IN THE UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF ARKANSAS
CENTRAL DIVISION

DYLAN BRANDT, et al.,

PLAINTIFFS,

v. **No. 4:21-CV-00450-JM**

LESLIE RUTLEDGE, et al.,

DEFENDANTS.

DEFENDANTS' SUPPLEMENTAL EXHIBITS

For the purpose of responding to Plaintiffs' new evidence submitted with their reply, including one entirely new witness (*see* Decl. of Jack Turban, Dkt. No. 51-1; Suppl. Decl. of Deanna Adkins, Dkt. No. 51-2; Suppl. Decl. of Armand H. Matheny Antommaria, Dkt. No. 51-3), Defendants submit the following exhibits:

30. **Supplemental Declaration of Stephen B. Levine, M.D.**

31. **Supplemental Declaration of Mark Regnerus, Ph.D.**

32. **Supplemental Declaration of Paul W. Hruz, M.D., Ph.D.**

33. Roberto D'Angelo, et al., "One Size Does Not Fit All: In Support of Psychotherapy for Gender Dysphoria," 50 Archives of Sexual Behavior 7 (2021).

Dated: July 19, 2021

Respectfully submitted,

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SUPPLEMENTAL DECLARATION OF STEPHEN B. LEVINE, M.D.

Pursuant to 28 U.S.C. 1746, I declare:

1. I have been retained by counsel for Defendants as an expert witness in connection with this litigation. I have actual knowledge of the matters stated in this declaration. My training, credentials, extensive experience, and significant history as an expert witness are detailed in my declaration in this matter dated July 8, 2021.

2. My opinions set forth in this declaration are based upon my knowledge and direct professional experience in the matters discussed. The material that I have relied upon are the same types of materials that other experts in my field rely upon when forming opinions on the subject, including hundreds of published, peer-reviewed scientific research (and clinical) articles.

3. I have reviewed the newly submitted supplemental declarations by Dr. Deanna Adkins (dated July 15, 2021) and Dr. Armand Antommaria (dated July 15, 2021), as well as the declaration submitted by the plaintiffs' new witness, Dr. Jack Turban (dated July 16, 2021). The declarations submitted by the plaintiffs' experts, and by Dr. Turban, in particular, contain numerous errors on matters that I have already addressed in my first declaration and that could be addressed beyond what I say here. Therefore, this declaration does not exhaust my opinions.

4. As I explain, Dr. Turban's account of the evidence is demonstrably distorted by his advocacy of experimental gender-transition procedures on minors and his opposition to other

approaches to treatment, which functions to harm youth with gender dysphoria by limiting access to psychotherapy. Dr. Turban would dismiss the international consensus that claims concerning safety and effectiveness of gender-transition procedures are not supported by the evidence because they threaten his life's work thus far. A fundamental issue that is not being addressed is what is the adult fate of teens treated with hormones and prepared for further surgery, if they so elect. This glaring unanswered question is central for two reasons: first is the fact that multiple objective scientific reviews have pointed out a lack of convincing evidence of improved mental health during adolescence; and, second, every study of adult trans populations indicates a high prevalence of various mental health problems.[1] Finally, the scientific community is moving to prioritize psychotherapy as the indicated treatment for adolescents with gender dysphoria.

I. DR. TURBAN'S MISEVALUATION OF THE EVIDENCE IS DRIVEN BY ITS THREAT TO HIS LIFE'S WORK.

5. Dr. Turban advocates for treating gender dysphoria throughout life with medical and surgical interventions first. Much of his research output is designed to prove the value of these treatments and to discredit any other approach. Relevant to this legal matter, he is likely the country's most visible advocate of performing gender-transition procedures on minors. His work reflects a single-minded focus on these procedures as treatment for adolescents with gender dysphoria. Indeed, his work has been soundly criticized for his "problematic analysis" and "flawed conclusions," which he has "use[d] to justify the misguided notion that anything other than 'affirmative' psychotherapy for gender dysphoria (GD) is harmful and should be banned." Further, his "notion that all therapy interventions for GD can be categorically classified" into a

[1] Dhejne, C., Van Vlerken, R., Heylens, G., & Arcelus, J. (2016). Mental health and gender dysphoria: A review of the literature. *Intl. Rev. Psychiatry (Abingdon, England)*, *28*(1), 44–57. https://doi.org/10.3109/09540261.2015.1115753

"simplistic 'affirmation' versus 'conversion' binary" betrays "a misunderstanding of the complexity of psychotherapy."[2] His use of a survey to suggest that puberty blockers reduce suicidality has been refuted.[3] The regrettable outcome of Dr. Turban's efforts is to "limit access to ethical psychotherapy for individuals suffering from GD, further disadvantaging this already highly vulnerable population."

6. In a recent article Dr. Turban frankly recognizes that "[s]ince the publication of the WPATH Standards of Care and the Endocrine Society guidelines, the use of pubertal suppression for transgender youth has become more common in the United States. There are limited data, however, regarding the mental health outcomes of pubertal suppression."[4] Unfortunately, Dr. Turban's description of the evidence in his declaration here does not display that same candor. His commitment to the cause of promoting "affirmative" gender-transition treatment distorts his evaluation of the actual state of the evidence. This is reflected in both his overstated assessment of low-quality studies that he claims "taken together" indicate that gender-transition procedures "improve[] mental health" and his dismissiveness of the international consensus that the safety and effectiveness of such procedures are not supported by the evidence.

7. Notably, neither Dr. Turban nor the plaintiffs' other witnesses claim that gender-transition procedures *reduce gender dysphoria itself*. Instead, Turban picks through a handful of

[2] Robert D'Angelo, Ema Syulnik, Sasha Aya, Lisa Marchiano, Dianna Theadora Kenny, and Patrick Clarke, Letter to the Editor: "One Size Does Not Fit All: In Support of Psychotherapy for Gender Dysphoria," *Arch. Sex. Behav.*, vol. 50, p. 7 (2021), https://doi.org/10.1007/s10508-020-01844-2

[3] Biggs, M. Puberty Blockers and Suicidality in Adolescents Suffering from Gender Dysphoria. *Arch. Sex. Behav.* 49**,** 2227–2229 (2020). https://doi.org/10.1007/s10508-020-01743-6

[4] Turban, J. L., King, D., Carswell, J. M., & Keuroghlian, A. S. (2020). Pubertal Suppression for Transgender Youth and Risk of Suicidal Ideation. *Pediatrics, 145*(2), e20191725. https://doi.org/10.1542/peds.2019-1725

low-quality studies for findings of any reduction (however insignificant) in various forms of psychopathology.[5] And, repeatedly, when such findings are absent, Dr. Turban claims the study was "underpowered"—suggesting that the contrary findings are merely the result of how the study was performed or how many subjects it included (Turban pars. 13, 14). Indeed, Dr. Turban's description ignores these studies' reports of continuing high rates of poor functionality[6] as well as suicidal ideation, suicide attempts, and completed suicides.

8. Revealingly, Dr. Turban dismisses as irrelevant the outcome of the one long-term study that sought to ascertain mental-health outcomes of gender-transition surgery. The publication of that study by Bränström and Pachankis in the *American Journal of Psychiatry* resulted in a correction.[7] That correction was published along with a comment from the editor, seven letters to the editor noting the study's serious methodological errors, and a retraction by the authors explaining that their conclusion that gender-transition surgery improves mental health was incorrect.[8] The data from that study actually *contradicts* claims that gender-transition surgery im-

[5] Dr. Antommaria's declarations recognize that the Endocrine Society guidelines' suggestions concerning the use of puberty blockers are based on very low quality, or at best, "low quality" evidence. By those guidelines' own terms, the weakness of such suggestions indicate doubt that those "who receive [puberty blockers] will derive, on average, more benefit than harm." Wylie C. Hembree, et al., Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline, *J. Clin. Endocr. & Metabolism*, vol. 102, p. 3872 (Nov. 2017).

[6] Zeluf, G., Dhejne, C., Orre, C., Nilunger Mannheimer, L., Deogan, C., Höijer, J., & Ekéus Thorson, A. (2016). Health, disability and quality of life among trans people in Sweden-a web-based survey. *BMC public health*, *16*(1), 903. https://doi.org/10.1186/s12889-016-3560-5

[7] Correction to Bränström and Pachankis, *Am. J. Psychiatry*, vol. 177, p. 734 (Aug. 2020), https://doi.org/10.1176/appi.ajp.2020.1778correction

[8] Ned H. Kalin, Reassessing Mental Health Treatment Utilization Reduction in Transgender Individuals After Gender-Affirming Surgeries: A Comment by the Editor on the Process, *Am. J. Psychiatry*, vol. 177, p. 764 (Aug. 2020), https://doi.org/10.1176/appi.ajp.2020.20060803

proves mental health. This important study is very inconvenient for Dr. Turban's efforts to advocate for "affirmative" gender-transition treatment. So it is not surprising that he seeks to minimize its significance.

9. Bränström and Pachankis are not the only advocates who have noted that there is a need for more evidence that gender confirming surgeries improve mental health. In their 2021 study in *JAMA Surgery*,[9] Almazan and Keuroghlian write: "Despite the growing demand for and access to gender confirming surgery, there is a paucity of high quality evidence regarding the effects on mental health of TGN [i.e., transgender and gender diverse] people." Methodological concerns focus on the reliance of retrospective self-report among a diverse group of clinically unknown trans-identified people and the lack of both a meaningful control group and measures of continuing gender dysphoria, psychological distress, or psychosocial functioning.[10] Even though most forms of gender-transition surgery are not performed on adolescents, discussion of surgery matters for treating adolescents because a significant minority of patients undergoing hormonal treatment will pursue surgery, and some actually undergo mastectomies before reaching 18 years old.

10. Claiming, as Dr. Turban does, that the data shows that "affirming" gender-transition treatment improves mental health is a distortion of all of the evidence. But even if there were reliable evidence of short-term improvements in adolescents' mental health, that would not

[9] Almazan, A. N., & Keuroghlian, A. S. (2021). Association Between Gender-Affirming Surgeries and Mental Health Outcomes. *JAMA surgery*, *156*(7), 611–618. https://doi.org/10.1001/jamasurg.2021.0952

[10] Biggs has criticized the limitations of Turban's data set, which was the same data set used by Almazan and Keuroghlian. See Biggs M. (2020). Puberty Blockers and Suicidality in Adolescents Suffering from Gender Dysphoria. *Archives of sexual behavior*, *49*(7), 2227–2229. https://doi.org/10.1007/s10508-020-01743-6

be sufficient to recommend gender-transition procedures. The issue is not simply whether adolescents feel better in the short term—which can be caused by cross-sex hormone-fueled euphoria or a misplaced adolescent conviction that such procedures will ameliorate psychosocial problems (including gender dysphoria itself). Rather, the important issue from a responsible psychiatric perspective is whether individuals who undergo gender-transition procedures have improved outcomes over their *life course*. But neither Dr. Turban nor the plaintiffs' other experts produce any evidence to support claims that there is such improvement. Puberty suppression began in the US in earnest only in 2014 and while it has been employed in many urban gender medicine clinics, there are no long-term follow-up data available. There is only belief that it is the proper treatment. The adult outcomes remain to be seen. And one can see from Dr. Turban's CV that he lacks years of experience of following adults patients and attempting to help them with their various symptoms and dilemmas.

11. Contrary to Drs. Turban and Antommaria, the "off-label" use of drugs is the least of the problems with "affirmative" gender-transition treatment. It is generally accepted by the scientific community that the outcomes of the so-called Dutch protocol (i.e., providing puberty blockers and cross-sex hormones to adolescents with early-onset gender dysphoria) are simply unknown and that the risks are significant. Only a few months ago, there was a sensation when Thomas Steensma, who helped develop the Dutch protocol, reportedly raised the alarm that "the rest of the world is blindly adopting our research" when in fact "[l]ittle research has been done so far on treatment with puberty blockers and hormones in young people. That is why it is also seen as experimental."[11] Indeed, in the United States, these "affirmative" treatments are being

[11] More Research is Urgently Needed into Transgender Care for Young People: "Where Does the Large Increase of Children Come From?" https://www.voorzij.nl/more-research-is-urgently-needed-into-transgender-care-for-young-people-where-does-the-large-increase-of-children-come-from/

performed even on adolescents with *late*-onset gender dysphoria—a group with a different developmental pathway that were unstudied by the Dutch protocol investigators. Indeed, De Vries, one of the main investigators who produced the Dutch protocol, has warned that their research does not "apply to adolescents who more recently present in overwhelmingly large numbers for transgender care, including those that come at an older age, possibly without a childhood history of [gender incongruence]." She urged "caution" because "some eventually detransition."[12] If the current practices of the gender transition industry do not qualify as *experimental*, then that word simply has no meaning.

