶ Although several systematic

⁷ de Vries, A. L., Steensma, T. D., Doreleijers, T. A., & Cohen-Kettenis, P. T. (2011). Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. *Journal of Sexual Medicine*, 8(8), 2276–2283. [link to this article](#).

⁸ Carmichael, P., Butler, G., Masic, U., Cole, T. J., De Stavola, B. L., Davidson, S., ... Viner, R. M. (2021). 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*, 16(2), e0243894. [link to this article](#).

⁹ Hembree et al., op. cit.

¹⁰ Coleman, E., Bockting, W., Botzer, M., Cohen-Kettenis, P., DeCuypere, G., Feldman, J., ... Zucker, K. (2012). Standards of care for the health of transsexual, transgender, and gender-nonconforming people, version 7. *International Journal of Transgenderism*, 13(4), 165–232. [link to this article](#).

¹¹ Sinai, J. (2022). The current gender-affirming care model in BC is unvalidated and outdated. *BC Medical Journal*, 64(3), 106.

¹² Malone, W. J., Hruz, P. W., Mason, J. W., & Beck, S. (2021). Letter to the Editor from William J. Malone et al: “Proper care of transgender and gender-diverse persons in the setting of proposed discrimination: A policy perspective.” *Journal of Clinical Endocrinology and Metabolism*, 106(8), e3287. [link to this article](#).

¹³ Dahlen, S., Connolly, D., Arif, I., Junejo, M. H., Bewley, S., & Meads, C. (2021). International clinical practice guidelines for gender minority/trans people: Systematic review and quality assessment. *BMJ Open*, 11(4), e048943. [link to this article](#).

¹⁴ Kraschel et al., op. cit.

¹⁵ Coleman, E., Radix, A. E., Bouman, W. P., Brown, G. R., de Vries, A. L. C., Deutsch, M. B., ... Arcelus, J. (2022). Standards of care for the health of transgender and gender diverse people, version 8. *International Journal of Transgender Health*, 23 (suppl.1), S1–S259, [link to this article](#).

¹⁶ Block J. (2023). Gender dysphoria in young people is rising—and so is professional disagreement. *BMJ (Clinical research ed.)*, 380, 382. [link to this article](#).

reviews were already publicly available (see below),^{17,18,19} WPATH SOC 8 stated that “a systematic review regarding outcomes of treatment in adolescents is not possible.”²⁰ It has been noted with regard to WPATH SOC 8 specifically that an entity making recommendations without a systematic review would be “violating standards of trustworthy guidelines;”²¹ furthermore, the WPATH SOC 8 methods are prone to bias.²²

It is worth mentioning that another influential set of recommendations, by the American Academy of Pediatrics (AAP), is also not evidence based.²³ A peer-reviewed critique found that “remarkably, not only did the AAP statement fail to include any of the actual outcomes literature on such cases, but it also misrepresented the contents of its citations, which repeatedly said the very opposite of what AAP attributed to them.”²⁴ A recent investigative report discusses differences between the WPATH SOC 8 and AAP recommendations and evidence-based medicine guideline requirements, as well as “serious problems” with the Endocrine Society recommendations.²⁵

Beyond the Endocrine Society GRADEs, several different evaluations of the evidence base for providing puberty blockers, hormones, and surgeries have been done, including:

- UK National Institute for Health and Care Excellence (NICE) evidence reviews for under 18: “The critical outcomes for decision making are the impact on gender dysphoria, mental health and quality of life. The quality of evidence for these outcomes was assessed as very low certainty using modified GRADE.”^{26,27}
- Swedish National Board of Health and Welfare (NBHW) (2022) for adolescents, finding: “The NBHW deems that the risks of puberty suppressing treatment with GnRH-analogues and gender-affirming hormonal treatment currently outweigh the possible benefits, and that the treatments should be offered only in exceptional cases.”²⁸
- Cochrane review “found insufficient evidence to determine the efficacy or safety of hormonal treatment approaches for transgender women in transition.”²⁹

¹⁷ National Institute for Health and Care Excellence. (2020). *Evidence review: Gonadotrophin releasing hormone analogues for children and adolescents with gender dysphoria*. [link to this article](#).

