Expert Report of

James Cantor, PhD.

Boe v. Marshall

United States District Court
Middle District of Alabama
Northern Division

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I. Credentials and Qualifications

A. Education and professional background

1. I am a sexual behavior scientist, with an internationally recognized record studying the development of human sexualities, and an expert in research methodology of sexuality. . My curriculum vitae is attached as Appendix 1 to this report. My publication record includes both biological and non-biological influences on sexuality, ranging from pre-natal brain development, through adulthood, to senescence. The primary, but not exclusive, focus of my own research studies has been the development of atypical sexualities. In addition to the studies I myself have conducted, I am regularly consulted to evaluate the research methods, analyses, and proposals from sexual behavior scientists throughout the world. The methodologies I am qualified to assess span the neurochemical and neuroanatomic level, individual behavioral level, and social and interpersonal levels.

2. I am trained as a clinical psychologist and neuroscientist, and I am the author of over 50 peer-reviewed articles in my field, spanning the development of sexual orientation, gender identity, hypersexuality, and atypical sexualities collectively referred to as *paraphilias*. Although I have studied many atypical sexualities, the most impactful of my work has been MRI and other biological studies of the origins of pedophilia. That work has revolutionized several aspects of the sex offender field, both with regard to the treatment of offenders and to the prevention of sexual abuse of children. In 2022, I received the Distinguished Contribution Award from the Association for the Treatment and Prevention of Sexual Abuse in recognition of my research and its integration into public policy. My efforts in this regard have been the subject of several documentary films.

3. Over my academic career, my posts have included Senior Scientist and Psychologist at the Centre for Addiction and Mental Health (CAMH), and Head of Research for CAMH's Sexual

Behaviour Clinic. I was on the Faculty of Medicine of the University of Toronto for 15 years and have served as Editor-in-Chief of the peer reviewed journal, *Sexual Abuse*. That journal is one of the top-impact, peer-reviewed journals in sexual behavior science and is the official journal of the Association for the Treatment and Prevention of Sexual Abuse. In that appointment, I was charged to be the final arbiter for impartially deciding which contributions from other scientists in my field merited publication. I believe that appointment indicates not only my extensive experience evaluating scientific claims and methods, but also the faith put in me by the other scientists in my field. I have also served on the Editorial Boards of *The Journal of Sex Research*, the *Archives of Sexual Behavior*, and *Journal of Sexual Aggression*. I am currently the Director of the Toronto Sexuality Centre in Canada. Thus, although I cannot speak for other scientists, I regularly interact with and am routinely exposed to the views and opinions of most of the scientists active in our field today, within the United States and throughout the world.

4. For my education and training, I received my Bachelor of Science degree from Rensselaer Polytechnic Institute, where I studied mathematics, physics, and computer science. I received my Master of Arts degree in psychology from Boston University, where I studied neuropsychology. I earned my doctoral degree in psychology from McGill University, which included successfully defending my doctoral dissertation studying the effects of psychiatric medication and neurochemical changes on sexual behavior, and included a clinical internship assessing and treating people with a wide range of sexual and gender identity issues.

5. I have a decades-long, international, and award-winning history of advocacy for destigmatizing people with atypical sexualities. While still a trainee in psychology, I founded the American Psychological Association's (APA) Committee for Lesbian, Gay, and Bisexual Graduate Students. Subsequently, I have served as the Chair for the Committee on Science Issues

for APA's Division for the Psychology of Sexual Orientation and Gender Diversity and was appointed to its Task Force on Transgender Issues. Throughout my career, my writings and public statements have consistently supported rights for transgender populations and the application of science to help policy-makers best meet their diverse needs. Because my professional background also includes neurobiological research on the development of other atypical sexualities, I have become recognized as an international leader also in the destigmatizing of the broader range of human sexuality patterns.

6. I am highly experienced in the application of sex research to forensic proceedings: I have served as the Head of Research for the Law and Mental Health Program of the University of Toronto's psychiatric teaching hospital, the Centre for Addiction and Mental Health, where I was appointed to the Faculty of Medicine.

7. I have served as an expert witness in 21 cases in the past four years, as listed on my *curriculum vitae*. These cases included criminal, civil, and custody proceedings, preliminary injunction and Frye hearings, as well as trials. I have testified in courts in Canada and throughout the U.S., including Alabama, Arizona, Florida, Illinois, Indiana, Kansas, Kentucky, Massachusetts, New York, Texas, Utah, and West Virginia. I have provided expert testimony concerning the nature and origins of atypical sexualities, as well as concerning gender dysphoria and gender identity in children.

8. For my work in this case, I am being compensated at the hourly rate of $400 per hour. My compensation does not change based on the conclusions and opinions that I provide here or later in this case or on the outcome of this lawsuit.

B. Clinical expertise vs. scientific expertise

9. In clinical science, there are two kinds of expertise: Clinicians' expertise regards

applying general principles to the care of an individual patient and the unique features of that case. A scientist's expertise is the reverse, accumulating information about many individual cases and identifying the generalizable principles that may be applied to all cases. Thus, different types of decisions may require different kinds of experts, such that questions about whether a specific patient represents an exception to the general rule might be better posed to a physician's expertise, whereas questions about establishing the general rules themselves might be better posed to a scientist's.

10. In legal matters, the most familiar situation pertains to whether a given clinician correctly employed relevant clinical standards. Often, it is other clinicians who practice in that field who will be best equipped to speak to that question. When it is the clinical standards that are themselves in question, however, it is the experts in the assessment of scientific studies who are the relevant experts.

C. The professional standard to evaluate treatment models is to rely on objective assessors, not treatment model users in a conflict of interest with its results.

11. I describe in a later section the well-recognized procedures for conducting reviews of literature in medical and scientific fields to evaluate the strength of evidence for particular procedures or treatments. Importantly, the standard procedure is for such evaluations to be conducted by objective assessors with expertise in the science of assessment, and not by those with an investment in the procedure being assessed. Because the people engaged in providing clinical services are necessarily in a conflict of interest when claiming that their services are effective, formal evaluations of evidence are routinely conducted by those *without* direct professional involvement and thus without financial or other personal interest in whether services are deemed to be safe or effective. This routine practice standard is exemplified by all of the only three

systematic, comprehensive research reviews that have been conducted concerning the safety and efficacy of puberty blockers and cross-sex hormones as treatments for gender dysphoria in children.