12. Dr. Turban's claim that the national reviews from the UK, Sweden, and Finland are "not peer-reviewed" is perverse. When a study is submitted to a peer-reviewed journal, it is reviewed by—at most—three people in the field. The national reviews from the UK, Sweden, and Finland have more than three reviewers, and they each considered numerous studies in the field, not just a single paper. The national reviews also include experts with greater expertise in study design and scientific method than the typical clinicians who review individual studies for a journal. These reviews speak with one voice that using puberty blockers and cross-sex hormones for gender transition is unsupported by reliable evidence of safety and effectiveness. That consensus is very inconvenient for Dr. Turban's life work, which is perhaps why his declaration would mislead the court to believe that these reviews are unreliable.[13]

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[12] Annelou L.C. de Vries, Challenges in Timing Puberty Suppression for Gender-Nonconforming Adolescents, *Pediatrics*, vol. 146(4) (October 2020), https://doi.org/10.1542/peds.2020-010611

[13] As if the national reviews were not enough, a peer-reviewed summary of the evidence came to a similar conclusion, finding "no long-term outcome data for either pre-pubertal or adolescent transgender youth . . . . Significant gaps in knowledge exist in nearly all aspects of gender variance, gender dysphoria and transgender experiences of children, adolescents and young adults." J. Olson-Kennedy, P.T. Cohen-Kettenis, B.P.C. Kreukels, H.F.L. Meyer-Bahlburg, R. Garofalo, W. Meyer, and S.M. Rosenthal, Research Priorities for Gender Nonconforming/Transgender Youth: Gender Identity Development and Biopsychosocial Outcomes, *Curr. Opin. Endocrinol. Diabetes Obes.*, vol. 23(2), p. 172 (April 2016), doi:10.1097/MED.0000000000000236

13. The international consensus is further bolstered by the Cochrane systematic review that Dr. Turban barely acknowledges. Cochrane researchers exhaustively combed through six medical databases, three "grey literature" databases, five clinical trial registries, and the scientific abstracts of the last two meetings of 14 different professional organizations. They contacted 15 different manufacturers of hormones and other experts in the field. After initially identifying 1057 studies, removing duplicates, screening, and inspecting them, the researchers concluded, "This systematic review has shown that well-designed, sufficiently robust randomised controlled trials (RCTs) and controlled-cohort studies do not exist." "Despite more than four decades of ongoing efforts to improve the quality of hormone therapy for women in transition, [the review] found that no RCTs or suitable cohort studies have yet been conducted to investigate the efficacy and safety of hormonal treatment approaches for transgender women in transition." The review further noted that the Endocrine Society, the UK National Health Service, and the NHS Guideline Panel had all reached the same conclusion. It highlighted the all-important issue: "If hormone therapy is highly valued in the treatment of gender dysphoria, then this raises the question: why are there no RCTs or appropriate cohort studies for this clinical condition?"[14]

II. THE SCIENTIFIC COMMUNITY IS MOVING TO PRIORITIZE PSYCHOTHERAPY FOR ADOLESCENTS WITH GENDER DYSPHORIA.

14. In asserting that I have misrepresented the "watchful waiting" approach, Dr. Turban actually misrepresents my position. The initial approach to youth with gender dysphoria, whether young children or adolescents, should be extended evaluation and therapy to address the post-natal forces that may be contributing to their self-understanding so that they can eventually make an informed decision about how to present themselves to the world.

[14] Claudia Haupt, et al., *Antiandrogen or Estradiol Treatment or Both during Hormone Ther-apy in Transitioning Transgender Women*, Cochrane Database of Systematic Reviews (Nov. 28, 2020).

15. This approach is also different from so-called conversion therapy. Indeed, there is a world of difference between trying to change how a patient identifies (on one hand) and providing psychotherapy that recognizes that how a patient identifies often does change as a result of maturation, life experience, intellectual growth, etc. (on the other). This is consistent with what Finland has recently discovered, that adolescents are still likely to undergo significant changes, some of which may cause them to find adaptations that render undesirable drastic bodily alterations. Indeed, the Finnish guidelines warn that "[b]rain development continues until early adulthood—about age 25, which also affects young people's ability to assess the consequences of their decisions on their own future selves for [the] rest of their lives." Those guidelines further note that it is uncertain whether puberty blockers *themselves* impair young peoples' judgment and decision making, which could negatively impact the ability to provide informed consent to subsequent hormonal and surgical stages of the intervention. "[T]hese factors," they explain, "are key reasons for postponing any [medical] interventions until adulthood" and instead prioritizing psychotherapy for adolescents.[15]

16. My colleagues and I note that most adolescents presenting with gender dysphoria have considerable indicators of underlying mental health problems before gender has become an issue for them. Therefore, they benefit greatly from psychotherapy. In contrast, Dr. Turban completely fails to address the role played by mental health comorbidities in the genesis of gender dysphoria. He does not deal with autism spectrum disorders, the impact of childhood adversities or preexisting depression, social anxiety, self-hatred, etc. He implausibly blames all resid-

[15] Palveluvalikoima, Recommendation of the Council for Choices in Health Care in Finland (PALKO / COHERE Finland), https://segm.org/sites/default/files/Finnish_Guidelines_2020_Minors_Unofficial%20Translation.pdf

ual problems that transgender-identifying persons have on society—i.e., the minority stress theory. Dr. Turban's ignoring of post natal experience in shaping a search for a comfortable sense of self reflected in the symptoms of gender dysphoria is facilitated by his belief that all gender dysphoria is prenatally biologically determined. He uses his biological causality hypothesis to ignore the problematic developmental experiences of so many of these trans teens, despite his research fellowship in child and adolescent psychiatry.

17. Neither Dr. Turban nor the plaintiffs' other experts provide any reliable evidence concerning how to determine which adolescents will persist in a transgender identification into adulthood. Persistence rates of the adolescents undergoing medical transition may be high, but that does not reflect the adolescents who only transiently identify as transgender, those who agree that time or psychotherapy is the best approach, those who recognize their intense fears and conflicts about cross gender expression, and those who know that they are deeply depressed and anxious but do not know why. Also, contrary to Dr. Turban, a high persistence rate for adolescents who have undergone medical transition is explained by the medical transition itself, which reinforces a transgender identity. The Endocrine Society guidelines recognize that "social transition (in addition to GD/gender incongruence) has been found to contribute to the likelihood of persistence."[16] It would strain credulity to maintain that social transition has this effect but medical transition does not.

18. In view of the indisputable fact that how a person identifies can change, Dr. Adkins draws a meaningless distinction between how one identifies (which she claims is "fixed") and how one "*understand*[*s*]" how one identifies (which, she claims, may "evolve"). In any

[16] Wylie C. Hembree, et al., Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons, p. 3879.

case, Dr. Adkins now claims that gender identity is "fixed" only in the sense that it cannot be changed simply at will or by "external" factors. That is very far from claiming that gender identity is immutable, and it obviously allows that a person's identification can change based on *internal* experiential factors and maturation itself. Most aspects of human identity evolve throughout life.[17] Those who return to presenting themselves as a member of their biological sex after hormones or surgery starkly contradict Dr. Adkins' belief system.

19. Dr. Adkins' claims that using puberty blockers for gender-transition procedures is "reversible" or that they merely "pause" puberty are also false and misleading. Based on concerns that virtually all adolescents who begin puberty blockers proceed to cross-sex hormones, the UK National Health Service has officially recommended against such language, stating that "[r]esearchers and clinical staff working in gender identity development should consider carefully the terms that they use in describing treatments e.g. avoid referring to puberty suppression as providing a 'breathing space,' to avoid risk of misunderstanding."[18] This is a wise recommendation, and it should be followed. Further, besides puberty blockers' physical side effects like inhibiting increase of height and bone density, the drugs also have irreversible psychosocial effects. That is because puberty blockers also halt the normal social and psychological process of maturation at that developmentally crucial stage, with lifelong effects. The Endocrine Society guidelines rightly recognize both "the sense of social isolation from having the timing of puberty to

[17] Levine SB. (2020). "The Gender Revolution" in Psychotherapeutic Approaches to Sexual Problems: An essential guide for mental health professionals. American Psychiatric Association Publications, Washington, DC., pp 81-98.

[18] Investigation into the Study "Early Pubertal Suppression in a Carefully Selected Group of Adolescents with Gender Identity Disorders," National Health Service Health Research Authority (October 14, 2019), https://www.hra.nhs.uk/about-us/governance/feedback-raising-concerns/investigation-study-early-pubertal-suppression-carefully-selected-group-adolescents-gender-identity-disorders/

be so out of sync with peers" and the "potential harm to mental health (emotional and social isolation) if initiation of secondary sex characteristics must wait until the person has reached 16 years of age."[19]

I declare under penalty of perjury that the foregoing is true and correct.

Executed on July 19, 2021.

Stephen B. Levine, M.D.

[19] Wylie C. Hembree, et al., Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons, p. 3885.

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DEFENDANTS.

SUPPLEMENTAL DECLARATION OF DR. MARK REGNERUS

Pursuant to 28 U.S.C. 1746, I declare:

1. My credentials, research, and professional qualification are detailed in my declaration in this matter dated July 7, 2021. Here, as there, my opinions are based upon my knowledge and research in the matters discussed. The materials I have used to research and write this report are the standard sources used by other experts in my field. I have actual knowledge of the matters stated in this declaration. This declaration does not exhaust my opinions.

2. I have reviewed the newly submitted supplemental declarations by Dr. Deanna Adkins (dated July 15, 2021) and Dr. Armand Antommaria (dated July 15, 2021), as well as the declaration submitted by the plaintiffs' new witness, Dr. Jack Turban (dated July 16, 2021). As I detail below, these new declarations contain numerous errors and mistakes.

3. As stated in my original report, I make no claims about the most prudent course of treatment for any particular patient. Rather, my assessment concerns the unscientific process by which "affirmative" treatment of transgender-identifying adolescents has come to be the default position advocated by various professionals and organizations. Dr. Turban makes a variety of criticisms of my report, but very few of them touch upon the primary concerns in my original report.

4. Dr. Turban accuses me (and other state's experts, as well as the Swedish and Finnish reports' authors) of misrepresenting and omitting "key research" on a variety of outcomes here, listing eight studies about pubertal suppression and six on gender-affirming hormonal treatment. My intention from the outset was not to offer a comprehensive literature review of the entire field of research in transgender science—especially but not exclusively that which focused on minors. That is a task unsuited to this document. Rather, one of the central purposes of my report was to describe how any supposition that there is a legitimate scientific consensus about treatment for adolescents is unmerited, and why. The research I cited and discussed is compelling evidence favoring a proper interpretation of this field as "in development" rather than as "settled science."

5. Dr. Turban offers the unsubstantiated claim that "[a]ll existing published data…points to the fact that gender-affirming medical interventions improve mental health for transgender adolescents." Such a categorical claim is simply untrue, as my original report already documented.

6. As an example of this erroneous categorical claim, Dr. Turban immediately highlights on the very same page an example of how "research has shown that sexual functioning (along with romantic development) improves" after gender-affirming medical interventions on adolescents.[1] The study he cites, however, reveals no such thing. "Improvement" cannot even be measured here, since the study was a cross-sectional one, not longitudinal. The study, rather, asked transgender youth a series of questions about sexual and romantic experiences and satisfaction (at a mean age of 14, no less). The results revealed that, in comparison to the general

[1] Bungener, S. L., Steensma, T. D., Cohen-Kettenis, P. T., & De Vries, A. L. (2017). Sexual and romantic experiences of transgender youth before gender-affirmative treatment. *Pediatrics*, *139*(3) e20162283. https://doi.org/10.1542/peds.2016-2283

population, transgender youth displayed less sexual and romantic experience. It is an odd study to reference in support of his (ironic) claim about state's experts' purported mischaracterizations.

7. Dr. Turban's attempt at explaining both the surge in gender dysphoria and the reversal in the sex ratio of presenting patients is weak and speculative, demonstrating my original claim that some researchers and clinicians are indeed uninterested in understanding a pair of important social developments that may shape how practitioners and their professional societies approach treatments. His disregard for Professor Littman's inquiry about the social cues of adolescent-onset gender dysphoria is obvious: her work is dismissed because "the scientific current understanding…does not focus on 'social contagion.'" Perhaps the problem is less with Littman than with purveyors of a "science" that is more interested in safeguarding particular answers than it is with asking questions.

8. A similar cavalier manner characterizes how Dr. Turban brushes off three European judicial and medical decision-making bodies, as if admitting any weakness undergirding the "consensus" of American professional societies is fatal. Instead, he simply claims that these too are "outlier views" not supported by the list of organizations that, as I demonstrated in the original report, themselves do not agree on definitions, terms, and even their own historical shift in understanding (e.g., minors' ability to consent). There's no trust in science here—only in patron professional associations and their client scholars.

9. My primary point in discussing Professor Littman's study is to highlight how rare it is for social and medical scientists today to be exploring the surge in adolescent gender dysphoria cases. Simply because Littman's is an opt-in sample is no cause for implying it is without value. Moreover, the "correction" of which Dr. Turban speaks (on page 31) is hardly of

the sort to compare with the correction the Bränström and Pachankis study yielded.[2] Whereas the latter study's primary narrative—that "affirmative" surgeries contributed to patient's subsequent mental health—evaporated, Littman's correction merely concerned the language she used and did not change the results of her study.

10. It is nevertheless ironic for Dr. Turban to criticize Littman's use of an opt-in, recruited "anonymous online survey," when he has published extensively—including citations in his own report—from the 2015 United States Transgender Study. The USTS recruited networked, self-identified transgender or nonbinary participants by advertising their survey among "active transgender, LGBTQ, and allied organizations."[3] Now, there's nothing inherently wrong with collecting data using a nonrandom approach like this, and it is common in this domain.[4] The problem, in this case, is when the conclusions based on such data are delivered to the reader in a way that suggests they are consonant with everyone who has identified as transgender or experienced gender identity disorder or dysphoria. Hence, to impugn Littman's strategy is to impugn Dr. Turban's own extensive use of the same method of collecting data from "some anonymous people recruited from the Internet…" (page 32).[5]

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[2] Bränström, R., & Pachankis, J. E. (2020). Reduction in mental health treatment utilization among transgender individuals after gender-affirming surgeries: a total population study. *American journal of psychiatry*, *177*(8), 727-734. https://doi.org/10.1176/appi.ajp.2019.19010080

[3] James, S. E., Herman, J. L., Rankin, S., Keisling, M., Mottet, L., & Anafi, M. (2016). The Report of the 2015 U.S. Transgender Survey. Washington, DC: National Center for Transgender Equality.