¹⁸ National Institute for Health and Care Excellence. (2020). *Evidence review: Gender-affirming hormones for children and adolescents with gender dysphoria*. [link to this article](#).

¹⁹ Swedish National Board of Health and Welfare. (2022). *Care of children and adolescents with gender dysphoria. Summary*. [link to this article](#).

²⁰ Coleman et al. (2022), op. cit., p. S46.

²¹ Block, op. cit.

²² Dahlen, S., Meads, C., & Bewley, S. (2022, October 21). WPATH Standards of Care: A new edition using outdated methods weakens the trustworthiness of content. Rapid Response. *BMJ Open*, 11(4), e048943. [link to this article](#).

²³ Rafferty, J., Committee on Psychosocial Aspects of Child and Family Health, Committee on Adolescence, & Section on Lesbian, Gay, Bisexual, and Transgender Health and Wellness (2018). Ensuring comprehensive care and support for transgender and gender-diverse children and adolescents. *Pediatrics*, 142(4), e20182162. [link to this article](#).

²⁴ Cantor J. M. (2020). Transgender and gender diverse children and adolescents: Fact-checking of AAP policy. *Journal of Sex & Marital Therapy*, 46(4), 307–313. [link to this article](#).

²⁵ Block, op. cit.

²⁶ National Institute for Health and Care Excellence, *Evidence review: Gonadotrophin releasing hormone analogues for children and adolescents with gender dysphoria*, op. cit.

²⁷ National Institute for Health and Care Excellence. (2020). *Evidence review: Gender-affirming hormones for children and adolescents with gender dysphoria*, op. cit.

²⁸ Swedish National Board of Health and Welfare, op. cit.

²⁹ Haupt, C., Henke, M., Kutschmar, A., Hauser, B., Baldinger, S., Saenz, S. R., & Schreiber, G. (2020). Antiandrogen or estradiol treatment or both during hormone therapy in transitioning transgender women. *Cochrane Database of Systematic Reviews*, 11(11), CD013138. [link to this article](#).

- Florida Medicaid undertook a broad evidence review of surgeries, hormones and puberty blockers³⁰ (including an umbrella review³¹); based upon it, the Department of Health characterized these treatments as “**experimental and investigational with the potential for harmful long term affects** [sic].”³²

These findings are consistent with the low quality found by the Endocrine Society, underscoring the difficulty in estimating likely outcomes with medical intervention.

Puberty Blocker Safety

Kraschel et al. (2022) state:

GnRHAs have been used in the treatment of central precocious puberty dating back to the 1970s, providing longitudinal safety data for their use in the pediatric population. ... However, there is some concern that going directly from pubertal suppression to gender-affirming hormones like estrogen or testosterone may impair fertility. For that reason, existing guidelines recommend fertility counseling prior to adolescent patients pursuing such care, so that they may consider fertility-preservation options.”³³

Although the authors wish to carry over results from treatment of a different population for a different condition, the Interim Cass report cautions that “it is important that it is not assumed that outcomes for, and side effects in, children treated for precocious puberty will necessarily be the same in children or young people with gender dysphoria.”³⁴ For fertility in particular, when puberty blockers are followed by hormones, “GnRH therapy prevents maturation of primary oocytes and spermatogonia and may preclude gamete maturation, and currently there are no proven methods to preserve fertility in early pubertal transgender adolescents.”³⁵

There are other risks of puberty blockers. They can significantly decrease bone mineral density,^{36,37} cause depression³⁸ and have been seen to decrease sexual desire in adult men.³⁹ Their effects on brain development are not understood; there is a concern

³⁰ Florida Medicaid. (2022). *Generally accepted professional medical standards determination on the treatment of gender dysphoria*. [link to this article](#).