12. In 2020, England's National Health Service (NHS) commissioned a major review of the use of puberty blockers and cross-sex hormones in children and young people and appointed prominent pediatrician Dr. Hilary Cass to lead that review, explicating that "Given the increasingly evident polarization among clinical professionals, Dr. Cass was asked to chair the group as a senior clinician with *no prior involvement* or fixed views in this area." (Cass 2022 at 35, italics added.) Dr. Cass's committee in turn commissioned formal systematic reviews of evidence from the England National Institute for Health & Care Excellence (NICE), a government entity of England's Department of Health and Social Care, established to provide guidance to health care policy, such as by conducting systematic reviews of clinical research, but without direct involvement in providing treatment to gender dysphoric individuals. (https://www.nice.org.uk/.) Similarly, the Finnish health care council commissioned its systematic review to an external firm, Summaryx Oy. (Pasternack 2019.) Summaryx Oy is a "social enterprise" (a Finnish organization analogous to a non-profit think-tank) that conducts systematic research reviews and other analyses for supporting that nation's medical and social systems. Its reviews are conducted by assessment professionals, not by clinicians providing services. (www.summaryx.eu/en/.) The systematic review by Sweden's National Board of Health and Welfare (NBHW) included four experts. (SBU Scoping Review 2019.) In addition to their own research fields, they provided clinical services in areas adjacent to but apart from gender dysphoric children, such as physical disorders of sexual development (Dr. Berit Kriström) or gender dysphoria in adults (Dr. Mikael Landén).

13. My own most-cited peer-reviewed paper relating to gender dysphoria in minors

illustrates the expertise in the evaluation of scientific evidence that I have and am recognized for. That is, that paper provided not clinical advice or a clinical study, but rather a review and interpretation of the available evidence concerning desistance in children who suffer from gender dysphoria, as well as of evidence (and lack of evidence) concerning the safety and efficacy of medical transition to treat gender dysphoria in minors. (Cantor 2019.)

14. My extensive background in the assessment of sexuality research and in the development of human sexuality places me in exactly the position of objectivity and freedom from conflict-of-interest required by the universal standards of medical research science.

15. I do not offer opinions about the best public policy. Multiple jurisdictions have attempted multiple different means of implementing that science into various public policies. Although I accept as an axiom that good public policy must be consistent with the scientific evidence, science cannot objectively assess societal values and priorities. Therefore, my opinions summarize and assess the science on which public policy is based, but I can offer no opinion regarding which public policy mechanisms would be best in light of that science.

II. Multiple international health care systems that had initially expanded medicalized transition to include minors have reversed that policy, as research on safety and effectiveness accumulated, in a growing international trend against the medicalized transition of minors.

16. Medicalized interventions for minors originated in European clinics (most prominently in the Netherlands and Sweden), and these precedents (and in particular the so-called "Dutch Protocol") are frequently cited by American clinicians. However, growing concerns about safety together with the continuing absence of reliable evidence of benefit even after more than 20 years of experience have led respected and far-from "conservative" European health care ministries to step back and discourage or even cease providing medicalized transition of minors, other than in exceptional and carefully limited circumstances, such as within registered and approved research trials. Instead, these authorities now endorse psychotherapy as the treatment of choice for minors, with medical interventions representing a method of last resort, if permitted at all. These range from medical advisories to outright bans on the medical transition of minors. I provide details concerning these policy changes below, and provide additional details regarding the underlying systematic reviews in Section II and V below.

A. England

17. The National Health Service (NHS) of the United Kingdom centralized gender counselling and transitioning services into a single clinic, the Gender Identity Development Service (GIDS) of the Tavistock and Portman NHS Foundation Trust. Between 2008 and 2018, the number of referrals to the clinic had increased by a factor of 40, leading to a government inquiry into the causes. (Rayner 2018.) The GIDS was repeatedly accused of approving and endorsing medical transition in minors without adequate justification, including by 35 members of the GIDS own staff, who resigned by 2019. (BBC News 2021; Donnelly 2019). An ex-governor and psychotherapist of the Trust who resigned, Marcus Evans, said staff feared being called

transphobic, which was impacting their objectivity in their work. (Doward 2019a).

18. In 2020, a former patient of the GIDS, Keira Bell, brought a lawsuit alleging that the GIDS practices with respect to prescribing puberty blockers for minors were unproven and potentially harmful in ways that meant that it was impossible for minors to give meaningful informed consent. After taking extensive expert evidence, the trial court concluded that puberty blockers might have "potentially irreversible" and "life-changing" effects on a young person (*Bell v. Tavistock*, [2020] EWHC 3274 (Admin), ¶148, 151), that there was "very limited evidence as to its efficacy" (¶134) such that "it is right to call the treatment experimental" (¶148), and that use of puberty blockers almost always led to use of cross-sex hormones that "may well lead to a loss of fertility" (¶¶ 137-138). While an appeals court later concluded that the trial court had exceeded the proper role of the court in making factual findings on these questions, the appeals court acknowledged that "Medical opinion is far from unanimous about the wisdom of embarking on treatment before adulthood. The question raises not only clinical medical issues but also moral and ethical issues, all of which are the subject of intense professional and public debate." (Bell v. Tavistock 2021 at ¶3.)

19. Perhaps prompted by the Kiera Bell litigation, also in 2020 the English National Health Service ("NHS") commissioned the thorough independent review of the use of puberty blockers and cross-sex hormones to be chaired by Dr. Cass that I have described above. After an extensive process that included obtaining the systematic reviews of all published studies bearing on safety or efficacy of these hormonal interventions in minors as well as "extensive" listening sessions with clinicians, patients, and families, in February 2022 Dr. Cass issued an extensive "Interim Report" summarizing the state of the relevant medical science and in particular highlighting the presence of serious but unstudied risks, and the lack of strong evidence of efficacy. I will quote specific

items from Dr. Cass's Report as relevant to specific topics below. At a high level, Dr. Cass concluded that to date there has been "very limited research on the sexual, cognitive, or broader developmental outcomes" from the use of puberty blockers for gender dysphoria (Cass 2022 at 19), that it is an unanswered question "whether the evidence for the use and safety of [puberty blockers] is strong enough as judged by reasonable clinical standards" (at 37), and that "the available evidence was not strong enough to form the basis of a policy position" with regard to use of both puberty blockers and cross-sex hormones in minors (at 35).

20. Following issuance of Dr. Cass's Interim Report, the English NHS has published a consultation document concerning a proposed revised service specification under which "NHS England will only commission [puberty blockers] in the context of a formal research protocol." (NHS Interim Service Specification at 12.)

B. Finland

21. In Finland, minors were made eligible for medicalized transition in 2011 by that country's health care service, the Council for Choices in Health Care in Finland (COHERE). Assessments of mental health and preparedness were centralized by law into two research clinics, Helsinki University Central Hospital and Tampere University Hospital.

22. In 2019, the Service Selection Council (Palko) of the Finnish Ministry of Social Affairs and Health commissioned a systematic review of the effectiveness and safety of medicalized transition (Pasternack 2019), and in 2020, Finnish researchers published an analysis of the outcomes of adolescents diagnosed with transsexualism and receiving cross-sex hormone treatment in Finland's Tampere University Hospital. (Kaltiala 2020.) Despite the purpose of medical transition being to improve mental health, the study showed:

> 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. (Kaltiala 2020 at 213.)