[4] Littman, L. (2020). The use of methodologies in Littman (2018) is consistent with the use of methodologies in other studies contributing to the field of gender dysphoria research: Response to Restar (2019). *Archives of sexual behavior*, *49*(1), 67-77. https://doi.org/10.1007/s10508-020-01631-z

[5] See, for example: Turban, J. L., King, D., Li, J. J., & Keuroghlian, A. S. (2021). Timing of social transition for transgender and gender diverse youth, K-12 harassment, and adult mental health outcomes. *Journal of adolescent health*. https://doi.org/10.1016/j.jadohealth.2021.06.001; Turban, J. L., Loo, S. S., Almazan, A. N., & Keuroghlian, A. S. (2021). Factors leading to "detransition" among transgender and gender diverse people in the United States: A mixed-methods analysis. *LGBT health*, *8*(4), 273-280. https://doi.org/10.1089/lgbt.2020.0437; Turban, J. L., King, D., Carswell, J. M., & Keuroghlian, A. S. (2020). Pubertal suppression for transgender youth and risk of suicidal ideation. *Pediatrics*, *145*(2), e20191725. https://doi.org/10.1542/peds.2019-1725; Turban, J. L., Beckwith, N., Reisner, S. L., & Keuroghlian, A. S. (2020). Association between recalled exposure to gender identity conversion efforts and psychological distress and suicide attempts among transgender adults. *JAMA Psychiatry*, *77*(1), 68-76. doi:10.1001/jamapsychiatry.2019.2285; Turban, J. L., King, D., Reisner, S. L., &

11. That Dr. Turban should commend the Almazan and Keuroghlian study (on page 25) is another irony, since it too is based on the USTS. Talk of a "control group" in medical research connotes a clinical trial, randomization, and/or some sort of multi-wave analysis in order to establish an obvious time order to events. The USTS, however, offers none of these values.

12. Moreover, the USTS creates the impression that the data collection effort was a population-based random sample, like the US Census. It is not. Indeed, the USTS yields information about the transgender population that is decidedly different from that which can be learned from the 2014 CDC's Behavioral Risk Factor Surveillance System (BRFSS) data, the product of a probability sample from 19 states (and Guam).[6] When the two are compared, stark differences are revealed, further suggesting that the empirical "truth" about the transgender population is simply difficult to discern—a fact of life in this domain of research. For example:

a. Unemployment: 15% in the USTS vs. 8% in the BRFSS

b. Sexual orientation: 47% of male-to-female identify as LGB in the USTS vs. 15% in the BRFSS; 24% of female-to-male identify as LGB in the USTS vs. 10% in the BRFSS

c. Currently married: 18% in the USTS vs. 50% in the BRFSS

d. Child in the household under 18: 14% in the USTS vs. 32% in the BRFSS

e. General health rated as fair or poor: 22% in the USTS vs. 26% in the BRFSS

Keuroghlian, A. S. (2019). Psychological attempts to change a person's gender identity from transgender to cisgender: Estimated prevalence across US States, 2015. *American journal of public health*, *109*(10), 1452-1454. https://doi.org/10.2105/AJPH.2019.305237

[6] Meyer, I. H., Brown, T. N., Herman, J. L., Reisner, S. L., & Bockting, W. O. (2017). Demographic characteristics and health status of transgender adults in select US regions: Behavioral Risk Factor Surveillance System, 2014. *American journal of public health*, *107*(4), 582-589. https://doi.org/10.2105/AJPH.2016.303648

13. On page 7 of his report, Dr. Turban favorably cites a study published in a 2015 issue of *Psychoendocrinology* that measured Child Behavior Checklist scores based on parental self-report. Thus, Dr. Turban, who criticizes (on page 32) Littman's reliance on a parental questionnaire, has no trouble with parental self-reports as a measurement technique so long as they support his position.

14. There are two conclusions to draw from this comparison of the USTS and BRFSS samples. First, opt-in samples like the USTS are for understanding processes and possibilities, not populations (as in the BRFSS). Second, Littman's use of an opt-in sample was hardly inappropriate. She sought to understand a process (that of rapid-onset gender dysphoria, or as others call it, late-onset or adolescent-onset gender dysphoria), one that curiously few scholars seem interested in understanding.

15. Dr. Turban seems far less curious about understanding surging gender dysphoria and the reversal in sex ratio than one would expect a purported expert about transgender identity to be. This matters. Professor Littman's exploratory research was lambasted because it introduced the possibility that transgender identity is—at an unknown rate—not innate but developmentally responsive to social cues for an unknown but significant number of cases. If she's right, it means greater attention to the diverse origins of gender dysphoria is in order, with possible ramifications for treatment options. This is not, however, in accord with claims of those advocating for "affirmative" treatment. Hence, her research is disparaged. This isn't how science is supposed to work.

16. While Dr. Turban is correct to note that the Bränström and Pachankis study concerns adults rather than minors, my discussion of it is intended to highlight the unsettledness of the science here, and to suggest that the line between activists and academics is a rather thin

one, provoking contests over the meaning of a study's results. Given that it is arguably the largest longitudinal dataset capable of tracking the long-term effects of hormones and surgery, its lack of findings (following the editor's requested correction) has ramifications for the treatment of adult and adolescent patients alike.

17. Dr. Turban's own attempt (beginning on page 33) to explain the surge in gender dysphoria and self-identified transgender cases is odd and under-documented, suggesting that he too—like most researchers in this domain—gives this important matter little thought. He claims that the "increase in referrals" is due to several causes.

18. Among these, Dr. Turban suggests that "parents in the past may have had limited literacy regarding gender diversity," something that has been ameliorated today. In other words, the level of true transgender identity may well have been stable in the past, but parents neither had the language nor the interest in aiding their children to live as their authentic selves, except perhaps in "extreme types" of gender dysphoria. Today, "owing to media attention and the internet, it is easier to access information…making the threshold lower to search for help" (page 34). But at the same time Dr. Turban maintains that Professor Littman's interest in understanding the role of "social" forces and "transgender-related content" on the internet in adolescent-onset gender dysphoria "is a fringe view not supported by evidence" (page 32). This is an obvious double standard.

19. Additionally, Dr. Turban seems to suggest that the rate of transgender "middle-aged adults" (about which I surmised in my report) would be comparable to that of adolescents today were it not for "decades of stigma" and "internalized transphobia," factors that "make it less likely for middle-aged transgender adults to come out, despite an increase in social acceptance" (page 34). This is pure speculation at best.

20. Finally, Dr. Turban attempts to explain why clinics are "seeing more birth-assigned females than males in recent years"—which is a rather mild way of describing what is not a mere uptick but a radical reversal and surge, as I previously described. Dr. Turban begins with the observation that "tomboys" were much more likely to be "accepted in society, whereas feminine boys are ridiculed." Perhaps so. But then he speculates that this phenomenon "likely led to more transgender males being satisfied with pushing gender expression toward more male without seeking support from a gender clinic…" In asserting this, Dr. Turban categorically and anachronistically redefines tomboys as transgender males who simply had no access to a gender clinic. Where are they today? Still hidden, having suppressed their true identity? This explanation beggars belief. Perhaps instead, yesterday's tomboys are largely content to have avoided medical dependency, living without health implications or impairments from lifelong treatments that were, at the time, unavailable. Their gender non-conformity fostered their own resilience.

21. Dr. Turban claims that "sex ratios that favor birth-assigned females" among the population of transgender patients is not unprecedented. While I can appreciate the subsequent international citations and consideration of international data, the sample sizes are simply too small (24 total cases of "female-to-male transsexuals" who "came from different parts of Poland" over four years in the study Dr. Turban cites[7]) to suggest anything about the sex ratio of transgender Poles in the 1970s. The rate of the much larger number seeking "sexologic" treatment from which this small pool is drawn, however, revealed the standard male-dominated pattern.

[7] Godlewski, J. (1988). Transsexualism and anatomic sex ratio reversal in Poland. *Archives of sexual behavior*, *17*(6), 547-548.

22. On page 36, Dr. Turban contests my claim that "there is no defined psychotherapeutic method for treating gender dysphoria that can be widely characterized and consistently identified as 'conversion therapy' in order to be banned." He misrepresents my claim. I did not state that there are no definitions. Rather, I assert that there are no "widely" and "consistently" agreed-upon definitions, like there is with the vast majority of clinical conditions, practices, and treatments. Only his reference to American Academy of Child and Adolescent Psychiatry (AACAP) offers a definition for conversion therapy. The subsequent citations each refer to conversion therapy but do not define it.

23. Following the AACAP's policy on conversion therapy, Dr. Turban employs a "frame alignment"[8] move to suggest efforts at conversion therapy for same-sex attraction and gender expression are equivalent, since both—he claims—specifically "aim to promote heterosexuality" (page 36). That is, he links interpretive orientations between two distinctive movements—the one to suppress gay conversion therapy and the one, noted above, on gender identity "conversion" efforts—in the hopes that overlapping interests, values, beliefs, and goals are complementary. But I am not talking about heterosexuality. I concur with another critic who has observed, "Studies of conversion therapy have been limited to *sexual orientation*, and, moreover, to the sexual orientation of *adults*, not to gender identity and not of children in any case."[9] Here again is evidence that a central framework for understanding the treatment of adolescent transgender patients is not that of mental and physical flourishing, but rather has become that of securing bodily autonomy and choice, as I explained in my original report.

[8] Snow, D. A., Rochford Jr., E. B., Worden, S. K., & Benford, R. D. (1986). Frame alignment processes, micromobilization, and movement participation. *American sociological review*, 464-481.

[9] 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. The quote is from page 308.

24. In published studies, Dr. Turban leans on the USTS's "definition" of conversion therapy, which—when posed to survey participants—was stated as follows: "Did any professional (such as a psychologist, counselor, or religious advisor) try to make you identify only with your sex assigned at birth (in other words, try to stop you being trans)?" Given the hundreds of questions and items the USTS posed to its respondents six years ago, the fact that it lumps any scenario that does not involve unqualified affirmation (including "watchful waiting") into one imprecise, binary measure is psychometrically irresponsible. In other words, it is foisting on people a one-size-fits-all definition. What one can learn from a poor-quality question posed to an opt-in sample of respondents motivated—even recruited—to participate is limited by definition. That such studies seem easily publishable today highlights the extent to which certain medical journals—officially sponsored by the same associations that have claimed a stake in the outcome here—have been "ideologically captured," a theme about which I wrote extensively in my original report. They seem uninterested in holding transgender research to standards comparable to other divisions of medicine.

25. Beginning on page 41, Dr. Turban makes much of the fact that the reports from the U.K., Sweden, and Finland "were not peer-reviewed" on his way to suggesting that each report "omits key studies," and/or were "poorly researched," before asserting that he would not recommend relying on their conclusions. Meanwhile, the NICE (UK) reports concluded that claims of benefit for medical gender interventions in children are based on "low quality evidence."[10] The same claim characterizes the Swedish report: "No studies explaining the increase of children and adolescents seeking [treatment] for gender dysphoria were identified….

[10] Society for Evidence Based Gender Medicine. (2021, May 5). Sweden's Karolinska ends all use of puberty blockers and cross-sex hormones for minors outside of clinical studies. https://segm.org/Sweden_ends_use_of_Dutch_protocol

All identified studies are observational, and few are controlled or followed-up over time."[11] Dr. Turban laments how "the NICE report also erroneously excluded" his own 2020 USTS-based *Pediatrics* study. But it is plausible—given the NICE reports' quality standards—that the decision to exclude his study was not erroneous or accidental, but quite intentional.

26. One conclusion is increasingly obvious in this interminable dispute over which published studies to include and which to ignore. We have rapidly reached a stage in the study of transgender medicine where the phrase "peer review" no longer guarantees quality analyses, apt measures, appropriate samples, thoughtful interpretations, and measured conclusions.

27. Referring to the UK, Swedish, and Finnish reports, Dr. Turban concludes that, together with the other (state's) experts, I "have inflated the importance of these reports…" (page 45). I see nothing to substantiate this. Rather, my modest original intention is to highlight how, despite advocates' rhetoric, there is both individual and organizational dissent to any purported "consensus" about "affirmative" gender treatment for minors.

28. My original assertion (in response to Dr. Antommaria's report) that there is "no obstacle to randomized trials *without* placebo groups to 'compare different types, dosages and methods of administration of active treatments'" is not, as Dr. Turban states, irrelevant.[12] It is yet another piece of evidence demonstrating the many ways in which randomized clinical trials research can be conducted here—but are not. Dr. Turban is correct that such a study "would not answer the question regarding the efficacy or effectiveness of the class of medications in

[11] Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU). (2019). Gender dysphoria in children and adolescents: An overview of the literature. *SBU.* Report No. 307: SBU 2019/427. https://www.sbu.se/en/publications/sbu-bereder/gender-dysphoria-in-children-and-adolescents-an-inventory-of-the-literature/

[12] 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,* p. 10. https://doi.org/10.1002/14651858.CD013138.pub2

general," but the lack of even dosage studies with control groups highlights the near lawlessness that this field of medicine seems to operate with, and provides further evidence of the "ideological capture" that I have thoroughly documented.

29. In his own response on this topic, Dr. Antommaria continues his appeal to clinical equipoise, adding a pitch for off-label drug use, which "may be well-supported by evidence" and "does not mean that the use is experimental, untested, or unsafe."[13] In the abstract, that is true. But there's a significant gap between "may be" and "is" in particular circumstances. Perhaps a test is in order.