³¹ Brignardello-Petersen, R., & Wierciuch, W. (2022). *Effects of gender affirming therapies in people with gender dysphoria: Evaluation of the best available evidence*. Agency for Health Care Administration Florida Medicaid Generally Accepted Professional Medical Standards Determination on the Treatment of Gender Dysphoria Attachment C. [link to this article](#).

³² Emphasis in the original.

³³ Kraschel et al., op. cit., p. 3.

³⁴ Cass Review. (2022). Cass Review Interim Report. [link to this article](#), p. 63.

³⁵ Bangalore Krishna, K. B., Fuqua, J. S., Rogol, A. D., Klein, K. O., Popovic, J., Houk, C. P., Charmandari, E., & Lee, P. A. (2019). Use of gonadotropin-releasing hormone analogs in children: Update by an international consortium. *Hormone Research in Paediatrics*, 91(6), 357–372. [link to this article](#), p. 365.

³⁶ Biggs, M. (2021). Revisiting the effect of GnRH analogue treatment on bone mineral density in young adolescents with gender dysphoria. *Journal of Pediatric Endocrinology and Metabolism*. [link to this article](#).

³⁷ Biggs M. (2022). The Dutch protocol for juvenile transsexuals: Origins and evidence. *Journal of Sex & Marital Therapy*, 1–21. Advance online publication. [link to this article](#).

³⁸ Abbvie Inc. Lupron Depot-Ped (leuprolide acetate for depot suspension). (March 2021). Package insert. US Food and Drug Administration website. [link to this article](#).

³⁹ This may or may not carry over to use with adolescents. Turner, D., & Briken, P. (2018). Treatment of paraphilic disorders in sexual offenders or men with a risk of sexual offending with luteinizing hormone-releasing hormone agonists: an updated systematic review. *Journal of Sexual Medicine*, 15(1), 77–93. [link to this article](#).

that “rather than buying time to make a decision, puberty blockers may disrupt that decision-making process.”⁴⁰

More importantly, the medical interventions under discussion do not only involve puberty blockers, but also hormones and surgeries. Medical risks are consequential: estrogen and testosterone for gender-affirming care degrade sexual organs,⁴¹ which can also cause, e.g., significant pain from vaginal and uterine atrophy⁴² and/or sexual dysfunction. Also observed are associated changes in the brain,^{43–46} increases relative to birth sex of adverse cardiovascular events such as blood clots (venous thromboembolism; more than a factor of 4 for male to female), strokes (factors of more than 1.6 for both sexes) and heart attacks (more than a factor of 4 for female to male)^{47,48}, as well as harmful changes to the endocrine system,⁴⁹ immune system (e.g., an increase in multiple sclerosis by a factor of 5 for male to female⁵⁰), and life span.^{51,52} Surgeries are also of

