features, but they cannot show which ones are *causing* which. It is a standard property of statistical science that when a study reports a correlation, there are necessarily three possible explanations. Assuming the correlation actually exists (rather than represents a statistical fluke or bias), it is possible that X causes Y, that Y causes X, or that there is some other variable, Z, that causes both X and Y. (More than one of these can be true at the same time.) To be complete, a research analysis of a correlation must explore all three possibilities.

57. For example, assuming a correlation between treatment of gender dysphoria in minors and mental health actually exists (rather than is a fluke): (1) It is *possible* that treatment causes improvement in mental health. (2) Yet, it is also possible that having good mental health is (part of) what enabled transition to occur in the first place. That is, because of gate-keeping procedures in the clinical studies, those with the poorest mental health are typically not permitted to transition, causing the higher mental health scores to be sorted into the transitioned group. (See Section IV.E on *Selection Bias*.) (3) It is also possible that a third factor, such as wealth or socioeconomic status, causes both the higher likelihood of transitioning (by being better able to afford it) and the likelihood of mental health (such as by avoiding the stresses of poverty or affording psychotherapy).

58. This principle of scientific evidence is why surveys do not (cannot) represent evidence of treatment effectiveness: Surveys are limited to correlations. (See Section III.F. on *Surveys*.)

C. When two or more treatments are provided at the same time, one cannot know which treatment caused observed changes (i.e., 'confounding').

59. Confounding is a well-known issue in clinical research design. As detailed in the present report, it applies throughout treatment studies of gender dysphoria. Patients who undergo medical transition procedures in research clinics routinely undergo mental health treatment (psychotherapy) at the same time. Without explicit procedures to distinguish them, it cannot be known which treatment produced which outcome (or in what proportions). Indeed, that mental health improvement came from mental health treatment

is a more parsimonious (and therefore, scientifically superior) conclusion than is medicalized treatment causing mental health improvement.

D. Extrapolation to dissimilar populations and dissimilar conditions.

60. The purpose of clinical science is to establish from a finite sample of study participants information about the effectiveness and safety, or other variables, of a treatment that can be generalized to other people. Such extrapolation is only scientifically justified with populations matched on all relevant variables. The identification of those variables can itself be a complicated question, but when an experimental sample differs from another group on variables already known to be related, extrapolation cannot be assumed but must be demonstrated directly and explicitly.

61. Each of the systematic reviews from the UK, Sweden, and Finland emphasized that the recently observed, greatly increased numbers of youth coming to clinical attention are a population different in important respects from the subjects of often-cited research studies. Conclusions from studies of adult-onset gender dysphoria and from childhood-onset gender dysphoria cannot be assumed to apply to the current patient populations of adolescent-onset gender dysphoria. The Cass Report correctly advised:

> It is also important to note that any data that are available do not relate to the current predominant cohort of later-presenting birth-registered female teenagers. This is because the rapid increase in this subgroup only began from around 2014-15. Since young people may not reach a settled gender expression until their mid-20s, it is too early to assess the longer-term outcomes of this group. (Cass 2022 at 36.)

The report also indicated:

> [I]t is important that it is not assumed that outcomes for, and side effects in, children treated for precocious puberty will necessarily be the same in children or young people with gender dysphoria. (Cass 2022 at 63.)

62. Finland's review repeated the observation of greatly (20 times) increased numbers, an entirely different demographic of cases, and increased proportions of psychiatric co-morbidities. (Finnish Palko Preparation Memo at 4-6.) The Swedish review

highlighted "the uncertainty that follows from the yet unexplained increase in the number of care seekers, an increase particularly large among adolescents registered as females at birth." (Swedish Socialstyrelsen Support 2022 at 11.)

63. It is well known that males and females differ dramatically in the incidence of many mental health conditions and in their responses to treatments for mental health conditions. Thus, research from male-to-female transitioners (the predominant population until recent years) cannot be extrapolated to female-to-male transitioners (the predominant population presenting at clinics today). Outcomes from patients who experienced clear pre-pubertal childhood gender dysphoria cannot be extrapolated to patients who first manifest diagnosable gender dysphoria well into puberty. Outcomes from clinics employing rigorous and openly reported gate-keeping procedures cannot be extrapolated to clinics or clinicians employing only minimal or perfunctory assessments without external review. Developmental trajectories and outcomes from before the social media era cannot be assumed to apply to those of the current era or the future. Research from youth with formal diagnoses and attending clinics cannot be extrapolated to self-identifying youth and those responding to surveys advertised on social media sites.

64. Further, treatment of gender dysphoria in children and adolescents presents novel-use cases very dissimilar to the contexts in which puberty blockers and cross-sex hormones have previously been studied. Whereas use of puberty blockers to treat precocious puberty *avoids* the medical risks caused by undergoing puberty growth before the body is ready (thus outweighing other risks), use of blockers to treat gender dysphoria in patients already at their natural puberty pushes them *away* from the mean age of the healthy population. Instead of avoiding an objective problem, one is created: Among other things, patients become subject to the issues and risks associated with being late-bloomers, *very* late-bloomers. This transforms the risk:benefit balance, where the offsetting benefit is primarily (however validly) cosmetic.

65. Similarly, administering testosterone to an adult male to treat testosterone deficiency addresses both a different condition and a different population than

administration of that same drug to an adolescent female to treat gender dysphoria; the benefits and harms observed in the first case cannot be extrapolated to the second.

E. Mental health assessment used for gate-keeping medicalized transition establishes a *selection bias,* creating a statistical illusion of mental health improvement among the selected.

66. Importantly, clinics are expected to conduct mental health assessments of applicants seeking medicalized transition, disqualifying from medical services patients with poor mental health. (The adequacy of the assessment procedures of specific clinics and clinicians remains under debate, however.) Such gate-keeping—which was also part of the original "Dutch Protocol" studies—can lead to misinterpretation of data unless care is explicitly taken. A side-effect of excluding those with significant mental health issues from medical transition is that when a researcher compares the average mental health of the gender dysphoric individuals first presenting to a clinic with the average mental health of those who completed medical transition, then the post-transition group would show better mental health—but only because of the *selection bias*, (Larzelere 2004; Tripepi 2010) even when the transition had no effect at all.

V. Childhood-onset gender dysphoria (prepubertal-onset) is characterized by high rates of desistance in the absence of social or medical transition. Of the 11 existing cohort studies, all showed the majority to desist feeling gender dysphoric upon follow-up after puberty.

67. Currently, the studies of outcomes among children who experience gender dysphoria before puberty that provide the most evidentiary strength available are only "cohort studies," which follow people over time, recording the outcomes of the treatments they have undergone. Such studies supersede (i.e., overrule) the outcomes of surveys, which are much more prone to substantial error. As I have explained above, however, cohort studies can describe developmental pathways, but cannot provide evidence of causation.

68. In total, there have been 11 cohort studies showing the outcomes for these

children, listed in Table 2. I first published this comprehensive list of studies in my own peer-reviewed article on the topic. (Cantor 2019.)

Table 2. Cohort studies of gender dysphoric, prepubescent children.

Count	Group	Study
2/16 4/16 10/16	gay trans-/crossdress straight/uncertain	Lebovitz, P. S. (1972). Feminine behavior in boys: Aspects of its outcome. *American Journal of Psychiatry, 128,* 1283–1289.
2/16 2/16 12/16	trans- uncertain gay	Zuger, B. (1978). Effeminate behavior present in boys from childhood: Ten additional years of follow-up. *Comprehensive Psychiatry, 19,* 363–369.
0/9 9/9	trans- gay	Money, J., & Russo, A. J. (1979). Homosexual outcome of discordant gender identity/role: Longitudinal follow-up. *Journal of Pediatric Psychology, 4,* 29–41.
2/45 10/45 33/45	trans-/crossdress uncertain gay	Zuger, B. (1984). Early effeminate behavior in boys: Outcome and significance for homosexuality. *Journal of Nervous and Mental Disease, 172,* 90–97.
1/10 2/10 3/10 4/10	trans- gay uncertain straight	Davenport, C. W. (1986). A follow-up study of 10 feminine boys. *Archives of Sexual Behavior, 15,* 511–517.
1/44 43/44	trans- cis-	Green, R. (1987). The "sissy boy syndrome" and the development of homosexuality. New Haven, CT: Yale University Press.
0/8 8/8	trans- cis-	Kosky, R. J. (1987). Gender-disordered children: Does inpatient treatment help? *Medical Journal of Australia, 146,* 565–569.
21/54 33/54	trans- cis-	Wallien, M. S. C., & Cohen-Kettenis, P. T. (2008). Psychosexual outcome of gender-dysphoric children. *Journal of the American Academy of Child and Adolescent Psychiatry, 47,* 1413–1423.
3/25 6/25 16/25	trans- lesbian/bi- straight	Drummond, K. D., Bradley, S. J., Badali-Peterson, M., & Zucker, K. J. (2008). A follow-up study of girls with gender identity disorder. *DevelopmentalPsychology, 44*, 34–45.
47/127 80/127	trans- cis-	Steensma, T. D., McGuire, J. K., Kreukels, B. P. C., Beekman, A. J., & Cohen-Kettenis, P. T. (2013). Factors associated with desistence and persistence of childhood gender dysphoria: A quantitative follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry, 52,* 582–590.
17/139 122/139	trans- cis-	Singh, D., Bradley, S. J., Zucker, K. J. (2021). A follow-up study of boys with Gender Identity Disorder. *Frontiers in Psychiatry*, 12:632784.