30. In the end, the field of transgender medicine—especially but hardly exclusively that branch that concerns adolescents—has gotten away with research conduct seldom tolerated in other branches of medicine. The field lacks randomized clinical trials, courtesy of a persistent appeal to clinical equipoise—which seems based more on popular demand than good judgment—and the wide use of off-label drugs. It is as if social media has functioned for this industry similar to the way that television advertising has functioned for pharmaceutical companies—by appealing to viewers to ask their doctors for what they want. If (1) the long-term physical and mental health results from "affirmative" treatments were demonstrably better—based on sensible methods and samples—or (2) the risks and invasiveness (and irreversibility of some) of the treatments were in turn modest, I would not be writing this response or the original report.

31. Dr. Turban signals little caution about the process of "affirmative" transitioning, and seems to disregard the losses incurred when patients regret walking through doorways that advocates enthusiastically open for them. He claims, "Although gender affirming hormones can

[13] Antommaria, A. H. M. (2021), p. 4.

cause some irreversible changes, such as body fat redistribution and vocal changes, these effects are primarily cosmetic."[14] Fat redistribution is hardly a more significant irreversible change than infertility. But for Dr. Turban, infertility seems largely irrelevant. He misrepresents a 2019 study, claiming that "fertility was similar between transgender men who had been on testosterone treatment and cisgender women."[15] In reality, the study is about comparing the pregnancy success rate of assisted reproductive technology—an expensive, demanding process with modest success rates—between self-identified transgender males (natal females) and a parallel group of women.[16] Given that over 98 percent of live births in the United States do not employ assisted reproductive technology[17] and involve no "fertility preservation" of the sort that WPATH recommends to counseled patients, the reference to "similar" fertility is apt to mislead.

32. Supporters of "affirmative" treatment approaches tend to formally endorse the Dutch protocol. Yet at the same time, that protocol is far more rigorous and exclusive in its selection than the majority of patients who make up published American transgender research samples.[18] In the Dutch protocol, baseline health and high functioning are *required* for adolescent patients to proceed through treatment. Psychiatric co-morbidities and the absence of

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[14] Turban, J. L., & Keuroghlian, A. S. (2018). Dynamic gender presentations: Understanding transition and "de-transition" among transgender youth. *Journal of the American academy of child & adolescent psychiatry*, *57*(7), 451–453. https://doi.org/10.1016/j.jaac.2018.03.016. The quote is from page 453.

[15] Turban, J. L. (2021), p. 12.

[16] Leung, A., Sakkas, D., Pang, S., Thornton, K. & Resetkova, N. (2019). Assisted reproductive technology outcomes in female-to-male transgender patients compared with cisgender patients: a new frontier in reproductive medicine. *Fertility and sterility 112*(5), 858-865. The quote is from page 859.
"To be included in this study, the patient had to identify as a transgender man and have completed an ovarian stimulation cycle for oocyte cryopreservation, embryo cryopreservation, or intended uterine transfer. Most couples who desired to conceive did so through reciprocal IVF, whereby the transgender patient provided the oocytes and their cisgender partner carried the pregnancy. The few transgender men who opted to carry the pregnancy themselves underwent several failed intrauterine insemination cycles before proceeding to IVF."

[17] Centers for Disease Control and Prevention. (2018). ART success rates. https://www.cdc.gov/art/artdata/index.html

[18] For a description of the protocol, see: 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.

childhood gender dysphoria (i.e., adolescent-onset only) are grounds for exclusion from subsequent treatment. This is inconsistent with the contemporary practice in American gender clinics, which offer "affirmative" gender treatment largely on-demand and with a much lower threshold for medical intervention. Hence, when Dr. Turban appeals to the results of studies employing the Dutch protocol—including much of Dr. de Vries's work—to support this practice, this is sleight of hand, since the panoply of American medical professional organizations to which he, Dr. Adkins, and Dr. Antommaria continue to appeal now disregard the Dutch protocol's rigor.

33. Drs. Adkins, Antommaria, and Turban are endorsing "affirmative" gender treatment based on research conclusions from a literature whose criteria for inclusion has long been quite different—more selective and rigorous—than it is today. To say, as does Thomas Steensma of the Dutch Center of Expertise on Gender Dysphoria, that "more research is really necessary, and very much needed" is an understatement.[19]

34. Finnish physicians confirm this: "During the past ten years the number of adolescents contacting gender identity services in order to seek for medical gender reassignment has increased across Western countries. The reasons for this are not known."[20] Moreover, researchers have noticed a difference in outcomes: "Those who did well in terms of psychiatric symptoms and functioning before cross-sex hormones mainly did well during real-life." This is the Dutch protocol, now disregarded in favor of "affirmative" treatment for all. How do adolescents fare when they are not screened? "Those who had psychiatric treatment needs or

[19] Tetelepta, B. (2021, February 27). More research is urgently needed into transgender care for young people. Where does the large increase of children come from? *Voorzij*.https://www.voorzij.nl/more-research-is-urgently-needed-into-transgender-care-for-young-people-where-does-the-large-increase-of-children-come-from/

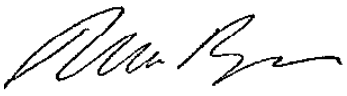
[20] Kaltiala-Heino, R., Sumia, M., Työläjärvi, M., & Lindberg, N. (2015). Two years of gender identity service for minors: overrepresentation of natal girls with severe problems in adolescent development. *Child and Adolescent Psychiatry and Mental Health*, *9*(1), 1-9.

problems in school, peer relationships and managing everyday matters outside of home continued to have problems…" Indeed, "[p]sychiatric comorbidities, particularly depression, anxiety disorders and autism spectrum disorders as well as suicidality and self-harming behaviors are common among adolescents seeking gender reassignment." Can "affirmative" treatment help them? We would have to suspend attention to any study conclusions employing the Dutch protocol in order to make this assessment. Steensma concludes with uncertainty: "We don't know whether studies we have done in the past can still be applied to this time."

35. As I concluded my original report, so here: Talk of a "consensus" among certain professionals in the field of transgender medicine is contrived and premature. The pace and extent of the ideological capture of professional organizations, researchers, and even patients demanding access to affirmative treatment is staggering. Protocols are in turn becoming more permissive, which leave practitioners in a position to only guess at what may result based on research conducted under quite different conditions. Given the state of disarray in the science, states have compelling reasons to protect their young people by requiring that they reach adulthood before submitting to experimental, life-altering gender transition treatments.

I declare under penalty of perjury that the foregoing is true and correct.

Executed on July 19, 2021.



Dr. Mark Regnerus

IN THE UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF ARKANSAS
CENTRAL DIVISION

DYLAN BRANDT, et al.,

PLAINTIFFS,

v. **No. 4:21-CV-00450-JM**

LESLIE RUTLEDGE, et al.,

DEFENDANTS.

SUPPLEMENTAL DECLARATION OF PAUL W HRUZ, M.D., PH.D.

Pursuant to 28 U.S.C. 1746, I declare:

1. I have been retained by counsel for Defendants as an expert witness in connection with the above-captioned litigation. I have actual knowledge of the matters stated in this declaration. A detailed summary of my background and credentials was provided in my initial declaration on this case, dated July 7, 2021. A true and accurate copy of my CV is attached as Exhibit A to that initial declaration.

2. I have reviewed the supplemental declarations provided by Drs. Adkins and Antommaria and the new declaration provided by Dr. Turban in reference to this case. I provide here additional scientific evidence and discussion of key assertions made by the Plaintiffs' witnesses that are false or highly misleading. This response is not exhaustive of all of my opinions. Many of the claims made by the Plaintiffs' witnesses were addressed in part or fully in my first declaration.

3. My opinions as detailed in this declaration are based upon my knowledge and direct professional experience in the subject matters discussed. The materials that I have relied upon are the same types of materials that other experts in my field of clinical practice rely upon when forming opinions on the subject including hundreds of published, peer reviewed scientific research (and clinical) articles.

4. Below is a summary of my supplemental opinions regarding the Plaintiffs' Supplemental Expert Witness Declarations and Dr. Turban's new declaration:

a. The studies cited by the Plaintiffs' experts suffer from methodological flaws. This includes the studies that Dr. Turban cites to argue that gender-transition procedures lead to long-term benefits. Accurate assessment of the relative strengths and weaknesses of current approaches to the care of children must include knowledge of the limitations of scientific study that is based upon convenience sampling, failure to include properly selected control groups, lack of randomization of study subjects, and *a priori* rejection of alternate hypotheses.

b. Neither the size nor number of professional organizations issuing endorsements for gender affirming medical interventions including use of puberty blockers and cross-sex hormones guarantees the veracity of the claims made. The relevant scientific community includes investigators who are able to objectively consider the merits of claims made.

c. The most recent studies addressing questions of psychological health in youth with gender dysphoria continue to have major weaknesses and limitations which prevent definitive conclusions to be made on long-term benefit.

d. In the absence of higher quality data in children, recently published evidence for lack of long-term benefit in treated adults must be considered.

e. Assertions regarding the experimental nature of the gender affirmation including use of puberty blockers and cross sex hormones are based upon lack of understanding of long term effects including treatment related side effects and efficacy in preventing suicide.

I. SUPPLEMENTAL DECLARATION OF DR. ADKINS:

5. Although Dr. Adkins continues to assert that youth who experience gender dysphoria after the onset of puberty do not desist, she provides zero experimental evidence to support this claim. Her single reference to a book chapter co-authored by Dr. Turban does not represent scientific evidence for this claim.

6. Dr. Adkins' reiteration of her claim that the number and size of professional organizations endorsing the affirmative model for addressing gender dysphoria guarantees the veracity of the recommendations made is not supported by high quality research. As discussed in more detail below, significant limitations and weaknesses are pervasive in the existing peer reviewed gender dysphoria literature. Dr. Adkins' claim that papers referenced by the Endocrine Society and WPATH represent rigorous research appear to reflect a lack of understanding of what constitutes scientific rigor. It is important to recognize that nearly all of the recommendations made in the Endocrine Society Guidelines were rated by the GRADE system as "low" or "very low" evidence. By definition, this rating means that that there is a high likelihood that the recommendations are likely to change once higher level evidence is gathered (Atkins D., et al. (2004). Grading quality of evidence and strength of recommendations. *BMJ, 328*(7454):1490). The mere number of published studies does not obviate these concerns. While this is not unique to the field of transgender medicine, the strength of recommendations made and the failure to consider alternate hypotheses regarding treatment are unique to this emerging discipline.

7. It is erroneous to draw conclusions on the purported safety of puberty blockers in adolescents with normally timed puberty based upon data collected in children treated for precocious puberty. These are different conditions and the effects of the timing of the intervention is highly relevant to assessment of safety. The statement that "there is no evidence

of short or long term negative effects on patients who receive puberty blockers" either reflects an ignorance of the published literature addressing this question or a failure to appreciate the significance of the data that was cited in my declaration. This includes information contained within the product labels for this class of medication. It is particularly relevant that "Psychiatric events have been reported in patients taking GnRH agonists, including LUPRON DEPOT-PED. Postmarking reports with this class of drugs include symptoms of emotional lability, such as crying, irritability, impatience, anger and aggression." (AbbVie, Lupron Depot (Leuprolide acetate) Product Monograph. 2018, AbbVie Corporation).

8. Dr. Adkins' statements regarding the effects of puberty blockade on bone density are inaccurate. She references two studies to assert that while bone density is lower during treatment, bone density normalizes after initiation of cross-sex hormones. The paper by Klink et al. (Klink, D., et al. (2015). Bone Mass in Young Adulthood Following Gonadotropin-Releasing Hormone Analog Treatment and Cross-Sex Hormone Treatment in Adolescents With Gender Dysphoria. *The Journal of Clinical Endocrinology & Metabolism, 100*(2): E270-E275) is a retrospective study that looked at bone mineral density (BMD) in 34 young gender dysphoric adults at the average age of 22, who had been given puberty blockers to suppress or delay puberty for 1.3–1.5 years, followed by cross-sex hormones for about 3 years. The main finding of this study is that young adults treated with GnRH agonists (i.e. puberty blockers) during adolescence have decreased bone mineral density (BMD) and loss of bone mass despite the subsequent administration of cross-sex hormones. Importantly, most of the study subjects were relatively late in their puberty when puberty blockers were initiated (average age 15 years), so much of their bone mass development had already occurred. From this study, it cannot be known how much BMD in children and younger adolescents treated with puberty blockers at a

younger age will be affected, nor can it be known whether these losses will lead to increased risk of fractures in later life. The second study she cites specifically addressed bone geometry not bone density. The authors note many limitations to the interpretation and application of the data generated. While assessment of bone geometry adds to the overall assessment of bone health, it does not negate the concern for adverse effects of pubertal suppression on bone density in adolescent youth.

9. Dr. Adkins' dismissal of published literature on known and potential adverse effects of cross-sex hormones by an ipse dixit statement that these side effects are rarely seen in patients with well managed treatment should not be accepted by this Court as a reliable source of evidence. Rather, rigorous examination of scientific studies examining verifiable outcomes with known error rates should be considered. The review article by Weinand and Safer that Dr. Adkins cites (Weinand, J. D. & Safer, J. D. (2015). Hormone therapy in transgender adults is safe with provider supervision; A review of hormone therapy sequelae for transgender individuals. *Journal of clinical & translational endocrinology*, *2*(2): 55–60) contains references to multiple studies reporting the same known and potential adverse effects included in my original declaration. In many cases, Weinand states that the evidence is inconclusive. Thus, despite the claim that cross-sex hormones are safe, the existing literature provides evidence for significant adverse effects including changes in body weight, insulin sensitivity and thromboembolism (i.e. stroke).