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- ⁴⁰ Cass, H. (2022, 9 July). *Independent review of gender identity services for children and young people—further advice*. Letter to John Stewart, National Director, Specialised Commissioning, NHS England. [link to this article](#).
- ⁴¹ Cheng, P. J., Pastuszak, A. W., Myers, J. B., Goodwin, I. A., & Hotaling, J. M. (2019). Fertility concerns of the transgender patient. *Translational Andrology and Urology*, 8(3), 209–218. [link to this article](#).
- ⁴² Obedin-Malover, J. (2016). Pelvic pain and persistent menses in transgender men. *UCSF Transgender Care*. [link to this article](#).
- ⁴³ Bjørnebekk, A., Kaufmann, T., Hauger, L. E., Klonteig, S., Hullstein, I. R., & Westlye, L. T. (2021). Long-term anabolic–androgenic steroid use is associated with deviant brain aging. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 6(5), 579–589. [link to this article](#).
- ⁴⁴ Fuss, J., Hellweg, R., Van Caenegem, E., Briken, P., Stalla, G. K., T’Sjoen, G., & Auer, M. K. (2015). Cross-sex hormone treatment in male-to-female transsexual persons reduces serum brain-derived neurotrophic factor (BDNF). *European Neuropsychopharmacology*, 25(1), 95–99. [link to this article](#).
- ⁴⁵ Holmes, D. (2016). Cross-sex hormones alter grey matter structures. *Nature Reviews Endocrinology*, 12(12), 686. [link to this article](#).
- ⁴⁶ Gómez, Á., Cerdán, S., Pérez-Laso, C., Ortega, E., Pásaro, E., Fernández, R., ... Guillamon, A. (2020). Effects of adult male rat feminization treatments on brain morphology and metabolomic profile. *Hormones and behavior*, 125, 104839. [link to this article](#).
- ⁴⁷ Getahun, D., Nash, R., Flanders, W. D., Baird, T. C., Becerra-Culqui, T. A., Cromwell, L., ... Goodman, M. (2018). Cross-sex hormones and acute cardiovascular events in transgender persons: A cohort study. *Annals of Internal Medicine*, 169(4), 205–213. [link to this article](#).
- ⁴⁸ Nota, N. M., Wiepjes, C. M., de Blok, C. J., Gooren, L. J., Kreukels, B. P., & den Heijer, M. (2019). Occurrence of acute cardiovascular events in transgender individuals receiving hormone therapy: results from a large cohort study. *Circulation*, 139(11), 1461–1462. [link to this article](#).
- ⁴⁹ Shadid, S., Abosi-Apeadu, K., De Maertelaere, A. S., Defreyne, J., Veldeman, L., Holst, J. J., ... & T’Sjoen, G. (2020). Effects of gender-affirming hormone therapy on insulin sensitivity and incretin responses in transgender people. *Diabetes Care*, 43(2), 411–417. [link to this article](#).
- ⁵⁰ Pakpoor, J., Wotton, C. J., Schmierer, K., Giovannoni, G., & Goldacre, M. J. (2016). Gender identity disorders and multiple sclerosis risk: A national record-linkage study. *Multiple Sclerosis Journal*, 22(13), 1759–1762. [link to this article](#).
- ⁵¹ de Blok, C. J., Wiepjes, C. M., van Velzen, D. M., Staphorsius, A. S., Nota, N. M., Gooren, L. J., Kreukels B. P. C., den Heijer, M. (2021). Mortality trends over five decades in adult transgender people receiving hormone treatment: a report from the Amsterdam cohort of gender dysphoria. *Lancet Diabetes & Endocrinology*. [link to this article](#).
- ⁵² Dhejne, C., Lichtenstein, P., Boman, M., Johansson, A. L., Långström, N., & Landén, M. (2011). Long-term follow-up of transsexual persons undergoing sex reassignment surgery: Cohort study in Sweden. *PLoS One*, 6(2), e16885. [link to this article](#).

concern for adolescents, and include double mastectomies at ages as young as 13⁵³ and vaginoplasties for minors.^{54,55}

Benefits of Gender-Affirming Care

Kraschel et al. state:

A substantial body of literature exists documenting the benefits of gender-affirming medical interventions, where indicated, for adolescents with gender dysphoria. Over a dozen studies have collectively linked such care to improvements in depression, anxiety, and suicidality.⁵⁶

The authors then reference Turban et al. (2022)⁵⁷ and van der Miesen et al. (2020).⁵⁸ Five of the six studies referenced by the former were rigorously evaluated in the NICE evidence reviews mentioned above, where they had their "overall quality assessed as poor." More detailed critiques of each can be found in these two NICE evidence reviews.^{59,60} For puberty blockers, NICE states: "Studies that found differences in outcomes could represent changes that are either of questionable clinical value, or the studies themselves are not reliable and changes could be due to confounding, bias or chance."⁶¹

Not covered by the NICE evidence reviews are the sixth Turban et al. reference,⁶² de Vries et al. (2014),⁶³ Turban et al.⁶⁴ itself, and van der Miesen et al.⁶⁵ De Vries et al.⁶⁶ is a small well-known study that reports short term (1–2 year) mental health and gender dysphoria outcomes of 55 young people after undergoing surgery, finding small psychological improvement. They reported large gender dysphoria improvement, but this appears to have been confounded by changing the measurement instrument

⁵³ Figure 2 of Olson-Kennedy, J., Warus, J., Okonta, V., Belzer, M., & Clark, L. F. (2018). Chest reconstruction and chest dysphoria in transmasculine minors and young adults: Comparisons of nonsurgical and postsurgical cohorts. *JAMA Pediatrics*, 172(5), 431–436. [link to this article](#).