They concluded that the youth who were functioning well after transition were those who were already functioning well before transition, and those who were functioning poorly before transition continued to function poorly after transition.

23. Importantly, the results of this study exemplify why correlations reported from surveys cannot be interpreted as evidence of causality. Mental health assessment would exclude the most poorly functioning youth from among those permitted to transition, but transition itself did not improve the functioning of those who were permitted to transition.

24. Consistent with the results of the independent evidence review by Summaryx Oy and analysis of the ethical issues involved, Finland's health care service ended the surgical transition of minors, ruling in 2020 that "Surgical treatments are not part of the treatment methods for dysphoria caused by gender-related conflicts in minors." (COHERE Summary 2020.) The review of the research concluded that "[N]o conclusions can be drawn on the stability of gender identity during the period of disorder caused by a psychiatric illness with symptoms that hamper development." (COHERE Summary 2020.) COHERE also greatly restricted access to puberty-blocking and cross-sex hormonal treatments, explicating that they may be considered for minors "only if it can be ascertained that their identity as the other sex is of a permanent nature and causes severe dysphoria," and only "if the need for it continues *after* [any] other psychiatric symptoms have *ceased* and adolescent development is progressing normally." (COHERE Summary 2020, italics added.) They restricted the procedures to their centralized research clinics. The council was explicit in noting the lack of research needed for decision-making, "There is also a need for more information on the disadvantages of procedures and on people who regret them." (COHERE Summary 2020.) In light of the special developmental and ethical considerations surrounding

minors, COHERE recommended that "no decisions should be made that can permanently alter a still-maturing minor's mental and physical development." (COHERE Recommendation 2020 at 7.)

C. Sweden

25. Sweden's national health care policy regarding trans issues has developed quite similarly to that of the UK. Already in place 20 years ago, Swedish health care policy permitted otherwise eligible minors to receive puberty-blockers beginning at age 14 and cross-sex hormones at age 16. At that time, only small numbers of minors sought medical transition services. An explosion of referrals ensued in 2013–2014. Sweden's Board of Health and Welfare ("Socialstyrelsen") reported that, in 2018, the number of diagnoses of gender dysphoria was 15 times higher than 2008 among girls ages 13–17. (Swedish Socialstyrelsen Support 2022 at 15.)

26. Sweden has long been very accepting with regard to sexual and gender diversity. In 2018, a law was proposed to lower the age of eligibility for surgical care from age 18 to 15, remove the requirement for parental consent, and lower the legal age for change of gender to age 12. A series of cases of regret and suicide following medical transition were reported in the Swedish media. (Orange 2020.) In 2019, the Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) therefore initiated its own systematic review of the research. The SBU released English-language results first as a summary and then published as a peer reviewed article. (Ludvigsson et al. 2023.) Like the UK, the Swedish investigation employed standardized review methods to ensure the encapsulation of the all the relevant evidence and came to the same conclusions: "This systematic review of almost 10 000 screened abstracts suggests that long-term effects of hormone therapy on psychosocial and somatic health are unknown, except that GnRHa treatment seems to delay bone maturation and gain in bone mineral density." (Ludvigsson 2023 at 12). They emphasized, "The absence of long-term studies is worrying because

many individuals start treatment as minors (<18 years) and CSHT is lifelong." (Ludvigsson 2023 at 10.) Regarding the full set of studies, "No randomised controlled trials were found, but we could identify 24 relevant observational studies. However, these were limited by methodological weaknesses, for instance lack of or inappropriate control group, lack of intra-individual analyses, high attrition rates that precluded conclusion to be drawn." (Ludvigsson 2023 at 9–10.)

27. In 2021, the leading Swedish pediatric gender clinic, at the Karolinska Institute, issued a new policy statement in which it stated that the Swedish evidence review "showed a lack of evidence for both the long-term consequences of the treatments, and the reasons for the large influx of patients in recent years." (Karolinska 2021.) The Karolinska Institute further stated that "These treatments are potentially fraught with extensive and irreversible adverse consequences such as cardiovascular disease, osteoporosis, infertility, increased cancer risk, and thrombosis." In a dramatic reversal of its policy, the Institute announced that "In light of the above, and based on the precautionary principle, which should always be applied, it has been decided that hormonal treatments (i.e., puberty blocking and cross-sex hormones) will not be initiated in gender dysphoric patients under the age of 16." Further, the Karolinska clinic announced that patients ages 16–18 would receive such treatments *only* within research settings (clinical trials monitored by the appropriate Swedish research ethics board). (Karolinska 2021.)

28. In 2022, the Swedish National Board of Health and Welfare published a major new national policy document concerning "Support, investigation and hormone therapy in gender incongruence in children and youth," including an English-language summary. (Swedish Socialstyrelsen Support 2022.) The National Board of Health noted "the continued lack of reliable scientific evidence concerning the efficacy and the safety of both [puberty blockers and cross-sex hormones]," and concluded (based on the commissioned evidence reviews) that "the evidence on

treatment efficacy and safety is still insufficient and inconclusive for all reported outcomes. Further, it is not possible to determine how common it is for adolescents who undergo gender-affirming treatment to later change their perception of their gender identity or interrupt an ongoing treatment." As a result, the Board of Health concluded that, "[f]or adolescents with gender incongruence, the . . . risks of puberty suppressing treatment with GnRH-analogues and gender-affirming hormonal treatment currently outweigh the possible benefits." (Swedish Socialstyrelsen Support 2022 at 10-12.) Accordingly, the Swedish Board of Health and Welfare "recommends restraint when it comes to hormone treatment." (Swedish Socialstyrelsen Updated Recommendations 2/22/22.)

D. France

29. While medical authorities in France have not issued any actual restriction, in 2022, the Académie Nationale de Médecine of France issued a strongly worded statement, citing the Swedish ban on hormone treatments:

> [A] great medical caution must be taken in children and adolescents, given the vulnerability, particularly psychological, of this population and the many undesirable effects, and even serious complications, that some of the available therapies can cause…such as impact on growth, bone fragility, risk of sterility, emotional and intellectual consequences and, for girls, symptoms reminiscent of menopause." (Académie Nationale de Médecine 2022.)

For hormones, the Académie concluded "the greatest reserve is required in their use," and for surgical treatments, "[T]heir irreversible nature must be emphasized." The Académie warned "the risk of over-diagnosis is real, as shown by the increasing number of transgender young adults wishing to 'detransition'." Rather than medical interventions, it advised health care providers "to extend as much as possible the psychological support phase." The Académie reviewed and emphasized the evidence indicating the very large and very sudden increase in youth requesting medical transition. It attributed the change, not to society now being more accepting of sexual

diversity, but to social media, "underlining the addictive character of excessive consultation of social networks which is both harmful to the psychological development of young people and responsible, for a very important part, of the growing sense of gender incongruence." (Académie Nationale de Médecine 2022.)