10. Contrary to the comments of Dr. Adkins in criticizing Dr. Levine regarding infertility following gender affirming medical interventions, concern for impaired fertility is a known and significant risk of cross-sex hormone administration, particularly when given to adolescent children who have not undergone full gonadal maturation, often because of pubertal

blockade. Recognition of this risk is the basis for offering counseling on fertility preservation prior to starting such interventions. Despite the routine offering fertility preservation, <5% of adolescents accept this intervention (Nahata, L., et al. (2017). Low Fertility Preservation Utilization Among Transgender Youth. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*, *61*(1): 40–44). However, studies have provided evidence that nearly half of transgender adults regret not being able to have biological children (see De Sutter, et al. (2002). The desire to have children and the preservation of fertility in transsexual women: A survey. *International Journal of Transgenderism, 6*(3): 215–221; and Wierckx, K., et al. (2012). Reproductive wish in transsexual men. *Human reproduction, 27*(2): 483–487). The attempt to minimize the significance of infertility in this patient population provides additional evidence of a biased assessment of the risk of gender affirming medical interventions.

11. Dr. Adkins incorrectly summarizes my conclusions regarding the most prudent approach to addressing morbidity associated with sex-gender identity discordance. My opinion, succinctly stated, is that with the current evidentiary base, provision of gender affirming medical interventions for gender dysphoric youth does not meet the minimum standards of risk–benefit analysis. Until higher quality evidence is available, such interventions should be reserved for properly controlled and supervised clinical trials. This can and should include studies to test alternate hypotheses regarding etiology and approaches to treatment.

II. DECLARATION OF DR. TURBAN:

12. Dr. Turban's portrayal of the concerns I and other Defense expert witnesses have raised about properly interpreting the statements made by professional organizations regarding the care of children with gender dysphoria, particularly the claim that this represents scientific consensus is inaccurate on multiple levels. There is no basis for dismissal of the emerging concerns in other countries regarding the "Dutch model" (i.e., pubertal suppression and cross-sex

hormones) for gender dysphoric youth. Dr. Turban assumes that the conclusion made in the evidence based reviews from Sweden, Finland and the United Kingdom are due to a lack of consideration of recently published literature. However, as discussed in detail below, each of the studies published in the past year that he cites contain several serious methodological weaknesses. This is in agreement with the conclusions reached in the NICE reports and the data that formed the basis of the decisions reached in Sweden and the UK.

13. Dr. Turban lists 8 studies on puberty blockers and 6 studies on cross-sex hormones to assert that these interventions have been demonstrated to be safe and effective in the medical treatment of gender dysphoria. It is therefore important to objectively review study design, data, and conclusions that can be made from these reports.

14. With respect to studies on the effect of pubertal blockade on gender dysphoric youth:

a. De Vries 2011 – While this study (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. The Journal of Sexual Medicine, 8(8), 2276-2283) did show improvement in psychological function over baseline with use of puberty blockers, the authors acknowledged that they do not know why these improvements occurred and that psychological support or other reasons may have been responsible for the observed effect. This study highlights the need for proper control groups.

b. De Vries 2014 – The strength of this study (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) is that it evaluated psychological outcomes from the start of pubertal blockade to at least one year following gender affirming surgery. It is limited by potential for selection bias, a relatively small cohort size (55 patients out of the 196 consecutively referred patients qualified for the study), and similar to the 2011 De Vries study did not contain a control group. It is also noteworthy there was a patient in this cohort who died from surgical complications.

c. Van der Miesen 2020 – This paper (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: official publication of the Society for Adolescent Medicine*, *66*(6): 699–704) reports on a cross-sectional study comparing 272 youth who had just been referred to the gender center and 178 youth who had received gender affirming medical interventions. These do not represent randomly selected patients such as what could be obtained from a non-clinical probability sample. The authors of this study themselves acknowledge: "The present study can, therefore, not provide evidence about the direct benefits of puberty suppression over time and long-term mental health outcomes. Conclusions about long-term benefits of puberty suppression should thus be made with extreme caution needing prospective long-term follow-up studies with a repeated measure design with individuals being."

d. Turban 2020 – This paper (Turban, J.L., et al. (2020). Pubertal Suppression for Transgender Youth and Risk of Suicidal Ideation. *Pediatrics, 145*(2): e20191725) was cited and discussed in my initial declaration. I note that Dr. Turban uses

this study as support for benefit of pubertal blockade. However, the only statistically significant difference related to "lifetime suicidality." This does not demonstrate that it improved suicidality. Since this measure includes the study subjects' entire lifetime, it is entirely possible that there were baseline differences in suicidality that influence whether or not study subjects were offered pubertal blockade. It is also important to note that the study did not show statistical difference in past year suicidality. Conjecture regarding the influence of social stress on outcomes, while perhaps a testable hypothesis, was not examined in this study. There are also concerns with the data used (i.e. the 2015 US Transgender Survey) as I will discuss in more detail below.

e. Achille 2020 – Similar to the studies described above, limitations of this study (Achille, C., 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 Endocrinolology, 2020*(1): 8) include small number of subjects, short-term follow up (1 year), potential for recruitment bias, and lack of any control group.

f. Kuper 2020 – This study (Kuper, L.E., et al. (2020). Body Dissatisfaction and Mental Health Outcomes of Youth on Gender-Affirming Hormone Therapy. *Pediatrics, 145*(4)) represents a larger cohort than previous studies (148 subjects) and assesses longitudinal changes in reported outcome measures. It is limited by only assessing short-term (1 year) follow up. It is important to recognize that reports of suicidal ideation, suicide attempt, and non-suicidal self-injury were not statistically improved during the follow-up period. Similar to the 2020 Turban paper, raw numbers were actually increased (see Table 5 of the Kuper paper).

g. Carmichael 2020 – I referenced this paper (Carmichael, P., et al. (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) in my initial declaration. It is notable that Dr. Turban dismisses the lack of evidence for psychological benefit in this study as reflective of insufficient power to detect this outcome. As already noted, small sample size and lack of randomization are general limitations to most of the studies in this field, including this study. The number of subjects in this study is on par with the other published studies discussed above. The power to detect differences is influenced by the magnitude of effect. Based upon the data presented in this report, the intervention clearly did not produce a major effect on psychological outcome.

h. Dr. Turban lists an eighth study comparing 101 subjects who received psychotherapy and 100 subjects who received pubertal suppression plus psychotherapy. He does not provide a reference in his declaration but presumably this is the 2015 paper by Costa et al (Costa, R., et al. (2015). Psychological Support, Puberty Suppression, and Psychosocial Functioning in Adolescents with Gender Dysphoria. *The journal of sexual medicine*, *12*(11): 2206–2214. https://doi.org/10.1111/jsm.13034). In this study, both groups demonstrated clinically significant improvement in psychological functioning. While the abstract from this paper reports that the improvement was better at 12 months in patients who received pubertal blockade, at the endpoint of the study (18 months) this difference was no longer present. An unbiased conclusion from this study is that it demonstrates that psychotherapy is beneficial in gender dysphoric youth, not that puberty blockade was responsible for this effect.

15. Of the 6 studies referenced by Dr. Turban to support his conclusion that cross-sex hormones provide psychological benefit, 3 are the same studies used to argue for benefits of puberty blockade. It is important to note that Dr. Turban appears to recognize the limited power of these studies due to small sample sizes, yet he nevertheless ignores this fact in an attempt to build a case that quality scientific evidence of benefit exists in the extant published literature.

a. Lopez de Lara 2020 – Similar to the previously discussed papers, this study is limited by small sample size (23 subjects from a single center), short-term follow up (1 year), significant potential for selection bias based upon convenience sampling, and lack of randomization. The "control group" in this study consisted of untreated children without gender dysphoria matched for age, ethnicity, and socioeconomic status.

b. Kaltiala 2020 – This study is a retrospective chart review. In this case, direct quotation of the study results and conclusions of the authors places this study in proper context. In the summary of results, the authors state: "Those who did well in terms of psychiatric symptoms and functioning before cross-sex hormones mainly did well during real-life. Those who had psychiatric treatment needs or problems in school, peer relationships and managing everyday matters outside of home continued to have problems during real-life." They conclude: "Medical gender reassignment is not enough to improve functioning and relieve psychiatric comorbidities among adolescents with gender dysphoria. Appropriate interventions are warranted for psychiatric comorbidities and problems in adolescent development." This is hardly an endorsement for cross-sex hormone use in this patient population.

c. Allen 2020 – The study, while longitudinal in design, is limited by small sample size, lack of randomization, no control group and short-term follow up. The mean duration of treatment was one year with a minimum of only 3 months.

16. In all of these studies, even if one accepts the weakly supported conclusions that there is short-term psychological benefit, this does not establish that this benefit is sustained long-term or that the primary goal of suicide prevention is achieved. In fact, when considering the available data in the papers referenced by Dr. Turban, current suicidality was not significantly impacted. While such long-term studies do not exist for treated adolescents, the analogous data in treated adults indicates that all cause mortality in patients who received gender affirming medical interventions started to diverge from the background population 8–10 years later (see Figure 1 from Dhejne, C., et al. (2011). Long-Term Follow-Up of Transsexual Persons Undergoing Sex Reassignment Surgery: Cohort Study in Sweden, *PloS One 6*(2): e16885). The patients who had received such medical interventions were more likely to have died from any cause and from suicide, in particular.

17. Dr. Turban fails to acknowledge the limitations and weaknesses of the 2015 US Transgender Survey which served as the basis for his 2020 Pediatrics paper on lifetime suicidality for patients who were provided puberty blockers and the 2021 JAMA Surgery paper mentioned in Dr. Turban's declaration (Almazan, A.N. & A.S. Keuroghlian. (2021). Association Between Gender-Affirming Surgeries and Mental Health Outcomes. *JAMA Surgery, 156*(7): 611–618.). This includes convenience sampling, recruitment of patients through transgender advocacy organizations, demand bias (a.k.a. the good subject effect), a high number of respondents who reported having not transitioned medically or surgically (and reported no desire to do so in the future), and several data irregularities. This included a high number of

respondents who reported that their age was exactly 18 years. As noted by D'Angelo and colleagues, these irregularities raise serious questions about the reliability of the USTS data (D'Angelo, R., et al. (2021). One Size Does Not Fit All: In Support of Psychotherapy for Gender Dysphoria. *Archives of sexual behavior*, *50*(1): 7–16. https://doi.org/10.1007/s10508-020-01844-2)

18. Dr. Turban restates the common but erroneous assertion that it is unethical to conduct randomized controlled trials. This error is reflected in the false conception of how such studies can be performed. Contrary to "randomization to placebo," the control group need not be left untreated. For a controlled trial to be performed, ideally all interventions would be the same in both the intervention and control groups except for the independent variable. In this context, for example, a randomized controlled trial might involve intervention and control groups both receiving psychological support and treatment of associated co-morbidities while being randomized for one of two possible intervention for a defined period of time with close monitoring for adverse effects under the supervision of a standard institutional review board. There is no claim that such studies can or should be double blinded. Dr. Turban's assertion is based on the assumption that gender-transition procedures will benefit patients. It is contrary to the scientific method, however, to assume that a hypothesis regarding the effects of a medical intervention is correct without first rigorously testing for evidence to reject the null hypothesis (i.e. that there is no difference between the intervention and control group).

19. In Dr. Turban's claim that the risks of gender affirming medical interventions are mischaracterized in the defense declarations, he makes several false or misleading statements about the effects of these interventions. A brief summary of these issues is presented in the following paragraphs:

20. Dr. Turban minimizes the risk of impaired fertility and in two important areas conflates data in adolescents to very different patient populations. It is not correct to equate effects of pubertal blockade for precocious puberty to blocking normally timed puberty. During pre-pubertal life, gonadotropin signaling is normally quiescent. Puberty represents a critical period for full gonadal maturation leading to reproductive capacity. Blocking gonadotropin release during puberty restores the body to its pre-pubertal state, with quiescent gonadotropin signaling. A patient placed on GnRH agonists to block normally timed puberty will not have undergone the gonadotropin release necessary to have reached full gonadal maturation and subsequent reproductive capacity. Because of this effect on reproductive development, it is incorrect to infer that the effects of cross-sex hormones on an adult patient who was allowed to complete gonadal maturation during puberty will be the same when applied to adolescents who have not been allowed to complete pubertal development. Additionally, arguing that puberty blockade alone, without proceeding to cross-sex hormones, is reversible ignores the existing data showing that the vast majority of patients who receive puberty blockers will proceed to this later stage of intervention (see De Vries, A. L., et al. (2011). Puberty suppression in adolescents with gender identity disorder A prospective follow-up study. *The Journal of Sexual Medicine, 8*(8), 2276–2283).

21. Dr. Turban's dismissal of the risk of impaired fertility is also belied by the counseling that patients receive prior to starting cross-sex hormones. Recognition of the adverse effect of cross-sex hormones on gonadal maturation is precisely the basis for the requirement to counsel patients on fertility preservation prior to starting this intervention. An entire industry has evolved to provide assisted reproductive technologies to assist transgender patients in conceiving biological children after engaging in gender affirming medical interventions (See Maxwell, S., et

al. (2017). Pregnancy Outcomes After Fertility Preservation in Transgender Men. *Obstetrics and gynecology*, *129*(6): 1031–1034 regarding the need for assisted reproductive technology as cited by Dr. Adkins in her declaration footnote 9). Thus, to argue that fertility is not affected is blatantly false.