*For brevity, the list uses “gay” for “gay and cis-”, “straight” for “straight and cis-”, etc.

69. The children in these studies were receiving professional mental health support during the study period, but did not "socially transition." In sum, despite coming from a variety of countries, conducted by a variety of labs, using a variety of methods, at various times across four decades, every study without exception has come to the identical conclusion: among prepubescent children who feel gender dysphoric, the majority cease to want to be the other gender over the course of puberty—ranging from 61–88% desistance across the large, prospective studies. Such cases are often referred to as "desisters," whereas children who continue to feel gender dysphoric are often called "persisters."

70. This interpretation of these studies is widely accepted, including by the Endocrine Society, which concluded:

> In most children diagnosed with GD/gender incongruence, it did not persist into adolescence. . . . [T]he large majority (about 85%) of prepubertal children with a childhood diagnosis did not remain GD/gender incongruent in adolescence. (Hembree 2017 at 3879.)

The developers of the Dutch Protocol, at the Vrije University gender clinic, likewise concluded based on these studies that "Although the persistence rates differed between the various studies…the results unequivocally showed that the gender dysphoria remitted after puberty in the vast majority of children." (Steensma & Cohen-Kettenis 2011 at 2.)

VI. Systematic reviews of safety and effectiveness have been conducted by the health care ministries/departments of several governments. They *unanimously* concluded the evidence on medicalized transition in minors to be of poor quality.

A. Understanding safety and efficacy.

71. At the outset, it is important to understand the meaning of "safety" in the clinical context. The criteria for assessing safety involve two independent components, and

discussion of the safety of hormonal interventions on the natural development of children requires consideration of both of them. The term *safety* in the clinical context represents a "risk:benefit ratio," not an absolute statement that can be extrapolated across applications. In clinical research, assessing safety requires simultaneous consideration of both components of the risk:benefit ratio. That is, treatments are not deemed simply "safe" or "unsafe." These dual components are reflected in FDA regulation:

> There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that *the probable benefits* to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh *any probable risks*. (Code of Federal Regulations Title 21 Sec. 860.7, italics added.)

72. Thus, for example, as I explain in further detail below, because the Endocrine Society did not undertake (or rely on) any systematic review of the efficacy of hormonal interventions to relieve gender dysphoria in minors (i.e., their benefits), and WPATH did not undertake (or rely on) any systematic review of the safety of hormonal interventions in minors (i.e., their risks), neither gathered the evidence necessary to assess the risk:benefit ratio of medicalized transition in minors.

73. In fact, as I also review below, after conducting systematic reviews, the English, Finnish, and Swedish national health care institutions all concluded that there is insufficient evidence to determine that hormonal interventions as treatments for gender dysphoria in minors are safe. Reasons for these consistent conclusions include lack of research, insufficient research quality among the existing investigations, and insufficient investigation of long-term safety.

74. To understand the uniform conclusions of these national health care bodies, it is

important to understand that—at least where there is *prima facie* reason to be concerned that certain harms may result—when the research has not been done, the absence of evidence cannot be taken as evidence of the absence of such harms. "We don't know" does not permit the conclusion "It is safe."

B. The McMaster University systematic review of systematic reviews.

75. McMaster University is recognized as a center of expertise in the performance of methodologically sound systematic reviews. In 2022, authors associated with that McMaster University team (Dr. Romina Brignardello-Petersen and Dr. Wojtek Wiercioch) conducted a systematic review, "Effects of gender affirming therapies in people with gender dysphoria: evaluation of the best available evidence," spanning all the available systematic reviews in this area, including their methodological strength, the evidence they cited, and the conclusions they reached. (Brignardello-Petersen & Wiercioch 2022.) Applying carefully disclosed criteria and methods, they identified on-point systematic reviews, and graded the methodological quality of each on-point review as high, moderate, low, or critically low. With regard to systematic reviews relating to the effects of puberty blockers or cross-sex hormones, the authors included in their analysis all reviews that achieved at least a "low" rating of methodological quality, while excluding those rated as "very low." No systematic reviews earned a "high" methodological rating, except a review performed by the highly respected Cochrane Library of the effects of cross-sex hormones on transitioning natal males (Haupt 2020), but that most careful review in turn found *no* published studies on this topic of sufficient methodological soundness to satisfy its inclusion criteria and thus merit review. After this careful review of the data and analysis contained in available systematic reviews, the McMaster authors concluded:

> Due to important limitations in the body of evidence, there is great uncertainty about the effects of puberty blockers, cross-sex hormones, and surgeries in young people with gender dysphoria. This evidence alone is not sufficient to support

whether using or not using these treatments. (Brignardello-Petersen & Wiercioch 2022 at 5.)

C. The quality of the systematic reviews from governmental bodies and professional associations.

76. To ensure consideration of all available evidence, I compiled into a single table all the cohort studies of safety and effectiveness included by any of the systematic reviews from the international health care systems and (although they were incomplete) by the U.S.-based clinical associations issuing guidelines or standards. I discuss their specific findings in the following sections.

77. New studies continue to be conducted and published. I have identified two additional studies that were published after these reviews were released, but that meet their inclusion criteria: Tordoff, *et al.,* 2022, and Chen, *et al.,* 2023. The findings from both these studies are consistent with those already included and are noted here for completeness.

Table 1. Cohort studies of effectiveness and safety of puberty-blockers and cross-sex hormones in minors.

	Finland (2019)	NICE (2020a,b)	Sweden (2022)	E.S. (2017)	AAP (2018)	Baker (2021) (WPATH)
Effectiveness GnRHa	Costa et al, 2015 de Vries et al, 2011	Costa et al, 2015 de Vries et al, 2011	Becker-Hebly et al, 2020 Carmichael et al, 2021 Costa et al, 2015 *** Hisle-Gorman et al, 2021			de Vries et al, 2011
Effectiveness Sex Hormones	de Vries et al, 2014*	Achille et al, 2020 Allen et al, 2019 Kaltiala et al, 2020 Lopez de Lara et al, 2020	*** *** Cantu et al, 2020* de Vries et al, 2014* ***			Achille et al, 2020 de Vries et al, 2014* López de Lara et al, 2020
Safety (Bones) GnRHa		Brik et al, 2020 Joseph et al, 2019 Khatchadourian et al, 2014 Klink et al, 2015 Vlot et al, 2017	Joseph et al, 2019 Klink et al, 2015 Navabi et al, 2021 Schagen et al, 2020 Stoffers et al, 2019 Vlot et al, 2017 Lee et al, 2020 van der Loos et al, 2021			
Safety (Bloods) GnRHa		Klaver et al, 2020 Schagen et al, 2016	Klaver et al, 2018 Klaver et al, 2020 Nokoff et al, 2020 Perl et al, 2020 Schagen et al, 2016 Schulmeister et al, 2021			
Safety (Bones) Sex Hormones	****	Khatchadourian et al, 2014 Klaver et al, 2020 Klink et al, 2015 Kuper et al, 2020 Stoffers et al, 2019 Vlot et al, 2017		Klink et al, 2015		
Safety (Bloods) Sex Hormones			Jarin, 2017 Mullins et al, 2021 Tack et al, 2016			

*Included both puberty-blockers and cross-sex hormones.
**The Endocrine Society review included bone/skeletal health, but did not explicate whether the scope included minors.
***Sweden explicitly excluded due to high risk of bias: Achille, *et al.,* (2020), Allen, *et al.* (2019), de Vries, *et al.,* (2011), and López de Lara, *et al.,* (2020).
****The Finnish review adopted the Endocrine Society review, but did not indicate whether minors were included.

D. United Kingdom

78. The National Health Service (NHS) of the United Kingdom conducted an independent review of its services for minors with gender dysphoria. (Cass 2022.) Included in that process were two systematic, comprehensive reviews of the research literature, conducted by England's National Institute for Health Care Excellence (NICE) in 2020. One regarded the efficacy, safety, and cost-effectiveness of Gonadotrophin-Releasing Hormone (GnRH) analogs (or "puberty blockers") in minors. (NICE 2020a.) The other regarded the efficacy, safety, and cost-effectiveness of cross-sex hormones, or "gender-affirming hormones," in minors. (NICE 2020b.) (Only efficacy and safety are relevant to the present report.)