E. Norway

30. In 2022, Norway's Healthcare Investigation Board (Ukom) began a review of that country's guidelines for the medicalized transition of minors. (Block, Norway's Guidance, 2023.) In 2023, it released its report, which concluded that the evidence for the use of puberty blockers and cross-sex hormone treatments in youth was insufficient, and acknowledged the international recognition of the dearth of evidence of safety and effectiveness. The report deemed medicalized transition to be experimental. (Ukom 2023, Summary and Section 11.) The report faulted the existing Norwegian guidelines, published in 2020, for concentrating on "equality and rights" while "deviating from the requirements for the development of knowledge-based guidelines." (Ukom 2023, Summary.)

31. The Norwegian report concluded that "The knowledge base, especially research-based knowledge for gender-affirming treatment (hormonal and surgical), is insufficient and the long-term effects are little known" and that "This applies particularly to the teenage population, which accounts for a large part of the increase in referrals to the specialist health service in the last decade." (Ukom 2023, Summary and Section 7.)

32. In an interview about the report with the *British Medical Journal,* the Ukom Medical Director, Stine Marit Moen, said, "We're concerned that there may be undertreatment, overtreatment, and the wrong treatment" and added:

> We've seen a marked increase in referrals to specialised healthcare services in Norway for teenagers, as seen in many other western countries, and nobody knows

> the reason. The stability of the gender dysphoria of these teenagers is not known, and the evidence of long term effects of gender affirming treatments for this young population is insufficient. (Block, Norway's Guidance, 2023.)

33. Ukom noted that referrals to its national treatment service increased by a factor of eight between 2007 and 2018, and that this increase was largely from young biological females. Seventy-five percent of the referrals to its National Treatment Service had other co-morbid psychiatric diagnoses, including not only depression and anxiety but also autism spectrum disorders, ADHD, and Tourette's Syndrome. (Ukom 2023, Summary and Section 7.)

F. Assertions by U.S. organizations and officials that there is 'no debate' over medicalized transition are false.

34. The international consensus is clearly demonstrated by the multiple recent analyses, statements, and policy decisions from the health care service systems around the world. These include England's National Health Service, which noted the "Scarce and inconclusive evidence to support clinical decision making [which] has led to a lack of clinical consensus on what the best model of care for children and young people experiencing gender incongruence and dysphoria should be." (NHS 2022 at 5.)

35. As these several recent national policy reviews, statements, and recommendations make very clear, there is a great deal of doubt and debate among the sophisticated international medical and mental health community as to whether the administration of puberty blockers and cross-sex hormones to children and young people is the best clinical practice, and as to whether these treatments have been shown to be safe and effective. Indeed, the lack of scientifically reliable data concerning safety and efficacy highlighted by the systematic evidence reviews commissioned by the English National Health Service, by the Swedish National Board of Health and Welfare, and by the Finnish Council for Choices in Health Care in Finland have caused those national health authorities and others to move sharply away from approving puberty blockers, cross-sex

hormones, or surgery for minors.

36. In this report, I explain the evidence and lack of evidence behind that doubt, that debate, and the emerging international consensus of caution reflected in the several recent European policy statements or changes.

37. I note that the plaintiffs' experts have excluded all mention of the international reversals of policy, falsely suggesting a consensus. In fact, practices at U.S. gender clinics and statements by U.S. advocacy voices increasingly represent an outlier view, failing to update policy despite the mounting evidence.

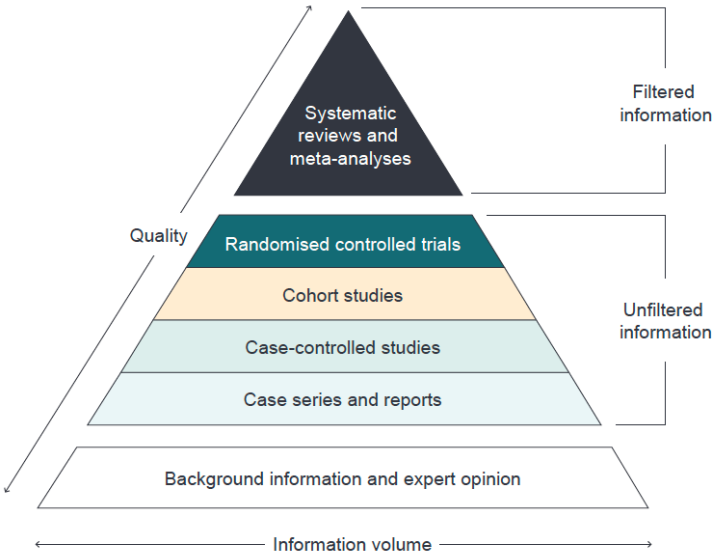
III. Clinical research has a standard *Pyramid of Evidence* that summarizes the relative strength of potential sources of information.

38. The widely accepted starting point in evidence-based medicine is the recognition that clinical experiences and recollections of individual practitioners (often called "expert opinion" or "clinical anecdote") do not and cannot provide a reliable, scientific basis for treatment decisions. Rather, in evidence-based medicine, clinical decision-making is based on objectively demonstrated evidence of outcomes from the treatment options. An essential first step in evidence-based medicine is identifying the relevant findings from among the immense flood of clinical journal articles published each year. Those studies and the evidence they report are then assessed according to the strength offered by the research methods used in each study. The research methods used in a study determine its reliability and generalizability, meaning the confidence one may have that using the same treatment again will have the same result again on other people. In this section, I explain the well-accepted criteria for evaluating the evidentiary value of clinical studies.

A. Clinical research comprises a standard *Pyramid of Evidence*, wherein studies from higher levels of evidence outrank even more numerous studies from lower levels of research.

39. The accepted hierarchy of reliability for assessing clinical outcomes research is routinely represented as a "Pyramid of Evidence" (Figure 1). Scientific questions are not resolved by the number of studies coming to one versus another conclusion. Studies representing higher levels of evidence outrank studies from lower levels. Even large numbers of lower-level studies cannot overcome a study representing a higher level of evidence. Indeed, because lower-level studies are generally faster and less expensive to conduct, it is typical for them to outnumber higher level studies. This is the property meant to be reflected by the pyramid's shape, which is larger at the base and smaller at the apex.

Figure 1: Pyramid of Standards of Evidence



Source: OpenMD. Retrieved from https://openmd.com/guide/levels-of-evidence.