22. The concern for the effects of pubertal blockade on bone density is primarily related to peak bone mass, not current fracture risk. It is well established that the teenage years are critical for bone mineral accrual (see NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy (2001). Osteoporosis prevention, diagnosis, and therapy. *JAMA*, *285*(6): 785–795). Studies that have examined the effects of pubertal blockade have consistently demonstrated significant effects on this process (See Vlot, M.C., et al. (2017). Effect of pubertal suppression and cross-sex hormone therapy on bone turnover markers and bone mineral apparent density (BMAD) in transgender adolescents. *Bone, 2017 Feb.* (95): 11–19). There is published literature indicating partial improvement with initiation of cross-sex hormones, but the relevant readout is not just change from baseline, but differences between achieved bone mass and the expected increase in untreated individuals (See Wiepjes, et al. (2017). Bone Mineral Density Increases in Trans Persons After 1 Year of Hormonal Treatment: A Multicenter Prospective Observational Study. *Journal of bone and mineral research, 32*(6): 1252–1260). Fracture risk at 5–10 years is not the relevant concern but rather osteoporosis and increased fracture risk later in life.

23. The apparent dismissal of published studies showing metabolic changes associated with increased cardiovascular risk reflects the general biased assessment of relative risk versus benefit among those advocating for gender-transition procedures. While it is correct to acknowledge that there are many contributing factors to cardiometabolic risk, this does not

diminish the concerns that cross-sex hormones have many known and unknown risks. Even if one accepts the proposition that results are inconclusive, this would imply that they have not been demonstrated to be "safe." Given the short duration that most adolescents have been exposed to cross-sex hormones (generally less than 10 years) and the time to which metabolic changes could lead to clinically detectable atherosclerosis and myocardial infarction, it is not surprising that the current data remains inconclusive for this outcome measure. The demonstrated increased risk of thromboembolic stroke in biological males exposed to estrogen is not insignificant.

24. Dismissal of known and potential cancer risk, similar to concerns about cardiometabolic risk, is unwarranted. This is another area where a longer timeframe is required to establish meaningful conclusions. At best, the available evidence indicates that the influence of cross-sex hormones on cancer risk is inconclusive. In addition to increased risk from hormone exposure, failure to perform regular cancer screening when presenting to medical providers as a sex that is not in accord with a patient's internal anatomy and genetics adds another potential risk. While data is limited, it is false to claim that there is no evidence of risk.

25. In addition to the known and potential adverse physical effects of puberty blockers when used to halt normally timed puberty, social harms must also be considered. The Endocrine Society Guidelines include acknowledgement that experiencing puberty on a different timeline than one's peers has "potential harm to mental health (emotional and social isolation) if initiation of secondary sex characteristics must wait until the person has reached 16 years of age" and that they may experience "the sense of social isolation from having the timing of puberty be so out of sync with peers." (See Hembree, W.C., et al. (2017). Endocrine Treatment of Gender-

Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab, 102*(11): 3869–3903.)

26. Claims by Dr. Turban that the reports from the United Kingdom, Sweden, and Finland do not accurately summarize the evidence (¶53) appear to reflect an underlying bias. The conclusions in these reports highlight the poor quality of research in this field and the many unanswered concerns about relative risk versus benefit of gender affirming medical interventions. As I have discussed above, the additional studies referenced by Dr. Turban in his declaration do not rectify these concerns but rather continue to reflect the weak evidentiary base. The data cited in formulating the Finland, Sweden, and U.K. reports support the recommendation for, at a minimum, a pause in the unquestioning advocacy for this gender affirming medical interventions as the best, and often only, approach to alleviate suffering in this vulnerable patient population. There remains a clear need for ongoing research that considers alternate hypotheses regarding etiology and approaches to treatment.

27. Similar to Dr. Adkins, Dr. Turban refers to his book chapter to perpetuate the unsubstantiated claim that desistance rarely if ever occurs if a patient continues to self-report a sex discordant gender identity after puberty has started. Yet in his declaration he fails to cite any scientific study to support this claim. As noted in my declaration, the only citation for this claim is another book that does not provide such evidence.

28. Dr. Turban provides an erroneous description of the data available regarding biological influences for sex-discordant gender identity. A key distinction must be made between genetic <u>influences</u> and genetic <u>determinants</u>. There are many conditions (e.g. alcoholism and compulsive gambling) that are known to have a genetic link. However, predisposition does not guarantee outcome. There are numerous ways in which genetic

predisposition can contribute to gender dysphoria but this does not prove that this outcome is predetermined at birth. The best example of this association is the established increased risk of sex-discordant gender identity in autistic children. Reference to neuroimaging studies also fail to establish a biological determinant of sex-discordant gender identity. Dr. Turban ignores the evidence I provided in my declaration regarding wide overlap in structural differences between males and females, neuroplasticity, and unresolved questions regarding cause versus effect.

29. Dr. Turban's dismissive comments regarding the methodological limitations and high potential for bias in the 2105 U.S. Transgender Survey require some comment to allow the Court to properly understand the concerns raised. This survey has been used in a number of recent publications including Dr. Turban's 2020 study published in Pediatrics on puberty blockers and lifetime suicidal ideation. One need not invoke a conspiracy theory to understand the high potential for recruitment bias, recall bias, and the inability to substantiate the claims of survey respondents. The most significant limitations of this survey are adequately outlined by the 2021 paper of D'Angelo et al. (see D'Angelo, et al. (2021), cited fully above).

III. SUPPLEMENTAL DECLARATION OF DR. ANTOMMARIA:

30. A major focus of Dr. Antommaria's first and supplemental declarations is on the question of what constitutes experimentation versus standard medical practice. Beyond formal definitions and colloquial uses of these terms, the underlying premise is that gender affirming medical interventions (including halting of normally timed puberty, administration of cross-sex hormones and surgical alteration of primary and secondary sexual anatomy) is known to be both safe and effective in alleviating distress in youth who experience sex-discordant gender identity. An associated presumption, used by each of the Plaintiffs' expert witnesses, is that this will prevent affected adolescents from committing suicide. This is reflected in Dr. Antommaria's comments of his supplemental declaration (¶6). Understanding of the pervasive limitations and

weaknesses in the published literature in this field, most notably the lack of evidence showing that this approach substantially improves long-term suicidality and mental health needs in children is the primary concern that led to the passing of the Arkansas SAFE act. Concerns are augmented by the failure to investigate alternate hypotheses with outright rejection of any intervention that may result, intended or unintended, in realignment of gender identity with biological sex. While medical practitioners in general, and pediatricians in particular, must often engage in attempts to provide care in the absence of definitive outcome data, the degree of caution used in engaging in such treatments is generally aligned with the ambiguities present. Such responsible conduct is largely absent in the rapidly expanding field of transgender medicine. Given the continued poor understanding of gender dysphoria and the relative risks and benefits of various treatment approaches, it is prudent to conduct medical interventions only as part of controlled clinical trials.

31. Dr. Antommaria correctly notes that many medications used in pediatric patients have not been FDA approved for children. There are many ways in which "off label" use is permissible. While in some cases "off-label use may be well-supported by evidence," this is not the case for halting normally timed puberty for gender dysphoric youth. In prescribing medications "off-label," physicians assume responsibility for the risk of an adverse event and must inform patients of such risk. As demonstrated by the comments of the Plaintiffs' witnesses in this case, it is doubtful that the use of puberty blockers to halt normally timed puberty is presented in this way. Repeatedly, the assertion is made that the use of puberty blockers is known to be safe and fully reversible. The falsehood of this claim was discussed in my initial declaration including reference to my published article that covers this in greater detail (see Hruz, P.W., L.S. Mayer, & P.R. McHugh. (2017). Growing Pains: Problems with Puberty

Suppression in Treating Gender Dysphoria. *The New Atlantis, 52*(Spring 2017): 3–36). In this context, acknowledgement of the off-label use of this class of medication is appropriate and informative without insinuation that the intent is to portray such use as illegal.

32. In making his assertion that it is justifiable to make strong recommendations based upon low quality of evidence, Dr. Antommaria fails to present the entire context for the importance of understanding bias in research and the reasons why the GRADE system was developed in the first place. The creation and intended use of the GRADE system is well described in a series of papers published in the BMJ in 2008. Details and links to these papers are readily available on the GRADE workgroup website (https://www.gradeworkinggroup.org/). There are unique aspects to the treatment of gender dysphoria that require specific comment regarding strong recommendations for interventions that are based upon low quality evidence. As clearly stated by the GRADE workgroup, "strong recommendations mean that most informed patients would choose the recommended management and that clinicians can structure their interactions with patients accordingly." Most patients who present to gender clinics desire (and often demand) gender affirming medical interventions. Under such circumstances, making a strong clinical recommendation does not ensure that this is based upon careful assessment of relative risk versus benefit.

33. Dr. Antommaria's dismissal (¶14) of the Bränström paper (Bränström, R., & Pachankis, J. E. (2020). Reduction in Mental Health Treatment Utilization Among Transgender Individuals After Gender-Affirming Surgeries: A Total Population Study. *The American journal of psychiatry, 177*(8): 727–734) as being irrelevant to the assessment of risks and benefits of gender affirmation medical interventions for gender dysphoric youth reflects the prevailing but erroneous assumption that this approach is founded on solid scientific grounds. It reflects my

stated concern regarding confirmation bias. When presented with new evidence that challenges the assertion that mental health is improved by cross-sex hormones and gender affirming surgery, Dr. Antommaria continues to rely on the low quality evidence contained in the Endocrine Society Guidelines. It is even more revealing that what was actually found in the data from the Bränström study (i.e. that cross-sex hormones and surgery provided no long-term change in mental health needs) is in stark contrast to how this paper was presented. The failure to appreciate or even consider these concerns is highly concerning regarding ability to objectively opine on the scientific evidence related to treatment of gender dysphoria.

34. The Plaintiffs' experts, including Dr. Antommaria, associate gender affirming medical interventions with the treatment of patients with disorders of sexual development ("DSDs"). It is important to note the major differences between these two conditions and the basis for medical care.

a. DSDs represent a unique situation where sexual identity can be ambiguous. This is the one situation where sex is tentatively assigned at birth. In the absence of a DSD, sex is correctly identified, not assigned, at birth. As data becomes available on etiology and expected outcomes related to sexual function, sex may be "reassigned." Note the importance of distinguishing the use of term "sex" and "gender" as they are intended to reflect different aspects of sexual form and expression.

b. Gender identity in patients with DSDs will be highly dependent on the underlying defect present.

c. Nearly all patients with gender dysphoria have normally formed and functional genitalia and gonads prior to the start of affirmative interventions. In contrast, many if not most patients with DSD have impaired or absent fertility.

d. Surgeries for minors with DSDs are generally directed to correcting anatomical defects with clinical significance. This would include defects that restrict urinary outflow, increase risk of urinary tract infections, or pose a cancer risk (e.g. intraabdominal testes or other dysgenetic gonads containing a Y-chromosome)

e. DSD advocacy groups strongly argue against medical interventions to change sexual appearance. The focus is on preventing surgeries in infancy. Older patients are quite vocal about the potential harms of genital surgeries.

f. The calculation of relative risk versus benefit of surgeries for DSDs most definitively is not the same as performing similar procedures for management of gender dysphoria.

35. Contrary to the biased and inaccurate conclusions of Drs. Turban, Adkins, and Antommaria as conveyed in their declarations, serious questions remain regarding the best approach to care for individuals who express an understanding of their gender identity that is discordant with their biological sex to alleviate dysphoria and associated psychological morbidity. Scientific deficiencies include understanding of etiology, the influence of gender affirming medical care on persistence versus desistence, long-term psychological health following gender affirming medical interventions in affected youth, and adverse physical effects of these interventions. Existing evidence claiming benefit remains of low quality and is hampered by major methodological limitations and weaknesses. When objectively reviewed, these data indicate that suicidality remains high in affected youth even after receiving hormonal interventions. This cannot be explained entirely by the social stress hypothesis. Emerging data challenges prevailing assumptions of the ability of hormonal and surgical interventions to reduce psychological morbidity in affected adults. Under these circumstances, it is appropriate to

restrict such interventions in children to properly designed and supervised clinical trials that explore a full range of alternative hypotheses.

I declare under penalty of perjury that the foregoing is true and correct.

Executed on July 19, 2021.

Paul W. Hruz, M.D., Ph.D.

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LETTER TO THE EDITOR

One Size Does Not Fit All: In Support of Psychotherapy for Gender Dysphoria

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Turban, Beckwith, Reisner, and Keuroghlian (2020) published a study in which they set out to examine the effects of gender identity conversion on the mental health of transgender-identifying individuals. Using the data from the 2015 U.S. Transgender Survey (USTS) (James et al., 2016), they found that survey participants who responded affirmatively to the survey question, "Did any professional (such as a psychologist, counselor, religious advisor) try to make you identify only with your sex assigned at birth (in other words, try to stop you being trans)?" reported poorer mental health than those who responded negatively to the question. From this, Turban et al. concluded that gender identity conversion efforts (GICE) are detrimental to mental health and should be avoided in children, adolescents, and adults. The study's conclusions were widely publicized by mass media outlets to advocate for legislative bans on GICE, with the study authors endorsing these calls (Bever, 2019; Fitzsimons, 2019; Turban & Keuroghlian, 2019).