⁵⁴ Milrod, C., & Karasic, D. H. (2017). Age is just a number: WPATH-affiliated surgeons' experiences and attitudes toward vaginoplasty in transgender females under 18 years of age in the United States. *The Journal of Sexual Medicine*, 14(4), 624–634.

⁵⁵ Terhune, C., Respaut, R., & Conlin, M. (October 6, 2022). *As more transgender children seek medical care, families confront many unknowns*. Reuters Investigates. [link to this article](#).

⁵⁶ Kraschel, op. cit., pp. 3–4.

⁵⁷ Turban, J. L., King, D., Kobe, J., Reisner, S. L., & Keuroghlian, A. S. (2022). Access to gender-affirming hormones during adolescence and mental health outcomes among transgender adults. *PLoS One*, 17(1), e0261039. [link to this article](#).

⁵⁸ van der Miesen, A., Steensma, T. D., de Vries, A., Bos, H., & Popma, A. (2020). Psychological functioning in transgender adolescents before and after gender-affirmative care compared with cisgender general population peers. *Journal of Adolescent Health : Official Publication of the Society for Adolescent Medicine*, 66(6), 699–704. [link to this article](#).

⁵⁹ National Institute for Health and Care Excellence. (2020). *Evidence review: Gender-affirming hormones for children and adolescents with gender dysphoria*, op. cit.

⁶⁰ National Institute for Health and Care Excellence. *Evidence review: Gonadotrophin releasing hormone analogues for children and adolescents with gender dysphoria*, op. cit.

⁶¹ Ibid., p. 13.

⁶² Turban et al., op. cit.

⁶³ de Vries, A. L., McGuire, J. K., Steensma, T. D., Wagenaar, E. C., Doreleijers, T. A., & Cohen-Kettenis, P. T. (2014). Young adult psychological outcome after puberty suppression and gender reassignment. *Pediatrics*, 134(4), 696–704. [link to this article](#).

⁶⁴ Turban et al., op. cit.

⁶⁵ Van der Miesen et al., op. cit.

⁶⁶ de Vries et al. (2014), op. cit.

before and after surgery,^{67,68} and in addition, preliminary reports of some of these patients' long-term outcomes are concerning, including reproductive regret in more than a quarter of the patients, one or more identity changes after treatment completion for a sizable percentage, and for male-to-female transitioners, apparent sexual difficulties for more than two-thirds.⁶⁹ Furthermore, two of the criteria for inclusion in this study were lifelong extreme gender dysphoria and psychological stability,⁷⁰ neither of which are part of the readiness requirements for medical interventions for young people as set out in the Endocrine Society or either set of WPATH guidelines, so the study's outcomes would not be expected to be relevant. The cross-sectional design of Turban et al.⁷¹ limits determination of cause and effect (an association or correlation does not indicate whether the intervention led to the symptom or vice versa, or whether something else caused both) and these same (non-representative⁷²) data also show an association between greater suicidality and taking estrogen.⁷³ The last reference provided in support, van der Miesen et al., explicitly says: "The present study can, therefore, not provide evidence about the direct benefits of puberty suppression over time and long-term mental health outcomes."⁷⁴ That is, it cannot show benefits due to medical intervention either. Benefits, when seen, have not been demonstrated to be due to medical intervention in either these or other research studies, and the risks are significant.