79. The puberty-blocker review was tasked with reviewing the research on two relevant questions. For one:

> *In children and adolescents with gender dysphoria, what is the clinical effectiveness of treatment with GnRH analogues compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention?* (NICE 2020a at 4.)

Clinical effectiveness of puberty-blockers was composed of three factors deemed "critical outcomes": impact on gender dysphoria, impact on mental health, and impact on quality of life. The second question addressed in the review was:

> *In children and adolescents with gender dysphoria, what is the short-term and long-term safety of GnRH analogues compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention?* (NICE 2020a at 6.)

Puberty-blocker safety was assessed as its effect on three categories of health: bone density, cognitive development or functioning, and "other."

80. The second review, for cross-sex hormone treatment, was tasked with the corresponding questions. For one:

> *In children and adolescents with gender dysphoria, what is the clinical effectiveness of treatment with gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention?* (NICE 2020b at 4.)

The critical outcomes were again deemed to be impact on gender dysphoria, on mental health, and on quality of life. The impact on mental health was composed of indicators of depression, anxiety, and suicidality and self-injury. The second question was:

> *In children and adolescents with gender dysphoria, what is the short-term and long-term safety of gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention?* (NICE 2020b at 7.)

Cross-sex hormone treatment safety was assessed as its effect on bone density and on "clinical parameters," which included insulin, cholesterol, and blood pressure levels.

81. These two reviews included a systematic consolidation of all the research evidence, following established procedures for preventing the "cherry-picking" or selective citation favouring or down-playing any one conclusion, carefully setting out the criteria for including or excluding specific studies from the review, and providing detailed analyses of each included study. The whole was made publicly available, consistent with good practice.

82. The reviews' results were unambiguous: For both puberty blockers and cross-sex hormones, "The critical outcomes for decision making are the impact on gender dysphoria, mental health and quality of life." The quality of evidence for these outcomes was assessed as "very low" using the established GRADE procedures for assessing clinical research evidence. (NICE 2020a at 4; NICE 2020b at 4.) The reviews also assessed as "very low" the quality of evidence regarding "body image, psychosocial impact, engagement with health care services, impact on extent of satisfaction with surgery and stopping treatment" or (in the case of cross-sex hormones) of "detransition." (NICE 2020a at 5; NICE 2020b at 6.) The review of puberty blockers concluded that of the existing research, "The studies included in this evidence review are all small, uncontrolled observational

studies, which are subject to bias and confounding," "They suggest little change with GnRH analogues [puberty blockers] from baseline to follow-up." (NICE 2020a at 13.) The cross-sex hormone review likewise reported a lengthy list of methodological defects or limitations affecting all available studies. (NICE 2020b at 13-14.)

83. The NHS changed the language on its website describing puberty blockers and cross sex hormones. It removed the statement that "The effects of treatment with GnRH analogues are considered to be fully reversible,"[2] replacing that text with:[3]

> Little is known about the long-term side effects of hormone or puberty blockers in children with gender dysphoria. . . . [I]t is not known what the psychological effects may be. It's also not known whether hormone blockers affect the development of the teenage brain or children's bones.

84. As mentioned in the McMaster review, the highly respected Cochrane Library, based in England, undertook a systematic review of studies of the safety and efficacy of the administration of cross-sex hormones to natal males. That review focused primarily on adults (age 16 and older). The results, including a detailed explanation of methodology and inclusion criteria, were published in 2020. Unfortunately, but importantly, the Cochrane review found *zero* studies, globally, that were sufficiently reliable to meet the inclusion criteria even at a "very low" level of evidentiary quality. The authors reported:

> Despite more than four decades of ongoing efforts to improve the quality of hormone therapy for women in transition, we 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….We found insufficient evidence to determine the efficacy or safety of hormonal treatment approaches…for transgender women in transition. The evidence is very incomplete, demonstrating

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[2] BBC. Retrieved from https://www.bbc.co.uk/sounds/play/m000kgsj; Kurkup, J. (2020, June 4). *The Spectator*. Available from https://www.spectator.co.uk/article/the-nhs-has-quietly-changed-its-trans-guidance-to-reflect-reality/

[3] NHS. Retrieved from https://www.nhs.uk/conditions/gender-dysphoria/treatment/

a gap between current clinical practice and clinical research. (Haupt 2020 at 10-11.)

The authors' frustration at the total lack of reliable research was evident: "The lack of reliable data on hormone therapy for transitioning transgender women should encourage the development of well-planned RCTs and cohort studies to evaluate widespread empirical practice in the treatment of gender dysphoria." (Haupt 2020 at 10.)

E. Sweden

85. Sweden similarly commissioned a systematic review, published in 2022 and charged with addressing these three questions:

> *Are there any scientific studies explaining the increase in numbers seeking for gender dysphoria?*
>
> *Are there any scientific studies on long-term effects of treatment for gender dysphoria?*
>
> *What scientific papers on diagnosis and treatment of gender dysphoria has been published after the National Board of Health and Welfare in Sweden issued its national support for managing children and adolescents with gender dysphoria in 2015?* (SBU Scoping Review Summary 2019.)

The databases searched included CINAHL (EBSCO), Cochrane Library (Wiley), EMBASE (Embase.com), PsychINFO (EBASCO), PubMed (NLM), Scopus (Elsevier), and SocINDEX (EBSCO). A total of 8,867 abstracts were identified, from which 315 full text articles were assessed for eligibility. The review concluded that "literature on management and long-term effects in children and adolescents is sparse," that no RCTs have been conducted, and that there remains no explanation for the recent and dramatic increases in numbers of minors presenting with gender dysphoria. (SBU Scoping Review Summary 2019.) I have quoted other conclusions from the Swedish systematic review in Section II above.

F. Finland

86. Finland's Ministry of Social Affairs and Health commissioned a systematic review, completed in 2019, of the effectiveness and safety of medicalized transition.

(COHERE Recommendation 2020.) The review spanned both minors and adults and included both puberty blockers and cross-sex hormones (Pasternack 2019). Three reviewers tabulated the results. In total, 38 studies were identified, of which two pertained to minors: de Vries (2011) and Costa (2015). The report noted that, because the methodological quality of the studies was already "weak" (no study including any control groups), the assessors declined detailed quality assessment of the existing studies. (Pasternack 2019 at 3.) I have quoted other conclusions from the Finnish systematic review in Section II above.

G. Norway

87. Norway's investigation of its health care policy for gender dysphoric minors also revealed substantial safety concerns:

> There are unsettled questions related to puberty blockers in young people. A published study shows that puberty-inducing hormones cause slower height growth and a slower increase in bone density. It is also noted that the effects on cognitive development have not been mapped. Unexplained side effects and long-term effects of both puberty blockers (hormone treatment) and gender-affirming hormone treatments are increasingly being questioned. However, experience with other patient groups shows that long-term use of sex hormones can affect disease risk. When people with gender incongruence are treated, it is with significantly longer duration and intensity of hormone treatment than hormone treatments for other conditions. (Ukom 2023.)

VII. The Endocrine Society, WPATH, and the American Academy of Pediatrics did not conduct systematic reviews of safety and efficacy in establishing clinical guidelines, despite systematic reviews being the foundation and gold standard of evidence-based care.

88. I have also examined the reviews conducted by the U.S.-based professional associations that have published standards and guidelines for the treatment of gender dysphoric youth. As detailed herein, and unlike the European reviews, none of the U.S.-

based professional associations conducted a systematic review of both effectiveness and safety, without which they are unable to assess the risk:benefit ratio posed by medicalized transition of minors.

A. The Endocrine Society reviewed cross-sex hormones, but not puberty blockers. They reviewed safety, but did not review effectiveness research.

89. The Endocrine Society appointed a task force which commissioned two systematic reviews as part of updating their 2009 recommendations. (Hembree 2017.) The scopes of the two reviews were limited to physiological effects of cross-sex hormones, narrowly defined: "The first one aimed to summarize the available evidence on the effect of sex steroid use in transgender individuals on lipids and cardiovascular outcomes….The second review summarized the available evidence regarding the effect of sex steroids on bone health in transgender individuals." (Hembree 2017 at 3873.) As described in the Endocrine Society Guidelines, those reviews did not, however, include the effectiveness of any treatment on mental health (quality of life, suicidality, rates of detransition, cosmetic or functional outcomes, or improvements in feelings of gender dysphoria). What appears to be the referenced review of lipids and cardiovascular outcomes (Maraka 2017) did not identify any study of adolescents, noting "literature addressing this clinical question in the pediatric/adolescent population is completely lacking." (Maraka at 3921.) What appears to be the referenced review of bone health (Singh-Ospina 2017) identified only one small study on adolescents, involving 15 male-to-female and 19 female-to-male cases. (Klink 2015.) Notably, the median duration of puberty-blocker administration was 1.2 years, leaving unknown the effects on children receiving blockers from puberty onset (usually age 9–10) to age 14 or 16.