We agree with Turban et al.'s (2020) position that therapies using coercive tactics to force a change in gender identity have no place in health care. We do, however, take issue with their problematic analysis and their flawed conclusions, which they use to justify the misguided notion that anything other than "affirmative" psychotherapy for gender dysphoria (GD) is harmful and should be banned. Their analysis is compromised by serious methodological flaws, including the use of a biased data sample, reliance on survey questions with poor validity, and the omission of a key control variable, namely subjects' baseline mental health status. Further, their conclusions are not supported by their own analysis. While they claim to have found evidence that GICE is associated with psychological distress, what they actually found was that those recalling GICE were more likely to be suffering from serious mental illness. Further, Turban et al.'s choice to interpret the said association as evidence of harms of GICE disregards the fact that neither the presence nor the direction of causation can be discerned from this study due to its cross-sectional design. In fact, an alternative explanation for the found association—that individuals with poor underlying mental health were less likely to be affirmed by their therapist as transgender—is just as likely, based on the data presented.

Arguably, even more problematic than the flawed analysis itself is the simplistic "affirmation" versus "conversion" binary, which permeates Turban et al.'s (2020) narrative and establishes the foundation for their analysis and conclusions. The notion that all therapy interventions for GD can be categorically classified into this simplistic binary betrays a misunderstanding of the complexity of psychotherapy. At best, this blunt classification overlooks a wide range of ethical and essential forms of agenda-free psychotherapy that do not fit into such a binary; at worst, it effectively mis-categorizes ethical psychotherapies that do not fit the "affirmation" descriptor as conversion therapies. Stigmatizing non-"affirmative" psychotherapy for GD as "conversion" will reduce access to treatment alternatives for patients seeking non-biomedical solutions to their distress.

We originally raised our concerns about the quality of Turban et al.'s (2020) study and the validity of their conclusions in a Letter to the Editor of *JAMA Psychiatry*, where the study had been published. However, our letter was rejected, apparently due to space limitations. In the ensuing months, as we observed Turban et al.'s unsupported claims of the harms of psychotherapy for GD taking root globally (United Nations, 2020), we felt compelled to write a more detailed critique of the study, which we present here. Our aim is to put the spotlight on the more problematic areas of Turban et al.'s analysis and to illustrate how heeding their recommendations will limit access to ethical psychotherapy for

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individuals suffering from GD, further disadvantaging this already highly vulnerable population.

Biased Sample

Turban et al.'s (2020) analysis used data from the 2015 USTS survey of transgender-identifying individuals (James et al., 2016). This survey used convenience sampling, a methodology which generates low-quality data (Bornstein, Jager, & Putnick, 2013). Specifically, the participants were recruited through transgender advocacy organizations and subjects were asked to "pledge" to promote the survey among friends and family. This recruiting method yielded a large but highly skewed sample. While Turban et al. acknowledged that the USTS may not be representative of the U.S. transgender population, they treat it as a valid source of data for major policy recommendations, disregarding the significant bias in the underlying data.

To demonstrate this apparent bias, we have constructed Table 1, which compares the demographic characteristics of the USTS participants to those of transgender participants from a high-quality probability sample collected by the Centers for Disease Control Behavioral Risk Factors Surveillance System (BRFSS) (Baker, 2019; CDC, 2014–2017). As Table 1 illustrates, even after applying weighting to correct for known survey biases, the USTS participants were far more likely to be young (42% vs. 22% were 18–24 years old) and educated (47% vs. 14% had completed post-secondary education) than BRFSS participants. They were far less likely to own a home (16% vs. 55%) or to be married or coupled (18% vs. 46%). They were also much more likely to have a non-binary identity (38% vs. 22%) and a markedly different self-reported sexual orientation: Only 15% of the USTS participants reported a heterosexual orientation, compared to 69% of the BRFSS participants. (It is not clear if sexuality in either case was reported relative to one's sex or gender identity.)

A number of additional data irregularities in the USTS raise further questions about the quality of data captured by the survey. A very high number of the survey participants (nearly 40%) had not transitioned medically or socially at the time of the survey, and a significant number reported no intention to transition in the future. The information about treatments received does not appear to be accurate, as a number of respondents reported the initiation of puberty blockers after the age of 18 years, which is highly improbable (Biggs, 2020). Further, the survey had to develop special weighting due to the unexpectedly high proportion of respondents who reported that they were exactly 18 years old. These irregularities raise serious questions about the reliability of the USTS data.

In addition to these demonstrable data problems, there are a number of other biases in the USTS data that likely skewed the responses. By targeting transgender advocacy groups, the survey underrepresented the experiences of transgender individuals who are not politically engaged. The emphasis on the survey's goals to highlight the injustices suffered by transgender people during the recruitment stage and in the introduction of the survey instrument itself made it vulnerable to overreporting of adverse experiences due to "demand bias" (also known as the "good subject effect"). This form of bias occurs when the researchers reveal their hypothesis and aims, which encourages participants to support the investigator's aims with their answers (Nichols & Maner, 2008; Orne, 1962; Weber & Cook, 1972). Finally, the experiences of detransitioners and desisters were not included, as they were disqualified from completing the survey. Failure to include detransitioned and desisted individuals in research regarding psychological interventions for GD is a serious oversight. These individuals, whose transgender identification was transient, may have been hurt by therapies that affirmed them as transgender, and may have benefitted from therapies that helped them successfully ameliorate their GD (D'Angelo, 2020b).

These serious limitations of the USTS survey greatly undermine the validity of the findings it produced. It is imperative that any analysis based on this low-quality biased sample is validated using a high-quality probability sample before any recommendations stemming from the analysis of these data can be used to shape clinical or policy decisions.

Invalid Measure of Gender Conversion Therapy

Turban et al.'s (2020) conclusions rest on the assumption that they have a valid way of determining whether or not a respondent was exposed to the unethical practice of conversion therapy. Yet, the USTS question they relied on (Question 13.2) is too non-specific to serve as a valid measure of gender conversion therapy. Firstly, the question conflates mental health encounters with interactions with other types of professionals. Secondly, there is no information about whether the recalled encounter was self-initiated or coerced. Thirdly, it does not differentiate between diagnostic evaluations or a specific therapeutic intervention. There is also no information about whether the focus of the encounter was gender dysphoria or another condition. And finally, it does not determine whether shaming, threats, or other unethical tactics were utilized during the encounter. This lack of context and detail renders the question incapable of differentiating between ethical non-affirmative (neutral) encounters and unethical conversion therapy.

Consider a common situation where the patient is seeking approval for medical treatment for GD, where the role of the therapist is to assess the individual's mental health to

Table 1 Comparison of demographic characteristics of transgender-identifying individuals in the 2015 US Transgender Survey (USTS) and the Behavioral Risk Factor Surveillance System Survey (BRFSS) 2014–2017

	USTS, 2015[a] Transgender ($n = 27{,}715$)	BRFSS, 2014–2017[b] Transgender ($n = 3075$)
Characteristic		
Gender identity		
Transgender women (male to female)	33%	48%[e]
Transgender men (female to male)	29%	30%[e]
Non-binary/gender-non-conforming	38%	22%[e]
Sexual orientation[c]		
Heterosexual	15%	69%
Lesbian or gay	16%	10%
Bisexual	14%	15%
Other[d]	55%	7%
Age		
18–24	42%	22%
25–44	42%	30%
45–64	14%	32%
65 +	2%	17%
Race/ethnicity		
White, non-Hispanic	62%	55%
Black, non-Hispanic	13%	16%
Asian, Native Hawaiian, or Pacific Islander	5%	5%
Other, non-Hispanic	3%	5%
Hispanic	17%	19%
Education level		
Did not graduate high school	2%	21%
Graduated high school	11%	33%
Some college or technical school	40%	32%
Graduated college or technical school	47%	14%
Annual household income		
< 25,000	38%	39%
25,000–49,999	24%	24%
50,000 +	38%	37%
Home ownership		
Own	16%	55%
Rent	44%	35%
Other arrangement	40%	10%
Marital status		
Married or coupled	18%	46%
Divorced, separated, or widowed	10%	21%
Never married	72%	33%

[a]US Transgender Survey, 2015 (James et al., 2016). Weighted data

[b]CDC BRFSS Survey, 2014–2017 (Baker, 2019). Weighted data

[c]Sexual orientation reported based on the respondent self-identification

[d]Combines all the response options other than "homosexual," "lesbian/gay," or "bisexual."

[e]Calculated using 2014–2017 BRFSS data (CDC, 2014–2017). Weighted data

ensure that GD is not secondary to another condition. Such encounters can be experienced by patients as an attempt to withhold the treatment they so desperately want (Chiland, 1997). Further, patients with psychiatric diagnoses, highly prevalent in transgender-identifying populations (Gijs, van der Putten-Bierman, & De Cuypere, 2013; Goodman & Nash, 2018; Wanta, Niforatos, Durbak, Viguera, & Altinay, 2019), can potentially experience or misinterpret neutral

interpersonal interactions as invalidating or rejecting (Barnow et al., 2009; Beck & Bredemeier, 2016; Gotlib, 1983). Not only does the survey question provide no detail to help discriminate between these essential therapy encounters and unethical conversion therapy, but it arguably biases the recall of neutral encounters toward recall of conversion by using emotionally charged language (e.g., "stop you being trans") and by conflating recall of religiously motivated encounters with clinical ones.

Turban et al. (2020) ignored these issues and instead created a veneer of certainty by referring to USTS question 13.2 as GICE and used it throughout the paper as though it were a valid equivalent of conversion therapy. Not only it the term itself novel (the lead author referred to the same USTS question by yet another term, "PACGI," in a publication just weeks earlier [Turban, King, Reisner, & Keuroghlian, 2019]), but its equivalency to conversion therapy is highly debatable, in part due to the fact that the term itself has not been defined, other than through a circular reference to USTS question 13.2 itself.[1] Accounting for the many gray areas in the question wording, we propose that GICE is "any professional encounter which the subject recalls as non-affirmative of their transgender identity." As we have demonstrated, it is not uncommon for agenda-free, neutral therapy interventions to be experienced by the subjects as non-affirmative. However, non-affirmative is not the same as "conversion," as the latter implies a therapist agenda and an aim for a fixed outcome (American Psychological Association, 2015). In fact, it is the utter inability of USTS question 13.2, and consequently, GICE, to differentiate between agenda-free ethical psychotherapy and coercive, agenda-driven therapy, that is the Achilles heel of Turban et al.'s entire argument.

Misinterpretation of a Key Scale

A key finding of Turban et al.'s (2020) analysis is that the USTS participants who recalled exposure to GICE were more likely to report severe psychological distress, as evidenced by their score of ≥ 13 on the K-6 scale. From this, Turban et al. concluded that GICE has adverse effects on mental health. We will address the unsupported claim of causation in a subsequent section. Here, we would like to further explore the use of the K-6 scale to make these claims, and its implications.

The K-6 scale, and its cutoff score of ≥ 13, was specifically developed by Kessler et al. (2003) in order to discriminate between cases of non-specific psychological distress and cases of serious mental illness (SMI). Scoring ≥ 13 is predictive of having a DSM diagnosis of schizophrenia, bipolar disorder, and a range of other major mental health conditions that cause serious functional impairment (Substance Abuse and Mental Health Services Administration, 2020). Thus, Turban et al.'s (2020) finding of an association between the recall of GICE and scoring ≥ 13 actually suggests that the USTS participants recalling GICE were more likely to have a severe mental illnesses diagnosis than those not recalling GICE. Further, any claim of causation, which Turban et al. continue to suggest throughout the paper (however unsupported by the study design), would imply that exposure to GICE caused serious mental illness, in previously mentally well populations. This is a highly speculative and implausible hypothesis, which further challenges their claims.

Omission of a Key Control Variable

Turban et al.'s (2020) hypothesis, namely, that GICE exposure (during lifetime, as well as in childhood) causes poor mental health and contributes to suicide attempts, is further weakened by a significant flaw in their data analysis: failure to control for the individuals' pre-GICE-exposure mental health status. Not only does this critical omission confound the association between exposure to GICE and present mental health, but it may mask reverse causation, namely, that it was the individual's underlying poor mental health that led to their experience of GICE in the first place.

Let us revisit the example of a common clinical encounter in which a person with GD and one or more comorbid psychiatric conditions presents for assessment with the goal of obtaining approval for cross-sex hormones. An assessment of such a complex presentation generally requires multiple sessions and involves ascertaining whether the GD is secondary to another condition. It is also likely that the clinician might focus on treating the comorbid condition(s) first, before pursuing "gender-affirming" interventions. While such a contact would be recalled by the respondent as non-affirmative and thus likely classified as GICE, it is the patient's poor mental health status that led to the non-affirming content of the encounter, rather than vice versa. If the said individual had attempted suicide in the past or continued to struggle with mental illness more recently, Turban et al.'s (2020) analysis would erroneously conclude that GICE was likely responsible for those difficulties, when, in fact, no such causation occurred.

In fact, failure to control for the subjects' baseline mental health makes it impossible to determine whether the mental health or the suicidality of subjects worsened, stayed the same, or potentially even improved after the non-affirming encounter. Given the high rate of co-occurring mental illness in transgender-identifying patients (Gijs et al., 2013; Goodman & Nash, 2018; Wanta et al., 2019), failure to control for prior mental health status is a serious methodological flaw.

[1] Psychological Attempts to Change Gender Identity.

Internal Inconsistencies in Mental Health Measures

Turban et al.'s (2020) finding that mental health outcomes of persons exposed to GICE are worse than those whose encounters were "gender-affirming" is weakened by internal inconsistencies in the mental health outcome measures. We have already discussed the fact that the threshold chosen by Turban et al. on the K-6 scale detects serious mental illness, rather than distress. Another measure of psychological distress chosen by Turban et al.—substance misuse—was not significantly different between GICE and the non-GICE group. More importantly, there is a lack of consistency in the suicide measures. While lifetime suicide attempts were elevated among the GICE group, total suicide attempts in the prior 12 months, as well as suicide attempts requiring hospitalization, which generally indicate more serious attempts rather than non-suicidal self-injury, were not significantly different between the two groups. Turban et al. did not address this inconsistency. Nor did they explore the relationship between suicidality and the higher levels of serious mental illness among the GICE group, despite the well-documented link between serious mental illness and suicide (Bertolote, Fleischmann, De Leo, & Wasserman, 2004). Turban et al. did not heed their own warning not to attribute the increased lifetime suicidality entirely to GICE since "other factors are also likely to be associated with suicidality among gender-diverse people." Instead, they treat the inconsistent and unclear association between GICE and suicidality as causative and infuse it with an air of certainty by elevating it into title of their paper.