These facts also undermine the claim by the authors that these interventions are "medically necessary care." The WPATH SOC7 guidelines do say medical intervention is "medically necessary," but qualify it with the phrase "for many people."⁷⁵ WPATH SOC7 does not provide a clinical test to identify the "many people" and no test has been established since. Identifying and excluding transient gender dysphoria from medical intervention is desirable (one WPATH SOC 8 requirement for hormones and surgery is that "Other possible causes of apparent gender incongruence have been identified and excluded"⁷⁶) but the requisite relevant and reliable long-term studies are absent and there is no agreement among experts as to how to determine how a given individual's gender

⁶⁷ Levine, S. B., Abbruzzese, E., & Mason, J. W. (2022). Reconsidering informed consent for trans-identified children, adolescents, and young adults. *Journal of Sex & Marital Therapy*, 1–22. Advance online publication. [link to this article](#).

⁶⁸ Abbruzzese, E., Levine, S. B., & Mason, J. W. (2023). 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*, 1–27. Advance online publication. [link to this article](#).

⁶⁹ Ibid.

⁷⁰ Delemarre-Van De Waal, H. A., & Cohen-Kettenis, P. T. (2006). Clinical management of gender identity disorder in adolescents: A protocol on psychological and paediatric endocrinology aspects. *European Journal of Endocrinology*, 155(suppl. 1), S131–S137. [link to this article](#).

⁷¹ Turban et al., op. cit.

⁷² D'Angelo, R., Syrulnik, E., Ayad, S., Marchiano, L., Kenny, D. T., & Clarke, P. (2021). One size does not fit all: In support of psychotherapy for gender dysphoria. *Archives of Sexual Behavior*, 50(1), 7–16. [link to this article](#).

⁷³ Biggs, M.. (2022). Comment on Turban et al. 2022: Estrogen is associated with greater suicidality among transgender males, and puberty suppression is not associated with better mental health outcomes for either sex (Version1). [link to this article](#).

⁷⁴ Van der Miesen et al., op. cit.

⁷⁵ Coleman et al. (2012), op. cit.

⁷⁶ Coleman et al. (2022), op. cit., p. S256.

dysphoria will develop, with or without medical intervention.^{77–80} (This significant lack of professional agreement about treatment protocols is also a challenge for the WPATH SOC 8 definition of “medical necessity,” which relies upon “generally accepted standards of medical practice” based upon “credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community”:⁸¹ the variation between expert protocols is so large that it appears difficult to establish any of them as “generally accepted.”)

Medical intervention has certainly not been shown to be medically necessary in general. The etiology and development of gender dysphoria is not yet well understood: it appears that there are many different pathways into and out of gender dysphoria.⁸² In particular, care for gender dysphoria is not synonymous with medical intervention. Some with gender dysphoria have had it resolve^{83–85} with mental health support such as psychotherapy^{86,87} and others have medically transitioned and found that it did not alleviate their distress or gender dysphoria;^{88,89} in particular, some have been badly harmed.⁹⁰ (The number who detransition, regret, and/or have been harmed is unknown due to the lack of adequate long-term outcome studies.^{91–94}) It has also long been observed in studies that in the absence of medicalization and social transition, the majority

⁷⁷ Block, op. cit.

⁷⁸ Levine et al., op. cit.

⁷⁹ Cohn J. (2022). Some limitations of “Challenges in the care of transgender and gender-diverse youth: An endocrinologist’s view.” *Journal of Sex & Marital Therapy*, 1–17. Advance online publication. [link to this article](#).

⁸⁰ Levine, S. B., & Abbruzzese, E. (2023). Current concerns about gender-affirming therapy in adolescents. *Curr Sex Health Rep*. [link to this article](#).

⁸¹ Coleman et al. (2022), op. cit., pp. S17–S18.

⁸² See the figure on page 57 in the Cass Interim Report, Cass Review (2022), op. cit.; note that medical and social transition pathways do not necessarily resolve gender dysphoria, for instance, either could lead to detransition.

⁸³ Churcher Clarke, A., & Spiliadis, A. (2019). “Taking the lid off the box”: The value of extended clinical assessment for adolescents presenting with gender identity difficulties. *Clinical Child Psychology and Psychiatry*, 24(2), 338–352. [link to this article](#).