90. Further, the Endocrine Society does not claim to have conducted or consulted any systematic review of the efficacy of puberty blockers or cross-sex hormones to reduce gender dysphoria or increase mental health or well-being by any metric. Nor does it claim to have conducted or consulted any systematic review of safety of any of these treatments

for minors with respect to brain development, future fertility, actual reversibility, or any other factor of safety or adverse event other than cardiovascular disease and bone strength.

91. For all these reasons, I concur with the opinion of Dr. Guyatt, who has said that he finds "serious problems" with the Endocrine Society guidelines, among other reasons because the only systematic reviews those guidelines refer to did not look at the efficacy of the recommended hormonal interventions to improve gender dysphoria, which he termed "the most important outcome." (Block, Gender Dysphoria 2023 at 4.)

92. The current Endocrine Society guidelines, released in 2017, include this disclaimer:

> The Endocrine Society makes no warranty, express or implied, regarding the guidelines and specifically excludes any warranties of merchantability and fitness for a particular use or purpose. The Society shall not be liable for direct, indirect, special, incidental, or consequential damages related to the use of the information contained herein. (Hembree 2017 at 3895.)

The previous, 2009, version included no disclaimers. (Hembree 2009.)

B. WPATH reviewed effectiveness, but not the safety of medicalized transition of minors.

93. WPATH engaged in a multi-step process in updating its Standards of Care from version 7 to version 8. That process included commissioning a systematic review, which was published as Baker, *et al.* (2021) which included the disclaimer "The authors are responsible for its content. Statements in this report do not necessarily reflect the official views of or imply endorsement by WPATH." (Baker 2021 at 14.)

94. The literature search was completed in June 2020, and spanned 13 questions. Two questions related to the effectiveness of medicalized transition of minors: Question #10 was "[W]hat are the effects of suppressing puberty with GnRH agonists on quality of life?", and question #11 was "[W]hat are the psychological effects (including quality of life) associated with hormone therapy?"(Sharma 2018; Baker 2021.) That is, the review included studies of the effectiveness of puberty blockers and cross-sex hormones, but,

remarkably did not include any effort to determine the *safety* of either.

95. Baker (2021) identified that among all experimental evidence published on medicalized transition, a total of "Three studies focused on adolescents." (Baker 2021 at 1.) These were Achille, *et al.* (2020), López de Lara, *et al.* (2020), and de Vries, *et al.* (2011, 2014). (Baker 2021 considered the two de Vries articles as a single study, because the later one included the subset of patients from the earlier one who continued in treatment. I will refer to this set as four studies, however, to be consistent with the other reviews.) Notably, in contrast with WPATH's review, the Swedish review entirely excluded Achille *et al.* (2020), López de Lara *et al.* (2020), and de Vries *et al.* (2011) due to their high risks of bias. (SBU Scoping Review Appendix 2.) The Baker team did not used the GRADE system for assessing the quality of evidence, instead using the Methods Guide for Conducting Comparative Effectiveness Reviews.

96. The Baker team noted "no study reported separate results by gender identity for transgender youth." (Baker 2021 at 3.) They also found that "No study reported on hormone therapy among nonbinary people." (at 3.) (Despite this finding, WPATH SOC-8 now includes recommendations for people who identify as nonbinary.)

97. My assessment of the Baker review revealed that there were substantial discrepancies and misleading ambiguities in their reporting: Baker, *et al.* indicated in the abstract that "Hormone therapy was associated with increased QOL [quality of life], decreased depression, and decreased anxiety" (Baker 2021 at 1,) and that "Associations were similar across gender identity and age" (Baker 2021 at 12). This is not what its actual data tables showed, however. Table 2 presented the only study of QOL specifically among adolescents included in the review and indicated that "Mean QOL scores did *not* change." (Baker 2021 at 7, italics added.)

98. The review, however, did not rate the quality of the studies of adolescents on their own, instead combining them with the studies of adults. (at 10, italics added.) Table 4 of that study presented three analyses of anxiety: One showed a decrease, and on the other two, "Mean anxiety score did *not* change." (at 11, italics added.) Finally, the review

also concluded, "It was impossible to draw conclusions about the effects of hormone therapy on death by suicide." (at 12.) Even for the combined set, the review read the strength of evidence to be "low" for each of QOL, depression, and anxiety, and to be "insufficient" for death by suicide. (Baker 2021 at 13, Table 6.) Specifically, the review indicated, "There is insufficient evidence to draw a conclusion about the effect of hormone therapy on death by suicide among transgender people." (at 13, Table 6.) Overall, "The strength of evidence for these conclusions is low due to methodological limitations." (at 12.) Of particular concern was that "Uncontrolled confounding was a major limitation in this literature." (at 12.)

99. Additionally, although WPATH commissioned the Baker review, WPATH did not follow its results. Baker 2021 indicated the use of two systematic quality assessment methods, called RoB 2 and ROBINS-I (Baker 2021 at 3); however, WPATH modified the conclusions that that process yielded. WPATH SOC-8 states, "This evidence is not only based on the published literature (direct as well as background evidence) but also on consensus-based expert opinion." (Coleman 2022 at S8.) Moreover:

> Recommendations in the SOC-8 are based on available evidence supporting interventions, a discussion of risks and harms, as well as feasibility and acceptability within different contexts and country settings. Consensus on the final recommendations was attained using the Delphi process that included all members of the guidelines committee and required that recommendation statements were approved by at least 75% of members. (Coleman 2022 at S8.)

100. By allowing "consensus-based expert opinion" to modify or overrule conclusions supported by systematic reviews that apply accepted criteria of evidentiary strength, WPATH has explicitly abandoned evidence-based medicine. As indicated already by the Pyramid of Evidence, "expert opinion" represents the *lowest* level of evidence in science, whereas systematic review, the highest. (Also, it is unclear what the authors mean by "background evidence.") To modify systematic results according to committee opinion is to re-introduce the very biases that the systematic process is meant to overcome. The

WPATH document attempts to claim the authority of a systematic review, while reserving the ability to "overrule" results that WPATH members did not like.

101. As to evidence supporting hormonal interventions in minors, WPATH asserted that "a systematic review regarding outcomes of [hormonal] treatment in adolescents is not possible" due to the lack of "outcome studies that follow youth into adulthood." (Coleman 2022 at S46.) WPATH is correct that essential outcome studies have not been done, but incorrect that this authorizes issuance of guidelines or standards in the absence of a systematic review. As Dr. Guyatt has stated, "systematic reviews are always possible"—and indeed an important conclusion from such a review may be (as here) that insufficient evidence exists to support any evidence-based guideline. As Dr. Guyatt further elaborated, if an organization issues recommendations without performing an on-point systematic review, "they'd be violating standards of trustworthy guidelines." (Block, Dysphoria Rising, 2023 at 3.)

102. Finally, the WPATH SOC-8 were revised immediately after their release, removing all age minimums to all recommendations. None of these studies and none of these reviews support such a change, and WPATH cites no studies or other document in support of the change.

103. In sum, the WPATH SOC8 cannot be called evidence-based guidelines under any accepted meaning of that term.

C. The American Academy of Pediatrics did not conduct a systematic review either of safety or effectiveness.

104. While the AAP policy statement is often referenced, the AAP did not report conducting any systematic review of any aspect of transgender care in producing its policy statement on gender-diverse children and adolescents. (Rafferty 2018.) Further, the AAP policy statement on its face is the work of a single author rather than of any committee or the membership more broadly (Dr. Rafferty "conceptualized," "drafted," "reviewed," "revised," and "approved" the statement), and the statement explicitly states that it does not "indicate an exclusive course of treatment" nor "serve as a standard of medical care."

(Rafferty 2018 at 1.)

VIII. Definitions of sex, gender identity, and gender dysphoria.

A. Sex and sex-assigned-at-birth represent objective features.

105. Sex is an *objective* feature: It can be ascertained regardless of any declaration by a person, such as by chromosomal analysis or visual inspection. Gender identity, however, is *subjective:* There exists no means of either falsifying or verifying people's declarations of their gender identities. In science, it is the objective factors—and only the objective factors—that matter to a valid definition. Objectively, sex can be ascertained, not only in humans or only in the modern age, but throughout the animal kingdom and throughout its long history in natural evolution.