B. The highest level of evidence for safety and effectiveness research is the systematic review of clinical experiments.

40. The most reliable and conclusive method of determining what is actually known or not known with respect to a particular treatment is the *systematic review.* Systematic reviews employ standardized procedures to assess comprehensively all available evidence on an issue, minimizing opportunities for bias in gathering and evaluating research evidence. As described by Dr. Gordon Guyatt, the internationally recognized pioneer in medical research who invented the term *evidence-based medicine,* "A fundamental principle to the hierarchy of evidence [is] that optimal clinical decision making requires systematic summaries of the best available evidence." (Guyatt 2015 at xxvi.)

41. I note that Dr. Antommaria's report for the plaintiffs correctly indicated that "It is best practice to ascertain the studies via systematic reviews of the literature." (Antommaria Report at 6.) Missing from Dr. Antommaria's report is that none of the systematic reviews he cited were systematic reviews of safety and efficacy, both of which are necessary for assessing the risk:benefit

ratio of a treatment. Moreover, I note that none of the plaintiffs' other experts cited any systematic reviews at all, failing to meet the standard Dr. Antommaria and I indicated.

1. Systematic reviews prevent the 'cherry-picking' of studies that favor a particular result.

42. Because systematic reviews are designed to prevent researchers from including only the studies they favor and other biases, systematic reviews are the routine starting point for developing clinical practice guidelines. (Moher 2009.) The methods of a systematic review include:

- Define the scope, including the "PICO": Population/Patient, Intervention, Comparison/Control, and Outcome(s);
- Select and disclose the keywords used to search the (massive) available clinical research database(s) for potentially relevant articles, identify the databases they were applied to, and the date(s) of the searches, including any subsequent updates;
- Select and disclose the inclusion/exclusion criteria to be used to filter the "hits" from the keyword searches to identify research studies to be included in the detailed review;
- Review abstracts to select the final set of studies, using at least two independent reviewers to allow for measuring inter-rater reliability on the criteria;
- Code each study's results impacting the research question(s), disclosing the list of all studies and the results coded from each;
- Evaluate the reliability of the results [risk of bias] of each included study, applying uniform criteria across them all.

43. As detailed in Section V, several systematic reviews have been conducted of the outcomes of medicalized transition of gender in minors. Their conclusions are highly consistent with each other. Much of the expert testimony offered by plaintiffs' experts, however, depends on levels of evidence far lower on the pyramid of evidence (e.g., "expert opinion") or beneath the pyramid entirely (e.g., survey studies) while ignoring the thorough, high-quality systematic reviews available in the research literature. Doing so is in direct conflict with foundational principles of evidence-based medicine.

2. Systematic reviews prevent biased assessment of individual studies by uniformly applying standard criteria to each study reviewed. The most widely used criteria set is "GRADE."

44. In order to produce unbiased assessment of the studies within the systematic review, all the studies must be evaluated using the same evaluation criteria. Without such criteria, assessments can become influenced by researchers who, intentionally or not, hold the evaluative bar higher or lower for studies according to whether the studies' conclusions support or challenge that researcher's perspective. Several such systems have been developed. The most widely used system is the "Grading of Recommendations, Assessment, Development and Evaluations" (GRADE). (Goldet & Howick 2013.) In the GRADE system, studies' findings are downgraded for:

- Risk of bias:[1]
    - Lack of clearly randomized allocation sequence,
    - Lack of blinding,
    - Lack of allocation concealment,
    - Failure to adhere to intention-to-treat analysis,
    - Trial is cut short,
    - Large losses to follow-up;
- Inconsistency;
- Indirectness of evidence;
- Imprecision; and
- Publication bias (when studies with 'negative' findings remain unpublished).

Studies' ratings are upgraded if their findings identify:

- A large effect of the treatment;
- A dose-response relationship (the size of the effect has a systematic association with the dose of the treatment given); or
- That all plausible biases only *reduce* the apparent effect of the treatment (necessarily making the estimated effect sizes conservative estimates).

[1] In science, including in the GRADE system, the term "bias" refers to any external influence leading to a systematic over- or underreporting of the outcome being measured. That is, in this context "bias" is not used in the sociopolitical sense of personal values.

45. GRADE assessments yield a four-point score representing the certainty that a reported treatment effect is true. These certainty scores are (GRADE Handbook, Section 5):

Certainty	Meaning
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

C. The highest level experimental study of clinical safety and effectiveness is the Randomized Controlled Trial (RCT). RCTs can demonstrate that a given treatment causes (rather than only correlates with) a given outcome.

46. Randomized Controlled Trials are the gold standard method of assessing the effects caused by an experimental treatment. The great scientific weight of RCTs follows from the randomization: people do not pick which research group they are in—a treatment group or a control group. Without random group assignment, it is not possible to identify which, if any, changes are due to the treatment itself or to the factors that led to who did and did not receive treatment.

47. Levels of evidence lower than RCTs are unable to distinguish when changes are caused by the experimental treatment, or by factors that can mimic treatment effects, such as 'regression to the mean' and the placebo effect.

48. In the absence of evidence that X causes Y, it is a scientific error to use language indicating there is causal relationship. In the absence of evidence of causality, it is scientifically unsupportable to describe a correlation with terms such as: increases, improves, benefits, elevates,

leads to, alters, influences, results in, is effective for, causes, changes, contributes to, leads to, yields, impacts, decreases, harms, and depresses. Scientifically valid terms for correlations include: relates to, is associated with, predicts, and varies with.

49. I note that the plaintiffs' experts repeatedly misrepresent studies using causal language to describe studies that are unable to demonstrate causality. Such language incorrectly asserts that the evidence is stronger than it actually is.

1. RCTs, but not lower levels of evidence, overcome biases representing 'regression to the mean' and other factors that can mimic clinical improvement.

50. 'Regression to the mean' arises when researching issues, such as mood, depression, or levels of emotional distress that typically fluctuate over time. People are more likely to seek out treatment during low points rather than high points in their emotional lives. Thus, when tracking emotional states over time, the average of a group of people in a treatment group may often show an increase; however, without an untreated control group to which to compare them, researchers cannot know whether the group average would have increased anyway, with only the passage of time.

51. Blinding or masking participants in an RCT from which group they are in has been described as a preferred strategy since the 1950s, in order to exclude the possibility that a person's expectations of change caused any changes observed (the "placebo effect"). In practice, however, it has often made little or no significant difference. For example, a study using very high quality methods—meta-analysis of meta-analysis research—has revealed no statistical difference in the sizes of the effects detected by blinded/placebo-controlled studies from non-blinded/non-placebo-controlled studies of depression. (Moustgaard 2019.) That is, the pre-/post- treatment differences found in placebo groups are not as attributable to participants' expectations of improvement as

they are to expectable regression to the mean. (Hengartner 2020.)