⁸⁴ Parkinson, J. (2014). Gender dysphoria in Asperger’s syndrome: A caution. *Australasian Psychiatry: Bulletin of Royal Australian and New Zealand College of Psychiatrists*, 22(1), 84–85. [link to this article](#).

⁸⁵ Withers, R. (2020). Transgender medicalization and the attempt to evade psychological distress. *Journal of Analytical Psychology*, 65(5), 865–889. [link to this article](#).

⁸⁶ Evans, S. & Evans, M. (2021). *Gender dysphoria: A therapeutic model for working with children, adolescents and young adults*. Oxfordshire: Phoenix Publishing House.

⁸⁷ Ayad, S., D’Angelo, R., Kenney, D., Levine, S.B., Marchiano, L., & O’Malley, S. (2022). *A clinical guide for therapists working with gender-questioning youth, Version 1*. Gender Exploratory Therapy Association. [link to this article](#).

⁸⁸ Littman, L. (2021). Individuals treated for gender dysphoria with medical and/or surgical transition who subsequently detransitioned: A survey of 100 detransitioners. *Archives of Sexual Behavior*, 50(8), 3353–3369. [link to this article](#).

⁸⁹ Vandebussche E. (2022). Detransition-related needs and support: A cross-sectional online survey. *Journal of Homosexuality*, 69(9), 1602–1620. [link to this article](#).

⁹⁰ D’Angelo, R. (2018). Psychiatry’s ethical involvement in gender-affirming care. *Australasian Psychiatry*, 26(5), 460–463. [link to this article](#).

⁹¹ Expósito-Campos, P., & D’Angelo, R. (2021). Letter to the Editor: Regret after gender-affirmation surgery: A systematic review and meta-analysis of prevalence. *Plastic and Reconstructive Surgery. Global Open*, 9(11), e3951. [link to this article](#).

⁹² Levine, Abbruzzese & Mason, op. cit.

⁹³ Levine & Abbruzzese, op. cit.

⁹⁴ Cohn, op. cit.

with childhood onset gender dysphoria have it resolve with time.^{95,96} For all who recovered with either time and/or mental health support, medical intervention was not necessary. For those who were instead harmed by medical intervention, this is even more true; in fact, some detransitioners report wishing they had been offered exploratory therapy instead of medical intervention which they now regret.⁹⁷

Discussion

No studies have shown how to identify, in a reliable way, young people for whom the medical intervention benefits may outweigh the significant long-term risks. Nor is there sufficient clinical knowledge to predict for whom gender dysphoria will resolve with time or exploratory psychotherapy, or will not resolve with medical transition after the initial honeymoon phase is over, or will turn out to have other root causes after medicalization has commenced.^{98,99} These concerns, backed by the numerous systematic evidence reviews described earlier, have led many countries to restrict medical intervention for young people, often alongside prioritizing psychotherapy, in order to provide them with support more in line with the low-quality evidence for medical intervention. For example, the French National Academy of Medicine has stated that “since there is no test to distinguish a ‘structural’ gender dysphoria from transient dysphoria in adolescence” it is “therefore advisable to extend as much as possible the psychological support phase.”¹⁰⁰ As noted above, Sweden provides medical interventions only in exceptional cases.¹⁰¹ Finland provides medical intervention on a case by case basis,¹⁰² Norway is revisiting its guidelines, now calling these interventions “treatment under trial”¹⁰³ and the UK is closing its main pediatric gender clinic as it is not safe or viable long term^{104,105} and will now aim to provide more holistic¹⁰⁶ treatment. Including supportive exploration and counseling allows gender dysphoria to be put into the context of the full situation of the young person, and addressed as part of other challenges they might be facing (many young people with gender dysphoria currently present with significant comorbidities¹⁰⁷).

⁹⁵ Ristori, J., & Steensma, T. D. (2016). Gender dysphoria in childhood. *International Review of Psychiatry*, 28(1), 13–20. [link to this article](#).

⁹⁶ Singh, D., Bradley, S. J., & Zucker, K. J. (2021). A follow-up study of boys with gender identity disorder. *Frontiers in Psychiatry*, 12, 632784. [link to this article](#).