Claim of Causation When Only an Association Has Been Found

Although a causative relationship between recalled GICE and adverse mental health status is possible (even if direction of the causality is unclear), the cross-sectional design of the USTS is not capable of determining causation. While Turban et al. (2020) acknowledged this limitation and correctly referred to the relationship they found as an association, they strongly implied causation throughout their discussion, as well as in their "Conclusions and Relevance" section, which states, "These results support policy statements from several professional organizations that have discouraged this [GICE] practice." Presenting a highly confounded association as causation is a serious error, given its potential to dangerously misinform and mislead clinicians, policymakers, and the public at large about this important issue.

Discussion

The fact that coercive techniques to force unwanted changes in individuals are unethical and have no place is modern psychotherapy is self-evident and needs no additional justification. However, as we have demonstrated, Turban et al. (2020) failed to prove that GICE, as defined by affirmative answers to the USTS question, caused poor mental health or suicide attempts in study subjects. Further, since Turban et al. failed to establish equivalence between GICE, which likely subsumes a range of ethical non-affirmative interventions, and "gender conversion therapy," which implies unethical and coercive attempts to force a change in one's identity, their use of the study findings in support of a ban on "gender conversion therapy" is without any foundation.

Rather than appropriately acknowledging the significant study limitations and calling for more research, Turban et al. (2020) used their flawed findings to engage in a media campaign promoting legislative bans of GICE. Two of the study authors penned an op-ed in which they state, "It's time for conversion efforts to be illegal in every state, before more people die" (Turban & Keuroghlian, 2019). Turban, the lead author, repeated these sweeping, emotive claims on several highly visible national media platforms (Bever, 2019; Fitzsimons, 2019). In contrast, the debate regarding this study in the scientific arena was not allowed to occur. To the best of our knowledge, all of the letters written to the Editor of *JAMA Psychiatry*, many by respected academics and clinicians who outlined the serious problems in the study, have been rejected (some of them were later submitted as non-indexed comments in the online publication). The omission of these important arguments from the scientific discourse stifles scientific debate and perpetuates the current politicization of transgender health care, where treatment decisions are increasingly legislated by politicians.

While the poor study methodology is unfortunate, arguably, the most problematic aspect of Turban et al.'s (2020) work is the choice to view psychotherapy through a binary of "affirmation" versus "conversion," resulting in a conflation of ethical non-affirmative psychotherapy with conversion therapy. The self-evident crudeness of the GICE versus "affirmation" binary, promoted by Turban et al., and the potential harms of such a simplistic view of psychotherapy are illustrated by the following examples.

Consider a female victim of sexual assault, who subsequently develops an intense discomfort with her female anatomy and expresses a desire to undergo biomedical interventions to change her body. It would be unethical for the

clinician to overlook the contribution of sexual victimization to this nascent GD. A therapist enthusiastically supporting this patient's new male identity would be failing to provide appropriate treatment for what amounts to a post-traumatic condition, instead providing an inappropriate treatment with the potential to harm. Similarly, a boy who has been traumatized by relentless bullying due to his gender "non-conformity" (e.g., interest in classical music or fashion and avoidance of sports) may conclude that if he were a girl then he would "fit in" and the humiliation would stop. In this case too, gender-affirming interventions miss the mark when what this traumatized young person requires is psychotherapy.

Another obvious difficulty arises when same-sex attracted adolescents report cross-sex identifications. Research shows that a high number of homosexual adults have experienced periods of "cross-sex" behaviors and cross-gender identification in childhood and adolescence, often to a degree that is severe enough to warrant the diagnosis of GD, or gender identity disorder, as it was previously known (Bailey & Zucker, 1995; Bell, Weinberg, & Hammersmith, 1981; Hiestand & Levitt, 2005; Li, Kung, & Hines, 2017). When a dysphoric same-sex attracted young person in the midst of this developmental process presents for mental health care, a clinician overtly affirming the patient's cross-sex gender identity would be failing this patient by not addressing the patient's struggle with same-sex attraction and/or internalized homophobia. In fact, some homophobic societies and indeed families that reject homosexuality among their children have embraced the "affirmative" biomedical pathway (Bannerman, 2020; Hamedani, 2014), which poses a question as to whether "affirmative" care in some instances serves the role of gay conversion therapy.

Further, GD can present as a transient symptom that resolves spontaneously or in the context of developmentally informed psychotherapeutic treatment. Some common examples of transient gender-dysphoric states include adolescents girls, often on the autism spectrum, experiencing distress around the physical and social changes of puberty or gender-non-conforming young women struggling with shame about being seen as "butch." These individuals, searching for ways to understand and remedy their distress, can incorrectly attribute their discomfort to being transgender. Several case reports (Churcher Clarke & Spiliadis, 2019; Lemma, 2018; Spiliadis, 2019) indicate that the distress of young people with GD can lessen or resolve with appropriate psychotherapeutic interventions that address the central issues.

If anything other than "affirmation" is viewed as GICE, it follows that the provision of psychotherapy in these clinical scenarios would be seen as harmful conversion efforts. Yet these therapeutic interventions do not aim to convert or consolidate an identity, but instead aim to help individuals gain a deeper understanding of their discomfort with themselves, the factors that have contributed to their distress, and their motivations for seeking transition (Bonfatto & Crasnow, 2018; D'Angelo 2020a). These exploratory questions are consistent with the principle of therapeutic neutrality—a cornerstone of ethical psychotherapy (Simon, 1992). In fact, both "conversion" and "affirmation" therapy efforts carry the risk of undue influence, potentially compromising patient autonomy. In contrast, the provision of a neutral, unbiased psychotherapeutic process that allows these patients to clarify their feelings and assess the various treatment options, which range from non-invasive to highly invasive, irreversible procedures, is arguably the only way that meaningful informed consent for the latter can be obtained (Levine, 2018).

Turban et al.'s (2020) unproven assertion that non-affirming therapies are dangerous stands in contrast to the documented risks and uncertainties associated with hormonal and surgical interventions that are a core part of the "affirmation" treatment path. Until recently, puberty blockers were considered safe and fully reversible, but there is now emerging evidence of their adverse effects on the bone and brain health (Klink, Caris, Heijboer, van Trotsenburg, & Rotteveel, 2015; Joseph, Ting, & Butler, 2019; Schneider et al., 2017). Additionally, since almost all of the children treated with puberty blockers proceed to cross-sex hormones (de Vries et al., 2014), concerns have been raised that puberty blockers may consolidate gender dysphoria in young people, putting them on a lifelong path of biomedical interventions.

Cross-sex hormones are associated with cardiovascular complications, including a fourfold increased risk of heart attacks in biological females, and a threefold increase in the incidence of venous thromboembolism in biological males (Alzahrani et al., 2019; Nota et al., 2019). "Gender-affirming" surgeries can cause urethral stricture, neo-vaginal stenosis and prolapse, and long-term post-mastectomy pain (Larsson, Ahm Sørensen, & Bille, 2017; Manrique et al., 2018; Rashid and Tamimy, 2013; Santucci, 2018). The effects of "gender-affirmative" care on fertility have not been adequately studied, but infertility is a likely outcome, depending on the specific treatments pursued. It remains unclear whether fertility concerns will be important to this group of patients as they mature, but increasingly, gender centers are recommending fertility preservation procedures prior to undergoing hormonal interventions.

Given the absence of robust long-term evidence that the benefits of biomedical interventions outweigh the potential for harm, especially among young people (Heneghan & Jefferson, 2019), it is self-evident that the least-invasive treatment options should be pursued before progressing to more risky and irreversible interventions. To the extent that psychological treatments can help an individual obtain relief from GD without undergoing body-altering interventions, ensuring access to these interventions is not only ethical and prudent but also essential.

The importance of continued access to non-affirmation–non-conversion, agenda-free evaluation, and treatment is further underscored by the increasing numbers of detransitioning patients speaking out in social media forums following gender transitions they have come to regret (Entwistle, 2020). The rate of regret, detransition, and desistance from transgender identification is largely unknown (Butler & Hutchinson, 2020). The majority of patients with classical, childhood-onset gender dysphoria (61%-98%) desist from transgender identification some time in adolescence or young adulthood (Korte et al., 2008; Steensma, McGuire, Kreukels, Beekman, & Cohen-Kettenis, 2013; Zucker, 2018). The minority who persist with their transgender identification into adulthood and undergo "gender-affirmative" surgeries have been reported to have low rates of regret (van de Grift, Elaut, Cerwenka, Cohen-Kettenis, & Kreukels, 2018) and detransition (Dhejne, Öberg, Arver, & Landén, 2014). However, these studies may understate true regret rates due to overly stringent definitions of regret (i.e., requiring an official application for reversal of the legal gender status), very high rates of participant loss to follow-up (22%-63%) (D'Angelo, 2018), and an unexplored relationship between regret and high rates of post-transition suicide (Dhejne et al., 2011).

The novel cohort of young GD patients increasingly presenting for help is poorly understood. It is overrepresented by adolescent females with recent-onset GD and with comorbid mental health and neurocognitive issues (Bewley, Clifford, McCartney, & Byng, 2019; de Graaf, Giovanardi, Zitz, & Carmichael, 2018; Kaltiala-Heino, Bergman, Työläjärvi, & Frisen, 2018; Littman, 2018; Zucker, 2019). The trajectory of GD among these young patients, including the rates of desistance and detransition, remains unknown. However, many of us, along with our colleagues, are seeing increasing numbers of detransitioners with adolescent-onset GD who regret not having received exploratory psychotherapy to help them understand their distress and the desire to transition before they underwent irreversible medical and surgical treatments. Equally concerning, a number report that when doubts about their own transgender status arose, their therapists continued to affirm them as transgender, attributing their doubts to internalized transphobia, and encouraging them to continue medical interventions, which, in turn, unnecessarily exacerbated the psychological and physical harms.

Advocates of "affirmative care" tend to downplay the risks of iatrogenic harms resulting from inappropriate transitions and minimize the seriousness of the resulting harms by describing them as merely "cosmetic" (Turban & Keuroghlian, 2018). In stark contrast to these assertions, we are seeing increasing numbers of patients who feel deeply traumatized by inappropriate transitions. They suffer from irreversible physical changes, including alterations to their genitals and sexual function, sterility, painful vaginal atrophy, chest/breast alteration and scarring, deepening of the voice, unwanted permanent changes to facial hair growth, male-pattern baldness, urinary incontinence, and other lasting effects. Apart from the distress that these changes cause, they also negatively impact many areas of their lives, including their ability to form a stable gender identity (many feel trapped in a "gender no-man's land"), to find romantic partners and supportive social networks, to bear children, or to secure employment. The process of coming to terms with these consequences of their transition is psychologically difficult and can be profoundly painful.

Given the risky and irreversible nature of "gender-affirming" treatments, it is concerning that for many years now, there has been a lack of systematic research into the role that developmentally informed psychotherapy can play in the amelioration of GD, especially among young people. The need for the continued development and evaluation of non-invasive psychological treatment alternatives for GD has never been more urgent, given the fact that over 3% of young people report transgender identification or ideation (Johns et al., 2019). Given the sheer magnitude of this change, and the potential for exponential growth in the number of individuals who are medically harmed, it is time to raise the bar on science and to heed the first and most fundamental tenet of medicine: "First, do no harm."

Conclusions

Turban et al.'s (2020) singular endorsement of "affirmative" therapies, which their data failed to substantiate, contributes to the alarming trend to frame any non-"affirming" approaches as harmful. We are deeply concerned that this false dichotomy, reinforced by Turban et al.'s unproven claims of the harms of GICE, will have a chilling effect on the ethical psychotherapists' willingness to take on complex GD patients, which will make it much harder for GD individuals to access quality mental health care. We maintain that availability of a broad range of non-coercive, ethical psychotherapies for individuals with GD is essential to meaningful informed consent, which requires consideration of the full range of treatment options, from highly invasive to non-invasive. Further, given the potential of agenda-free psychotherapy to ameliorate GD non-invasively among young people with GD, withholding this type of intervention, while promoting "affirmation" approaches that pave the way to medical transition, is ethically questionable.

We believe that exploratory psychotherapy that is neither "affirmation" nor "conversion" should be the first-line treatment for all young people with GD, potentially reducing the need for invasive and irreversible medical procedures. This is especially critical now, when we are witnessing an exponential rise in the incidence of young people with GD who

have diverse and complex mental health presentations and require careful assessment and treatment planning.

We are concerned about the deficit in our knowledge base about psychological interventions for GD, beyond a few successful but small case studies, and we fear that the erroneous conclusions presented by Turban et al. (2020) will make it less likely that such research will be carried out in the future. We call on the scientific community to resist the stigmatization of psychotherapy for GD and to support rigorous outcome research investigating the effectiveness of various psychological treatments aimed at ameliorating or resolving GD. The outcomes of psychotherapeutic treatments must be compared to those of biomedical interventions, so that evidence-based standards of care that allow patients and clinicians to make fully informed decisions about how best to alleviate GD can be developed and put into practice.

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