2. When a 'no treatment control group' is untenable, RCTs use an 'active comparator' group instead.

52. It is not always possible to compare a group receiving a treatment to a group receiving only an inactive procedure, such as a placebo treatment or no treatment at all. In such situations, the standard, ethical, clinical research method is to compare two active treatments with each other.

53. The systematic reviews from England explicitly called for 'active comparator' studies to test whether medicalized transition of minors shows mental health benefits superior to those obtained from psychotherapy. (NICE 2020a at 40; NICE 2020b at 47.) Risk:benefit analysis cannot justify the greater risks associated with medicalization without evidence of correspondingly greater benefit.

D. Cohort studies are the highest level of evidence about medicalized transition currently available.

54. The highest-level study of medicalized transition of minors conducted thus far are cohort studies: gathering a sample of individuals who chose to undergo treatment and tracking them over time. Cohort studies are able to answer some questions that lower-level studies cannot, such as whether a high-functioning group improved over time versus having been composed of people who were already high-functioning. Cohort studies are, however, unable to demonstrate causality, to identify how much of any change was due to regression to the mean, or to detect any placebo effects.

E. Expert opinion represents the least reliable evidence.

55. As Figure 1 illustrates, evidence-based medicine opinion based on clinical experience is identified as the *least* reliable source of medical knowledge. Among other reasons, this is because non-systematic recollections of unstructured clinical experiences with self-selected

clientele in an uncontrolled setting is the most subject to bias. Indeed, mere "clinical experience" was long the basis of most medical and mental health clinical decisions, and it was precisely the scientific and clinical inadequacy of this type of "knowledge" that led to the development and widespread acceptance of the importance of evidence-based medicine. As Dr. Guyatt has written, "EBM places the unsystematic observations of individual clinicians lowest on the hierarchy," both because EBM "requires awareness of the best available evidence," and because "clinicians fall prey to muddled clinical reasoning and to neglect or misunderstanding of research findings." (Guyatt 2015 at 10, 15.)

F. Surveys and cross-sectional studies cannot demonstrate treatment effectiveness.

56. Surveys represent observational research rather than experimental research. (In science, experiments are studies involving a manipulation, not merely observation, by the researcher.) Surveys and cross-sectional studies can provide only correlational data and cannot demonstrate causality. (See Section IV below). It is not possible for a survey to yield evidence that a treatment is effective. No number of surveys can test a treatment, advancing it from 'experimental' to 'established' status.

57. Survey studies do not even appear on the *pyramid of evidence.* In accordance with the routine standards, systematic reviews of treatment studies exclude surveys.

58. I note that the plaintiffs' experts' reports rely largely on survey studies.

IV. Methodological defects limit or negate the evidentiary value of many studies of treatments for gender dysphoria in minors.

A. In science, to be valid, a claim must be objective, testable, and falsifiable.

59. In behavioral science, people's self-reports do not represent objective evidence. It is when emotional and other pressures are strongest that the distinction between and need for objective over subjective evidence is greatest. Surveys do not represent objective evidence. This is especially true of non-random surveys and polls, recruited through online social networks of the like-minded.

B. Correlation does not imply causation.

60. Studies representing lower levels of evidence are often used because they are faster and less expensive than studies representing higher levels. A disadvantage, however, is that they are often limited to identifying which features are *associated* with which other 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.

61. 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).

62. 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').

63. 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.

64. 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.

65. 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.)

66. 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.)

67. 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.

68. 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.

69. 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.

70. 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. 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. Plaintiffs' experts assert that use of puberty blockers and cross-sex hormones on adolescents is "safe." This claim is unsupported by any substantial scientific evidence, depreciates widely recognized risks of serious harm to minors so medicalized, and ignores both the many unknowns and the growing international doubts about their use.

72. 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," as the plaintiffs' experts repeatedly use those words. 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.)

73. 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.

74. 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.

75. 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." Plaintiffs' experts and many advocates in the field of transgender medicine make this error.

B. The McMaster University systematic review of systematic reviews.

76. 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.

77. 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.

78. 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

79. 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.)

80. 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."

81. 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.

82. 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.

83. 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.)

84. 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.

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

The authors' frustration at the total lack of reliable research was evident: "The lack of reliable data

[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/

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 at 10.)

E. Sweden

86. 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

87. 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

88. 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.)

VI. 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.

89. 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.

90. 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 identitify 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.

91. 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.

92. 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.)

93. 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.

94. 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.)

95. 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.

96. 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.

97. 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.)

98. 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.)

99. 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.)

100. 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.)

101. 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.

102. 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.)

103. 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.

104. 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.

105. 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.)

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

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

106. 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.

107. 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."

108. 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.

109. 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.

VIII. Gender Dysphoria is a mental health diagnosis.

110. Gender Dysphoria is a mental health condition defined by diagnostic criteria set out in the *Diagnostic and Statistical Manual of Mental Disorders* ("DSM") 5-TR. (American Psychiatric Ass'n 2022.) While the definitions contain multiple components and vary modestly for children, adolescents, and adults, all cases are characterized by a strong and lasting desire to be the opposite sex, and "clinically significant" distress of sufficient severity to impair the individuals' ability to function in their daily life setting. Gender dysphoria is nowhere defined as a medical (as opposed to mental health) condition, and it is not characterized by any disability or impairment or ill health affecting any part of the physical body.

IX. Distinct mental health phenomena must not be—but frequently are—confused or conflated.

111. One of the most widespread public misunderstandings about transsexualism and people with gender dysphoria is that all cases of gender dysphoria represent the same phenomenon; however, the clinical science has long and consistently demonstrated that prepubescent children expressing gender dysphoria represent a phenomenon distinct from that of adults starting to experience it. That is, gender dysphoric children are not simply younger versions of gender dysphoric adults. They differ in virtually every objective variable measured, including in their responses to treatments. A third presentation has recently become increasingly observed among people presenting to gender clinics: these cases appear to have an onset in adolescence—after the onset of puberty and before adulthood—and occur in the absence of any childhood history of gender dysphoria. Such cases have been called adolescent-onset or "rapid-onset" gender dysphoria (ROGD). Despite having only recently been observed, they have quickly and greatly outnumbered the better characterized types. Moreover, large numbers of adolescents are today self-identifying in surveys as "gender fluid" and "non-binary." These are not recognized mental health diagnoses, and do not relate in any known way to gender dysphoric groups that have been the subject of previous treatment outcome studies. Because each of these phenomena differ in multiple objective features, it is scientifically invalid to extrapolate findings from one type to the others.