⁹⁷ Fox A. (September 2021). *An open letter*. Genspect. [link to this article](#).

⁹⁸ Levine, Abbruzzese, & Mason, op. cit.

⁹⁹ Levine & Abbruzzese, op. cit.

¹⁰⁰ French National Academy of Medicine. (2022). Medicine and gender transidentity in children and adolescents, [link to this article](#).

¹⁰¹ Swedish National Board of Health and Welfare, op. cit.

¹⁰² Society for Evidence Based Gender Medicine [SEGM]. (2021, July 5). *one year since finland broke with WPATH “Standards of Care.”* News Spotlight. [link to this article](#).

¹⁰³ Block, J. (2023). Norway’s guidance on paediatric gender treatment is unsafe, says review. *BMJ*, 380, 697. [link to this article](#).

¹⁰⁴ Cass, op. cit.

¹⁰⁵ Andersson, J. & Rohden-Paul, A. (2022, 28 July). NHS to close Tavistock child gender identity clinic. *BBC News*. [link to this article](#).

¹⁰⁶ Cass Review, op. cit.

¹⁰⁷ Kaltiala-Heino, R., Bergman, H., Työlajärvi, M., & Frisé, L. (2018). Gender dysphoria in adolescence: Current perspectives. *Adolescent Health, Medicine and Therapeutics*, 9, 31–41. [link to this article](#).

Many current US treatment protocols are based upon the affirmative model espoused by the AAP,^{108,109} but rejected by several other countries.^{110,111} Casting objections to these protocols as solely political obscures the serious outcome uncertainties, risks of medical intervention, and the significant disagreements between experts in this field.^{112,113} (Nor are the medical concerns elaborated upon here “science-denialist”¹¹⁴ as some have claimed.) Such accusations can mislead clinicians, patients, and their families, and impede efforts to determine the best way to help these young people. It is important that they all have access to accurate information about these treatments, their uncertain outcomes, their risks and their alternatives, and the professional disagreements: serious healthcare issues are involved.

Given the low-quality evidence and the lack of understanding around the different ways gender dysphoria can arise and resolve, substantive questions remain. For instance, long-term follow-up of all currently medicalized patients in a controlled research setting would provide crucial and desperately needed information to guide care of this vulnerable population, as knowledge of outcomes to improve their care is greatly needed. Similarly, more studies to better understand and improve mental health support approaches are also needed, as well as improved support for the growing (but as yet uncounted) ranks of detransitioners. It is tragic that many young people are misinformed as to the effectiveness and necessity of risky and irreversible medical intervention for gender dysphoria and believe that their happiness depends upon getting it; in order to decrease the risk of iatrogenic harm, it is crucial to better inform clinicians and the wider community of these serious concerns, of alternatives such as ethical explorative psychotherapy, and of the need for further research. No politics is required. Just prioritization of evidence-based healthcare.

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¹⁰⁸ Levine & Abbruzzese, op. cit.

¹⁰⁹ Cohn, op. cit.

¹¹⁰ What America has got wrong about gender medicine: Too many doctors have suspended their professional judgment. (2023, April 8). *The Economist*. [link to this article](#).

¹¹¹ Abbasi, K. (2023). Caring for young people with gender dysphoria. *BMJ*, 380, 553 [link to this article](#).

¹¹² Vrouenraets, L. J., Fredriks, A. M., Hannema, S. E., Cohen-Kettenis, P. T., & de Vries, M. C. (2015). Early Medical treatment of children and adolescents with gender dysphoria: An empirical ethical study. *Journal of Adolescent Health: Official Publication of The Society for Adolescent Medicine*, 57(4), 367–373. [link to this article](#).

¹¹³ Block, Gender dysphoria in young people is rising, op. cit.

¹¹⁴ McNamara, M., Lepore, C., & Alstott, A. (2022). Protecting transgender health and challenging science denialism in policy. *New England Journal of Medicine*, 387(21), 1919–1921. [link to this article](#).