106. I use the term "sex" in this report with this objective meaning, which is consistent with definitions articulated by multiple medical organizations:

Endocrine Society (Bhargava 2021 at 220.)

> "Sex is dichotomous, with sex determination in the fertilized zygote stemming from unequal expression of sex chromosomal genes."

American Academy of Pediatrics (Rafferty 2018 at 2 Table 1.):

> "An assignment that is made at birth, usually male or female, typically on the basis of external genital anatomy but sometimes on the basis of internal gonads, chromosomes, or hormone levels."

American Psychological Association (APA Answers 2014):

> "Sex is assigned at birth, refers to one's biological status as either male or female, and is associated primarily with physical attributes such as chromosomes, hormone prevalence, and external and internal anatomy."

American Psychological Association (APA Resolution 2021 at 1):

> "While gender refers to the trait characteristics and behaviors culturally associated with one's sex assigned at birth, in some cases, gender may be distinct from the physical markers of biological sex (e.g., genitals, chromosomes)."

American Psychiatric Association (Am. Psychiatric Ass'n Guide):

> "Sex is often described as a biological construct defined on an anatomical, hormonal, or genetic basis. In the U.S., individuals are assigned a sex at birth based on external genitalia."

107. The phrases "assigned male at birth" and "assigned female at birth" are increasingly popular, but they lack any scientific merit. Science is the systematic study of natural phenomena, and nothing objective changes upon humans' labelling or re-labelling it. That is, the objective sex of a newborn was the same on the day before as the day after the birth. Indeed, the sex of a fetus is typically known by sonogram or amniocentesis many months before birth. The use of the term "assign" insinuates that the label is arbitrary and that it was possible to have been assigned a different label that is equally objective and verifiable, which is untrue. Infants were born male or female before humans invented language at all. Indeed, it is exactly because an expected child's sex is known before birth that there can exist the increasingly popular "gender reveal" events. Biologically, the sex of an individual (for humans and almost all animal species) as male or female is irrevocably determined at the moment it is conceived. Terms such as "assign" obfuscate rather than clarify the objective evidence.

B. Gender identity refers to subjective feelings that cannot be defined, measured, or verified by science.

108. It is increasingly popular to define gender identity as a person's "inner sense," however, neither "inner sense" nor any similar phrase is scientifically meaningful. In science, a valid construct must be both objectively measurable and falsifiable with objective testing. The concept of an "inner sense" fits none of these requirements.

IX. Suicide and suicidality are distinct phenomena representing different mental health issues and indicating different clinical needs.

109. *Suicide* refers to completed suicides and the sincere intent to die. It is substantially associated with impulsivity, using more lethal means, and being a biological male. (Freeman 2017.) *Suicidality* refers to *para*-suicidal behaviors, including suicidal

ideation, threats, and gestures.

A. Rates of suicidality among all adolescents have skyrocketed with the advent of social media.

110. The CDC's 2019 Youth Risk Behavior Survey found that 24.1% of female and 13.3% of male high school students reported "seriously considering attempting suicide." (Ivey-Stephenson 2020 at 48.)

111. The CDC survey reported not only that these already alarming rates of suicide attempt were still increasing (by 8.1%–11.0% per year), but also that this increase was occurring only among female students. No such trend was observed among male students. That is, the demographic increasingly reporting suicidality is the same demographic increasingly reporting gender dysphoria. (Ivey-Stephenson 2020 at 51.)

112. The U.S. Substance Abuse and Mental Health Services Administration (SAMHSA) produces a series of evidence-based resource guides which includes their Treatment for Suicidal Ideation, Self-Harm, and Suicide Attempts Among Youth. It noted (italics added):

> [F]rom 1999 through 2018, the suicide death rate doubled for females aged 15 to 19 and 20 to 24. For youth aged 10 to 14, the suicide death rate more than tripled from 2001 to 2018. Explanations for the increase in suicide may include bullying, social isolation, increase in technology and *social media*, increase in *mental illnesses*, and economic recession. (SAMHSA 2020 at 5.)

The danger potentially posed by social media follows from suicidality spreading as a social contagion, as suicidality increases after media reports, occurs in clusters of social groups, and in adolescents after the death of a peer. (Gould & Lake 2013.)

113. Social media voices today loudly advocate "hormones-on-demand" while issuing hyperbolic warnings that teens will commit suicide unless this is not granted. Both adolescents and parents are exposed to the widely circulated slogan that "I'd rather have a living son than a dead daughter," and such baseless threats or fears are treated as a justification for referring to affirming gender transitions as 'life-saving' or 'medically

necessary'. Such claims grossly misrepresent the research literature, however. Indeed, they are unethical: Suicide prevention research and public health campaigns repeatedly warn against circulating messages that can be taken to publicize or even glorify suicide, due to the risk of copy-cat behavior they encourage. (Gould & Lake 2013.)

114. Systematic review of 44 studies of suicidal thoughts and behaviors in LGBTQ youth and suicidality found only a small association between suicidality and sexual minority stress. (Hatchel 2021.) The quantitative summary of the studies (an especially powerful type of systematic review called *meta-analysis*) found no statistically significant association between suicidality and any of having an unsupportive school climate, stigma and discrimination, or outness/openness. There were, however, significant associations between suicidality and indicators of social functioning problems, including violence from intimate partners, victimization from LGBT peers and from non-LGBT peers, and sexual risk taking.

B. *Suicidality* is substantially more common among females, and *suicide*, among males. Sexual orientation is strongly associated with suicidality, but much less associated with suicide.

115. Notwithstanding public misconceptions about the frequency of suicide and related behaviors, the highest rates of death by suicide are among middle-aged and elderly men in high income countries. (Turecki & Brent 2016 at 3.) Males are at three times greater risk of death by suicide than are females, whereas suicidal ideation, plans, and attempts are three times more common among females. (Klonsky 2016; Turecki & Brent 2016.) In contrast with completed suicides, the frequency of suicidal ideation, plans, and attempts is highest during adolescence and young adulthood, with reported ideation rates spanning 12.1–33%. (Borges 2010; Nock 2008.) Relative to other countries, Americans report elevated rates of each of suicidal ideation (15.6%), plans (5.4%), and attempts (5.0%). (Klonsky 2016.) Suicide attempts occur up to 30 times more frequently than completed suicides. (Bachmann 2018.) The rate of completed suicides in the U.S. population is 14.5 per 100,000 people. (WHO 2022.)

116. There is substantial research associating sexual orientation with suicidality, but much less so with completed suicide. (Haas 2014.) More specifically, there is some evidence suggesting gay adult men are more likely to die by suicide than are heterosexual men, but there is less evidence of an analogous pattern among lesbian women. Regarding suicidality, surveys of self-identified LGB Americans repeatedly report rates of suicidal ideation and suicide attempts 2–7 times higher than their heterosexual counterparts. Because of this association of suicidality with sexual orientation, one must apply caution in interpreting findings allegedly about gender identity: because of the overlap between people who self-identify as non-heterosexual and as transgender or gender diverse, correlations detected between suicidality and gender dysphoria may instead reflect (be confounded by) sexual orientation. Indeed, other authors have made explicit their surprise that so many studies, purportedly of gender identity, entirely omitted measurement or consideration of sexual orientation, creating the situation where features that seem to be associated with gender identity instead reflect the sexual orientation of the members of the sample. (McNeil 2017.)

C. There is no evidence that medicalized transition reduces rates of suicide or suicidality.

117. It is repeatedly asserted that despite the known risks, despite the lack of research into the reality or severity of unquantified risks, it is essential and "the only ethical response" to provide medical transition to minors because medical transition is known to reduce the likelihood of suicide among minors who suffer from gender dysphoria. This is simply untrue. *No studies* have documented any reduction in suicide rates in minors (or any population) as a result of medical transition. No methodologically sound studies have provided meaningful evidence that medical transition reduces suicidality in minors. Instead, multiple studies show tragically high rates of suicide after medical transition, with that rate beginning to spike several years after medical transition.

118. Among post-transition adults, completed suicide rates remain elevated. (Wiepjes 2020.) Among post-operative transsexual adults in Sweden's highly tolerant society, death

by suicide is 19 times higher than among the cisgendered. (Dhejne 2011.) Systematic review of 17 studies of suicidality in transsexual adults confirmed suicide rates remain elevated even after complete transition. (McNeil 2017.) Among post-operative patients in the Netherlands, long-term suicide rates of six times to eight times that of the general population were observed depending on age group. (Asscheman 2011 at 638.) Also studying patients in the Netherlands, Wiepjes et al. (2020) reported the "important finding" that "suicide occurs similarly" before and after medical transition. (Wiepjes 2020 at 490.) In other words, *transition did not reduce suicide*. A very large dataset from the U.K. GIDS clinic showed that those referred to the GIDS clinic for evaluation and treatment for gender dysphoria committed suicide at a rate five times that of the general population, both before and after commencement of medical transition (Biggs 2022). Finally, in a still-ongoing longitudinal study of U.S. patients, Chen *et al.* have reported a shockingly high rate of completed suicide among adolescent subjects in the first two years *after* hormonal transition, although they provide no pre-treatment data for this population to compare against. (Chen 2023 at 245.)