A. Adult-Onset Gender Dysphoria consists predominantly of males sexually attracted to females.

112. Whereas Childhood-Onset Gender Dysphoria occurs in biological males and females and is strongly associated with later homosexuality (next section), Adult-Onset Gender Dysphoria consists primarily of biological males sexually attracted to females. (Lawrence 2010.) They typically report being sexually attracted to women and rarely showed gender atypical (effeminate)

behavior or interests in childhood (or adulthood). Some individuals express being sexually attracted to both men and women, and some profess asexuality, but very few indicate having a primary sexual interest only in men. (Blanchard 1998.) Cases of adult-onset gender dysphoria are typically associated with a sexual interest pattern involving themselves in female form (a paraphilia called autogynephilia). (Blanchard 1989a, 1989b, 1991.)

113. Because of the numerous objective differences between adult-, childhood-, and adolescent-onset gender dysphoria, it is not possible to extrapolate from these results to juvenile populations, which responsible authors are careful not to do.

B. Childhood-onset gender dysphoria (prepubertal-onset) is a distinct phenomenon characterized by high rates of desistance in the absence of social or medical transition.

114. For many decades, small numbers of prepubescent children have been brought to mental health professionals for help with their unhappiness with their sex and in the belief they would be happier living as the other sex. The large majority of childhood onset cases of gender dysphoria occur in biological males, with clinics reporting 2–6 biological male children to each female. (Cohen-Kettenis 2003; Steensma Evidence 2018; Wood 2013.)

1. Eleven cohort studies followed children not permitted social transition, all showing the majority to desist feeling gender dysphoric upon follow-up after puberty.

115. 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.

116. 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. *Developmental Psychology, 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.

117. 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."

118. 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.)

119. The consistent observation of high rates of desistance among pre-pubertal children who present with gender dysphoria demonstrates a pivotally important—yet often overlooked—feature: because gender dysphoria so often desists on its own, clinical researchers cannot assume that therapeutic intervention cannot facilitate or speed desistance for at least some patients. That

is, it cannot be assumed that gender identity is immune to influence such as from psychotherapy. Such is an empirical question, and there has not yet been any such research.

120. These same studies are often vaguely cited to assert that the high desistance rates uniformly reported in these 11 studies do not apply to children who have persisted until "the start of puberty" (which is taken to mean Tanner Stage 2), or in an alternative phrasing, that children "who persist until the start of puberty" are likely to continue to persist into adulthood. But these studies taken together do not support that degree of precision. Rather, the studies do not specify at exactly what developmental stage the reported desistance occurred—what they report is that the subjects had desisted by late adolescence or early adulthood. I am aware of no systematic study that establishes that— in the absence of social and/or medical transition—children who experience gender dysphoria are unlikely to desist if they have not desisted by the start of Tanner Stage 2.

2. One cohort study followed children who were permitted social transition. In contrast with children not permitted to transition socially, most persisted in expressing gender dysphoria.

121. In contrast, Olson et al. have now published a single cohort study of prepubescent children, ages 3–12 (average of 8), who had already made a complete, binary (rather than intermediate) social transition, including a change of pronouns. (Olson 2022.) The study did not employ DSM-5 diagnosis, as "Many parents in this study did not believe that such diagnoses were either ethical or useful and some children did not experience the required distress criterion." (Olson 2022.) Unlike the prior research studies, only 7.3% of these (socially transitioned) children ceased to feel gender dysphoric.

122. Although the team publishing this cohort study did not discuss it, their finding matches the prediction of other researchers, that social transition itself represents an active intervention, such that social transition may *cause* the persistence of gender dysphoria when it would have

otherwise resolved, avoiding any need for subsequent medicalization and its attendant risks. Conversely stated, social transition seems to prevent desistance. (Singh 2021; Zucker 2018, 2020.)

123. As recognized by multiple authors, the potential impact of social transition on rates of desistance is pivotal. The Endocrine Society cautions that "social transition...has been found to contribute to the likelihood of persistence." (Hembree 2017 at 3879.) WPATH has stated that after social transition, "A change back to the original gender role can be highly distressing and [social transition can] even result in postponement of this second transition on the child's part." (Coleman 2012 at 176.) In 2013, prominent Vrije University researchers observed:

> Childhood social transitions were important predictors of persistence, especially among natal boys. Social transitions were associated with more intense GD in childhood, but have never been independently studied regarding the possible impact of the social transition itself on cognitive representation of gender identity or persistence. [Social transition] may, with the hypothesized link between social transitioning and the cognitive representation of the self, influence the future rates of persistence. (Steensma 2013 at 588-589.)

3. There is no reliable method for predicting for which children who present with gender dysphoria will persist versus desist.

124. The Endocrine Society Guidelines stated in 2017 that "With current knowledge, we cannot predict the psychosexual outcome for any specific child" (Hembree 2017 at 3876), and this remains true today. Research has not yet identified any reliable procedure for discerning which children who present with gender dysphoria will persist, as against the large majority who will desist, absent transition and "affirmation." Such a method would be valuable, as the more accurately that potential persisters can be distinguished from desisters, the better the risks and benefits of options can be weighted. Such "risk prediction" and "test construction" are standard components of applied statistics in the behavioral sciences. Multiple research teams have reported that, on average, groups of persisters are somewhat more gender non-conforming than desisters, but not so different as to usefully predict the course of any particular child. (Singh 2021;

Steensma 2013.)

125. In contrast, one research team (the aforementioned Olson group) claimed the opposite, asserting that they developed a method of distinguishing persisters from desisters, using a single composite score representing a combination of children's "peer preference, toy preference, clothing preference, gender similarity, and gender identity." (Rae 2019 at 671.) They reported a statistical association (mathematically equivalent to a correlation) between that composite score and the probability of persistence. As they indicated, "Our model predicted that a child with a gender-nonconformity score of .50 would have roughly a .30 probability . . . of socially transitioning. By contrast, a child with gender-nonconformity score of .75 would have roughly a .48 probability." (Rae 2019 at 673.) Although the Olson team declared that "social transitions may be predictable from gender identification and preferences" (Rae 2019 at 669), their actual results suggest the opposite: the gender-nonconforming group who went on to transition (socially) had a mean composite score of .73 (which is less than .75), and the gender-nonconforming group who did not transition had a mean composite score of .61, also less than .75. (Rae 2019, Supplemental material at 6, Table S1.) Both of those are lower than the value of .75, so both of those would be more likely than not to desist, rather than to proceed to transition. That is, Olson's model does not distinguish likely from unlikely to transition; rather, it distinguishes unlikely from even less likely to transition.

126. Further, in the absence of long-term follow-up, it cannot be known what proportion of those who transition and persist through the early stages of puberty will later (for example as young adults) come to regret having transitioned and then *de*transition. Because only a minority of gender dysphoric children persist in feeling gender dysphoric in the first place, "transition-on-demand" increases the probability of unnecessary transition and unnecessary medical risks.

4. Temple Newhook's attempts to dismiss evidence of high rates of desistance from childhood gender dysphoria are invalid.