119. WPATH's systematic review of the effectiveness of puberty blockers and cross-sex hormones on suicide in minors concluded that "It was impossible to draw conclusions about the effects of [either] hormone therapy on death by suicide." (Baker 2021 at 12.) In short, I am aware of no respected voice that asserts that medical transition reduces suicide among minors who suffer from gender dysphoria.

120. As to the separate and far more common phenomenon of suicidality, of course, that claim is widely made. McNeil's systematic review revealed, however, a complicated set of interrelated factors rather than supporting the common hypothesis that rates of suicidal ideation and suicidal attempts would decrease upon transition. Rates of suicidal ideation did not show the same pattern as suicide attempts, male-to-female transitioners did not show the same patterns as female-to-male transitioners, and social transition did not show the same patterns as medical transition. Importantly, the review included one study that reported "a positive relationship between higher levels of social support from

leaders (e.g., employers or teachers) and increased suicide attempt, which they suggested may be due to attempts instigating increased support from those around the person, rather than causing it." (McNeil 2017 at 348.)

121. Moreover, the 2020 Kuper, *et al.* cohort study of minors receiving hormone treatment found *increases* in each of suicidal ideation (from 25% to 38%), attempts (from 2% to 5%), and non-suicidal self-injury (10% to 17%). (Kuper 2020 at Table 5.) Research has found social support to be associated with *increased* suicide attempts, suggesting the reported suicidality may represent attempts to evoke more support. (Bauer 2015; Canetto 2021.)

122. Overall, the research evidence is only minimally consistent with the hypothesis that an absence of transition causes mental health issues and suicide, but very strongly consistent with the hypothesis that mental health issues, such as *Borderline Personality Disorder* (BPD), cause both suicidality and unstable identity formation (including gender identity confusion). BPD is repeatedly documented to be greatly elevated among sexuality minorities (Reuter 2016; Rodriguez-Seiljas 2021; Zanarini 2021), and both suicidality and identity confusion are symptoms of that disorder. Thus, diverting distressed youth towards transition necessarily diverts youth away from receiving the psychotherapies designed for treating the issues actually causing their distress.

123. Despite that mental health issues, including suicidality, are repeatedly required by clinical standards of care to be resolved before transition, threats of suicide are instead oftentimes used as the very justification for labelling transition a "medical necessity". However plausible it might seem that failing to affirm transition causes suicidality, the epidemiological evidence does not support that hypothesis.

X. Neuroimaging studies have associated brain features with sex and with sexual orientation, but not gender identity.

124. Claims that transgender identity is an innate property resulting from brain structure remain unproven. Neuroimaging and other studies of brain anatomy repeatedly identify patterns distinguishing male from female brains, but when analyses search for

those patterns among transgender individuals, "gender identity and gender incongruence could not be reliably identified." (Baldinger-Melich 2020 at 1345.) Although much smaller than male/female differences, statistically significant neurological differences are repeatedly associated with sexual orientation (termed "homosexual" vs "nonhomosexual" in the research literature). Importantly, despite the powerful associations between transsexuality and homosexuality, as explicated by Blanchard, many studies analyzing gender identity failed to control for sexual orientation, representing a problematic and centrally important confound. I myself pointed this out in the research literature, noting that neuroanatomical differences attributed to gender dysphoria should instead be attributed to sexual orientation. (Cantor 2011, Cantor 2012.) A more recent review of the science, by Guillamon, et al. (2016), agreed, stating:

> Following this line of thought, Cantor (2011, 2012, but also see Italiano, 2012) has recently suggested that Blanchard's predictions have been fulfilled in two independent structural neuroimaging studies. Specifically, Savic and Arver (2011) using VBM on the cortex of untreated nonhomosexual MtFs and another study using DTI in homosexual MtFs (Rametti et al., 2011b) illustrate the predictions. *Cantor seems to be right*". (Guillamon 2016 at 1634, italics added; see also Italiano 2012.)

In addition to this confound, because snapshot neurobiological studies can provide only correlational data, it would not be possible for such studies to distinguish whether brain differences cause gender identity or if gender atypical behavior modifies the brain over time, such as through neuroplasticity. As noted by one team of neuroscientists, "[I]t remains unclear if the differences in brain phenotype of transgender people may be the result of a sex-atypical neural development or of a lifelong experience of gender non-conformity." (Fisher 2020 at 1731.) In sum, at present assertions that transgender identity is caused by neurology represent faith, not science.

XI. Known and potential harms associated with administration of puberty blockers and cross-sex hormones to children and adolescents.

A. Hormonal treatments during puberty interfere with neurodevelopment and cognitive development.

125. It is well known that pubertal hormone levels drive important stages of neural development and resulting capabilities, although the mechanisms are not yet well understood. Dr. John Strang (Research Director of the Gender Development Program at Children's National Hospital in Washington, D.C.) (Terhune 2022), the Cass Report from the U.K., and the systematic review from Finland all reiterated the central importance and unknown effects of GnRH-agonists on windows, or "sensitive periods," in brain development, notably including adolescence. As Dr. Cass put it:

> A further concern is that adolescent sex hormone surges may trigger the opening of a critical period for experience-dependent rewiring of neural circuits underlying executive function (i.e. maturation of the part of the brain concerned with planning, decision making and judgement). If this is the case, brain maturation may be temporarily or permanently disrupted by puberty blockers, which could have significant impact on the ability to make complex risk-laden decisions, as well as possible longer-term neuropsychological consequences. To date, there has been very limited research on the short-, medium- or longer-term impact of puberty blockers on neurocognitive development. (Cass Review Letter 2022 at 6.)

126. In a meta-analysis (a highly rigorous type of systematic review) of studies of neuropsychological performance, non-transsexual males undergoing puberty earlier show a different cognitive profile than those underdoing puberty later. The association of brain development with age of pubertal onset exists in humans as well as non-human animals. (Shirazi 2022.)

127. Even in adults, neuroscience studies employing MRI and other methods have shown that the blockade of normal levels of hormones associated with puberty and adulthood degrade brain performance. Thus, when GnRH-agonists are administered to

adult biological women, several brain networks decrease in activity and cognitive performance, such as in working memory, declines. (Craig 2007; Grigorova 2006.)

128. In light of this science, multiple voices have expressed concern that blocking the process of puberty during its natural time could have a negative and potentially permanent impact on brain development (Cass 2022 at 38–39; Chen 2020; Hembree 2017 at 3874.) As Chen *et al.* (2020) observed:

> [I]t is possible these effects are temporary, with youth 'catching up'…However, pubertal suppression may prevent key aspects of development during a sensitive period of brain organization. Neurodevelopmental impacts might emerge over time, akin to the 'late effects' cognitive findings associated with certain [other] oncology treatments. (Chen 2020 at 249.)

Chen et al. (2020) noted that no substantial studies have been conducted to identify such impacts outside "two small studies" (at 248) with conflicting results. I have not identified any systematic review of neurodevelopment or cognitive capacity.

129. A related concern is that by slowing or preventing stages of neural development, puberty blockers may impair precisely the mature cognitive capabilities that would be necessary to evaluation of, and meaningful informed consent to, the type of life-changing impacts that accompany cross-sex hormones.

B. Substantially delayed puberty is associated with medical harms.

130. The research cited by the WPATH Standards of Care includes the evidence that children whose natural puberty started very late (top 2.3% in age) have elevated risks of multiple health issues in adulthood. (Zhu & Chan 2017.) These include elevations in metabolic and cardiovascular disease, lower height, and decreased bone mineral density. It has not been studied whether these correlations also occur in children whose puberty is chemically delayed. Undergoing puberty much later than one's peers is also associated with poorer psychosocial functioning and lesser educational achievement. (Koerselman & Pekkarinen 2018.)

C. Reduced bone density.

131. The systematic reviews by Sweden, Finland, and England all included bone health as an outcome. *The New York Times* also recently commissioned its own independent review of the available studies. (Twohey & Jewett 2022.) These reviews all identified subsets of the same group of eight studies of bone health. (Carmichael 2021; Joseph 2019; Klink 2015; Navabi 2021; Schagen 2020; Stoffers 2019; van der Loos 2021; Vlot 2017.) These studies repeatedly arrived at the same conclusion. As described by *The New York Times* review:

> [I]t's increasingly clear that the drugs are associated with deficits in bone development. During the teen years, bone density typically surges by about 8 to 12 percent a year. The analysis commissioned by *The Times* examined seven studies from the Netherlands, Canada and England involving about 500 transgender teens from 1998 through 2021. Researchers observed that while on blockers, the teens did not gain any bone density, on average—and lost significant ground compared to their peers.[4] (Twohey & Jewett 2022.)

132. There is some evidence that some of these losses of bone health are regained in some of these youth when cross-sex hormones are later administered. The rebounding appears to be limited to female-to-male cases, while bone development remains deficient among male-to-female cases.

133. The long-term effects of the deficient bone growth of people who undergo hormonal interventions at puberty remain unstudied. The trajectory of bone quality over the human lifetime includes decreases during aging in later adulthood. Because these individuals may enter their senior years with already deficient bone health, greater risks of fracture and other issues are expectable in the long term. As the *New York Times'* analysts summarized, "That could lead to heightened risk of debilitating fractures earlier than would be expected from normal aging—in their 50s instead of 60s." Such harms, should they

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[4] The eighth study was Lee, *et al.,* 2020, which reported the same deficient bone development.

occur, would not be manifest during the youth and younger adulthood of these individuals. This distinction also represents one of the differences between adult transitioners and childhood transitioners and why their experiences cannot be extrapolated between them.

134. There does not exist an evidence-based method demonstrated to prevent these outcomes. The recommendations offered by groups endorsing puberty blockers are quite limited. As summarized by *The Times:*

> A full accounting of blockers' risk to bones is not possible. While the Endocrine Society recommends baseline bone scans and then repeat scans every one to two years for trans youths, WPATH and the American Academy of Pediatrics provide little guidance about whether to do so. Some doctors require regular scans and recommend calcium and exercise to help to protect bones; others do not. Because most treatment is provided outside of research studies, there's little public documentation of outcomes. (Twohey & Jewett 2022.)

D. Short-term/Immediate side-effects of puberty blockers include sterile abscesses, leg pain, headache, mood swings, and weight gain.

135. The Cass Report summarized that "In the short-term, puberty blockers may have a range of side effects such as headaches, hot flushes, weight gain, tiredness, low mood and anxiety, all of which may make day-to-day functioning more difficult for a child or young person who is already experiencing distress." (Cass 2022 at 38.)

136. In 2016, the U.S. FDA began requiring drug manufacturers to add a warning about the psychiatric side effects, after reports of suicidal ideation and a suicide attempt began to emerge among children prescribed GnRH-agonists (for precocious puberty).[5] The warning label on Lupron reads that "Psychiatric events have been reported in patients…such as crying, irritability, impatience, anger and aggression."

137. Other than the suicide attempt, such adverse effects may seem minor relative to the major health and developmental risks I have reviewed above, and they may be

[5] Reuters Special Report; 2022, Oct. 6. Retrieved from https://www.reuters.com/investigates/special-report/usa-transyouth-care/

dismissed by children and by parents confronted by fears of suicidality and an urgent hope that transition will resolve the child's unhappiness and mental health issues. However, when assessing risk:benefit ratio for "safety" against the undemonstrated benefits claimed for hormonal interventions, these observed harms should not be ignored.

E. Long-term use of cross-sex hormones in adult transsexuals is associated with unfavorable lipid profiles (cholesterol and triglycerides) and other issues.

138. As the Cass Report correctly and succinctly indicated, "Sex hormones have been prescribed for transgender adults for several decades, and the long-term risks and side effects are well understood. These include increased cardiovascular risk, osteoporosis, and hormone-dependent cancers." (Cass 2022 at 36.)

139. Minors who begin puberty blockers and proceed to cross-sex hormones—as almost all do—will require continuing treatment with cross-sex hormones for life, unless they go through the very difficult process of detransition. Because a lifetime dependence on cross-sex hormones is the expected course, the known adverse effects of cross-sex hormones on adults must also be part of the risk:benefit analysis of the "safety" of putting a minor on cross-sex hormones (and indeed, of the initial decision to put a child on puberty blockers).

140. Systematic review identified 29 studies of the effects of cross-sex hormone treatment on cardiovascular health in adults. (Maraka 2017.) By the two-year follow-up mark among female-to-male transitioners, hormone administration was associated with increased serum triglycerides (indicating poorer health), increased low-density-lipid (LDL) cholesterol (indicating poorer health), and decreased high-density-lipid (HDL) cholesterol (indicating poorer health). Among male-to-female transitioners at the two-year mark, cross-sex hormone treatment was associated with increased serum triglycerides (indicating poorer health).

XII. Assessment of plaintiffs' experts' reports.

141. Dr. Shumer indicated he was an expert witness for the plaintiffs in the following

cases, for which I am an expert witness for the defense: Dekker v Weida, Boe v Marshall, Roe v Utah High School Activities Association, Bridge v Oklahoma Department of Education.

142. Dr. Budge indicated she was an expert witness for the plaintiffs in Bridge v Oklahoma Department of Education. I am an expert witness for the defense in that case, which is currently in process.

A. Dr. Shumer's declaration does not include the evidence upon which an expert would rely for developing an expert opinion.

143. Dr. Shumer's entire declaration included exactly one citation, providing no support whatsoever for the many assertions he asserted. His submission does not provide evidence of meeting any expert or professional standard.

144. In his declaration, Dr. Shumer asserted specific conclusions about the medical status of specific people not under his care, which is a violation of medical ethics. The plaintiffs are not Dr. Shumer's patients. He has not examined them or their medical records. Dr. Shumer has made explicit that his information about them is "based solely on the information that I have been provided by Plaintiff's attorneys." (Shumer ¶15.) He is not able to diagnose their pubertal, hormonal, transgender, or mental health status versus their having been misdiagnosed by the health care providers who did.

B. Dr. Shumer's are unsupported by the research literature and contradict the research literature.

145. Dr. Shumer claimed without support that gender identity "has a strong biological basis" (Shumer ¶19) and is a "largely biological phenomenon" (Shumer ¶22), citing no support for his assertion. As already noted herein, the research has demonstrated a biological basis for sexual orientation, not gender identity. (See Section X. *Neuroimaging Studies.*)

146. Dr. Shumer claimed gender identity "cannot be changed by medical or psychological intervention" (Shumer ¶23). He cites no support for this assertion. In actual clinical practice, that is rarely the relevant issue. The far more typical situation is youth

who are *mistaken* about their gender identity, wherein youth misinterpret their experiences to indicate they are transgender. Moreover, it has been the unanimous conclusion of every follow-up study of gender dysphoric children ever conducted, not only that gender identity does change, but also that it changes in the large majority of cases. (See Section V. *Childhood-Onset Gender Dysphoria.*)

147. Dr. Shumer similarly claimed "attempts to 'cure' transgender individuals…are harmful and ineffective" (Shumer ¶25), citing no support for the assertion. Activists and social media increasingly, but erroneously, apply the term "conversion therapy," moving farther and farther from what the research has reported. "Conversion therapy" (or "reparative therapy" and other names) has referred to efforts to change a person's sexual orientation. More recently, any therapy failing to provide affirmation-on-demand is labeled "conversion therapy." (D'Angelo, *et al.,* 2020.) Although the media and social media habitually add "T" to "GLB" in discussing these issues, the research on "conversion therapy" has investigated only sexual orientation, and its results cannot be extrapolated to gender identity by mere analogy.

148. Dr. Shumer claimed that "a person's sex is comprised of several components, including…gender identity" (Shumer ¶26), citing no support for his claim. As already indicated herein, however, gender identity is in fact excluded from the definitions of sex. (See Section VIII.A. *Sex and Sex Assigned-at-Birth*.) (See also ¶160 herein.)

149. Dr. Shumer claimed "The WPATH Standards of Care represent expert consensus" and is "based on the best science" (Shumer ¶31). As detail already, expert consensus is the *lowest* level of evidence in clinical research (see Section III.E. *Expert Opinion*), and WPATH did not engage in any systematic review of the safety of transition. (See Section VII.B. *WPATH.*)

150. Dr. Shumer claimed the Endocrine Society (and WPATH) "establish the prevailing standards" for the treatment of gender dysphoria. (Shumer ¶32–33), citing no evidence for his claim. That the Endocrine Society did not engage in any systematic review of the effectiveness of transition and that the E.S. explicitly indicated the evidence for its

safety to be low is already reviewed herein. (See Section VII.A. *Endocrine Society.*)

151. Dr. Shumer claimed that "before puberty, there are no significant differences in athletic performance between girls and boys." (Shumer ¶38.) Peer reviewed research studies from around the world have repeatedly demonstrated the very opposite. Although the differences increase upon puberty, biological males already show even before puberty a 2–5% advantage in swimming, running, jumping, and a range of strength tests. Such differences have been repeatedly identified in studies of children from Australia (Catley 2013), Germany (Woll 2011), Norway (Tønnessen 2015), Spain (Gulias-González 2014), and Latvia (Sauka 2011). Dr. Shumer's declaration did not contest or mention the research studies cited among the legislative findings.

152. The single source cited within Dr. Shumer's entire declaration was Handelsman et al. (2018), to support the claim that testosterone was the "driver" of the post-pubertal male advantage in muscle mass and strength. Missing from the Shumer report, however, was the other study from Handelsman (2017), which reported, again, that the male advantage already existed *before* puberty:

> In track and field athletics, the effects of age on running performance… showed that the *prepubertal differences of 3.0%* increased to a plateau of 10.1% with an onset (ED20) at 12.4 years and reaching midway (ED50) at 13.9 years. For jumping,…the *prepubertal difference of 5.8%* increased to 19.4% starting at 12.4 years and reaching midway at 13.9 years. (Handelsman 2017 at 70, italics added)

C. Dr. Budge's assertions are unsupported by the research literature and contradict the research literature.

153. In referring to the basis of her assertions, Dr. Budge claimed she relied on "the same types of material that experts in my field of study regularly rely upon." (Budge ¶13.) The contents of her declaration show the opposite. Dr. Budge's asserted very many claims about transgender youth (Budge ¶¶17–22) and the medical care for transgender youth (Budge ¶¶23–34). Her claims are entirely unsupported, failing to include even a single peer reviewed research article to support even a single claim about the nature, causes, diagnosis,

or treatment of gender dysphoria. The materials upon which experts in this field rely is the peer reviewed literature, culminating in systematic reviews of their findings. (See Section III. *Clinical Research Pyramid of Evidence.*) Dr. Budge did not cite or indicate considering the conclusions of any of the systematic reviews conducted by the international health care bodies. (See Section VI *Systematic Reviews of Safety and Effectiveness.*)

154. Dr. Budge misrepresents "APA" and the "DSM." In ¶10 of her declaration, she refers to the "American *Psychological* Association" as "APA," and she notes affiliations she has with that organization. (Budge ¶11.) Her declaration subsequently refers to aspects of the diagnostic category "which the *APA* calls gender dysphoria." (Budge ¶23 line 22, italics added.) That organization, however, is the American *Psychiatric* Association, of which Dr. Budge is not a member: She clearly identified herself as a psychologist, not a psychiatrist. (Budge ¶3.) In the next sentence, Dr. Budge cites "APA's Diagnostic and Statistical Manual of Mental Disorders (DSM-5)" (Budge ¶23), from 2013, by the American *Psychiatric* Association. That edition is outdated, having been superseded by its text revision (the DSM-5-TR), published by American *Psychiatric* Association in 2022.

155. Dr. Budge asserted without support that "gender identity is well-established in psychology and medicine." (Budge ¶17.) Her claim does not reflect the status of the field. Indeed, the DSM-5-TR itself says the very opposite: "The area of sex and gender is highly controversial and has led to a proliferation of terms whose meanings vary over time and within and between disciplines." (American Psychiatric Association 2022 at 511.) (See also Section VIII.A. *Sex and Sex-Assigned-at-Birth.*)

156. Dr. Budge claimed that "sex" is comprised of multiple characteristics, and she included among them "gender identity." (Budge ¶19.) As already indicated herein, gender identity is *excluded* from the definition of sex. (See also Section VIII.B. *Subjective feelings.*) The same is true of the DSM-5-TR, which also says the opposite of Dr. Budge's unsourced claim:

> In this chapter [on gender dysphoria], *sex* and *sexual* refer to the biological indicators of male and female (understood in the context of reproductive capacity),

such as in sex chromosomes, gonads, sex hormones, and nonambiguous internal and external genitalia. (American Psychiatric Association at 511, italics in original.)

157. Dr. Budge's unsourced claim that gender identity is innate (Budge ¶20) is untrue. The peer reviewed research shows *sexual orientation* is innate, not gender identity. (See Section X. *Neuroimaging.*)

158. Dr. Budge offers a brief summary indicating potential benefits to participating in school-sponsored athletics (Budge ¶¶35–37), which is not in contention. The large majority of transgender adolescents are biologically female, and under SB-1165, continue to be permitted to participate on male designated teams, and these benefits remain available to them. Because SB-1165 explicitly permits participation in coed and mixed teams, such benefits remain available to everyone else. Moreover, the majority of adolescents who identify as transgender specifically identify as "non-binary" or "gender fluid." Teams designated mixed or coed represent a *closer* match to such identities than those designated female.

159. Dr. Budge was explicit that her opinion about SB-1165 being "psychological damaging" was "based on my experience working with transgender youth." (Budge ¶39). As indicated in the present report, such opinions represent the very lowest level of evidence. (See Section III.E. *Expert Opinion.*) In the absence of studies comparing participation on female designated teams versus coed- or mixed- teams, it is not possible for Dr. Budge to know what she claims.

160. Dr. Budge included no evidence to support her dramatic claim "irreversible and severe damage" including trauma, suicidal ideation, and suicide attempts. (Budge ¶39.) Dr. Budge's citation of Hughes et al. (2022) insinuates that Hughes to have been a study showing those results; however, it was not a study of impact at all. Rather, it was a survey of physicians and nurses providing the very hormones and other procedures whose safety and effectiveness are being challenged by the international health care community. (See Section VI. *Systematic Reviews of Safety and Effectiveness.*) As noted herein, such surveys

do not constitute meaningful scientific evidence (See Section III.F. *Surveys*), and this survey in particular made no effort to hide its political rather than objective purpose of the four questions it asked:

> Participants were asked to provide their thoughts about these proposed laws in four separate open-ended survey questions: ‘‘What do laws like this mean to you as a gender-affirming care provider for transgender and gender diverse youth?’’ ‘‘How do you think laws like this would impact your practice?’’ ‘‘How do you think laws like this would impact your patients?’’ ‘‘What steps, if any, do you think would be helpful to ensure transgender and gender diverse youth are not banned from participating in sports?’’ (Hughes 2022 at 248.)

161. Dr. Budge conveyed a warning “that the physical consequences for transgender youth of not being able to participate in sports include worse cardiovascular outcomes, poor bone mineral density, and poor neurocognitive development when compared to non-transgender youth” (Budge ¶39), citing Barrera et al. (2022). First, Barrera et al. (2022) is an editorial, not a peer-reviewed research finding. Second, the protection of mixed and coed activities prevents the situation Barrera warns against. Finally, and perhaps most relevantly, the listed health consequences are not caused by lack of exercise—They are caused by the *puberty-blockers and cross-sex hormones* used on the children. As Barrera wrote: “Increased access to physical activity for TGD [(transgender and gender-diverse)] youth is important for improving cardiovascular risk and mediating *the expected changes that occur with GAH* [(gender affirming hormones)].” (Barrera 2022 at 223, italics added.) (See also Section XI. *Known and Potential Harms.*)

162. The three remaining sources cited by Dr. Budge (Tebbe 2021; Kosciw 2022; McLemore 2015) are all surveys as well. They do not represent empirical research capable of demonstrating the causal connections which Dr. Budge attributes to them. They reflect the beliefs and political views of the people taking the surveys, not the accuracy of those views and beliefs. The recent Washington Post-Kaiser Family Foundation survey found both that a majority of Americans support laws prohibiting discrimination against trans

people *and at that same time* support restricting female sports teams to biological females. (Meckler & Clement 2023.)

D. Dr. Budge's report did not contest, or even address, the pertinent scientific or psychological issues or their implications.

163. Dr. Budge's declaration did not address the legislative findings of SB-1165 acknowledging the biological differences between males and females. Her declaration did not address any of the peer reviewed studies cited in SB1165 and did not cite any peer reviewed studies with conclusions that contradict the conclusions of the studies in SB-1165. Dr. Budge's analysis did not include any issues regarding competitive fairness from including people other than biological females on teams of biological females. It is not possible to develop an objective balance by considering only one side of such an issue.

164. Dr. Budge's analysis did not include the psychological effects on biological females of the participation of biological males. Because adolescents do not typically undergo genital surgery until adulthood, people with an intact penis and testicles would be present in the females' showers, locker rooms, and other areas designated female-only.

165. Dr. Budge's analysis did not address the capacity of mixed or coed teams to prevent the potential negative effects she postulated.

I swear or affirm under penalty of perjury that the foregoing is true and correct.

Dated: May 18, 2023 Signed: */s/ Dr. James M. Cantor, Ph.D.*

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