127. The unanimous consistency across all 11 cohort studies of (non-transitioned) gender dysphoric children offers high confidence in the conclusion that most childhood-onset cases desist during the course of puberty. In 2018, however, a commentary was published, contesting that conclusion, criticizing four studies. (Temple Newhook 2018.) Multiple accomplished international researchers studying outcomes of gender dysphoric children responded (Zucker 2018; Steensma & Cohen-Kettenis 2018), to which the Temple Newhook team wrote a rejoinder. (Winters 2018.) I have reviewed each of these arguments, finding that the Temple Newhook comments rely on demonstrable falsehoods, whereas the responses remain consistent with the peer-reviewed evidence. The Temple Newhook commentary has not altered the consensus of the international medical community, which continues to cite and rely upon these cohort studies.

128. Before delineating each of their arguments, it should be noted that the Temple Newhook team based their analysis on the wrong research reports, attacking only a straw-person version of the contents of the research literature. Table 3 repeats the 11 cohort studies (on the left left) and the four studies Temple Newhook criticized (right):

Table 3.

- Lebovitz (1972)
- Zuger (1978)
- Money & Russo (1979)
- Zuger (1984)
- Davenport (1986)
- Green (1987)
- Kosky (1987)
- Wallien & Cohen-Kettenis (2008)
- Drummond, *et al.* (2008)
- Steensma, *et al.* (2013)
- Singh, 2012/Singh, *et al.* (2021)[4]

- Wallien & Cohen-Kettenis (2008)
- Drummond, *et al.* (2008)
- Steensma, *et al.* (2011, 2013)

129. It should be noted that the Temple Newhook 2018 commentary does not represent a systematic review. Temple Newhook did not indicate search strategies, inclusion/exclusion criteria, coding methods, reliability checks, or other standard procedures used for ensuring objective and unbiased assessment of all relevant studies. Rather, the Temple Newhook analysis targeted a small and selective subset of the research available—a scientifically invalid endeavor, which the systematic review process is meant to prevent. Not only did Temple Newhook skip most of the relevant science, but conversely, Temple Newhook inserted the Steensma 2011 study, which should have been rejected. (The data it reported was already included in Wallien & Cohen-Kettenis 2008.) The Temple Newhook commentary claimed it was "systematically engaging scholarly literature." (Temple Newhook 2018 at 2.) However, as the above reference lists demonstrate, that commentary involved no such systematic procedures.

130. Temple Newhook does not report any research evidence of its own. Rather, the commentary hypothesizes issues they assert could, theoretically, have affected the rates of desistance consistently detected. Scientifically, such a criticism is vacuous: In science, it is always

[4] At the time of the 2018 Temple Newhook commentary, the Singh *et al.,* 2021 study was available as Singh, 2012.

possible for additional, external factors to have affected what was observed.

131. Also, as already detailed herein, the currently available level of evidence for outcomes of medicalized transition is the cohort study. The methodological issues highlighted by Temple Newhook are exactly why randomized, controlled trials (RCTs) need to be conducted, as such studies would be capable of resolving exactly those questions (in whichever direction). In the absence of randomized, controlled studies, however, the correct scientific process is to follow the results of the cohort studies (that is, the systematic reviews of the cohort studies).

132. In the science process, one cannot merely continue to retain a desired hypothesis, rejecting all counter-evidence until a perfect study emerges. This is especially important in clinical science, when the hypothesis relates to physical interventions, in children, with the potential to affect them for their entire lives. Rather, the scientific process proceeds by successive approximation, with results from the best available research replacing lesser quality research, increasing in confidence, but always with the possibility of changes imposed by future evidence.

133. By involving only a few of the full set of cohort studies, the Temple Newhook commentary removes one of the most compelling implications of the existing (cohort) studies: Their results are unanimous. However unlikely it might be for four studies to produce the same result randomly, it is even more unlikely for eleven studies all to come to the same result randomly.

134. Temple Newhook emphasized that gender identity issues differ across times and contexts/political environments, hypothesizing that children attending her clinic might differ from children attending the Toronto and the Amsterdam clinics. Returning once again to the full set of all studies, however, the evidence shows the very opposite: All studies yielded the same result, whether from the 1970s, 80s, 90s, 2000s, 2010s, and wherever in the world any clinic was. Acknowledging the possibility that future studies may lead to a different conclusion, the existing

evidence shows majority desistance, constantly and across all time periods.

135. Consideration of the full set of studies also indicates that the contrast is not Toronto and Amsterdam versus whatever "reality" Temple Newhook perceives. Rather, they show the contrast is between Temple Newhook and every facility in every country ever reporting desistance data on childhood-onset gender dysphoria. Moreover, despite Temple Newhook's mention of influences of political cultures, that commentary does not point out that Canada and the Netherlands are much more politically liberal than the U.S. Although the commentary offers the hypothesis that the Canadian and Dutch contexts might decrease persistence, the commentary does not include the inverse possibility: that these liberal environments might be *"iatrogenic"*—that is, causing dysphoria to continue when it might otherwise remit.

136. Also, the very evidence suggesting that gender dysphoria can be influenced by local environmental factors is itself evidence that gender identity is not, in fact, an innate and immutable feature, potentially amenable to change.

C. Adolescent-Onset Gender Dysphoria, the predominant clinical population today, is a distinct and largely unstudied phenomenon.

137. Concurrent with the advent of social media, a third profile began appearing clinically and socially, characteristically distinct from the two previously identified profiles. (Kaltiala-Heino 2015; Littman 2018.) Despite lacking any history before the current generation, this profile has now numerically overwhelmed the previously known and better characterized types in clinics and on Internet surveys. Unlike adult-onset or childhood-onset gender dysphoria, this group is predominately biologically female. This group typically presents in adolescence, but lacks the history of cross-gender behavior in childhood like the childhood-onset cases have. It is that feature

which led to the term Rapid Onset Gender Dysphoria (ROGD). (Littman 2018.)[5] Cases commonly appear to occur within clusters of peers in association with increased social media use (Littman 2018), and among people with autism or other mental health issues. (Kaltiala-Heino 2015; Littman 2018; Warrier 2020.) (See section XI on Mental Health.) The patterns reported by Littman have now been independently replicated by another study which also found it to be a predominantly female phenomenon, associated with very high rates of social media use, among youth with other mental health issues, and in association with peers expressing gender dysphoria issues. (Diaz 2023.) Due to the multiple differences across the epidemiological and other objective variables, there is no justification for extrapolating findings from adult-onset or childhood-onset gender dysphoria to this new presentation.

138. There do not yet exist any cohort studies of people with adolescent-onset gender dysphoria undergoing medicalized transition. Current studies are limited to surveys typically of volunteers from activist and support groups on the Internet.

139. Moreover, no study has yet been organized in such a way as to allow for a distinct analysis of the adolescent-onset group, as distinct from childhood-onset or adult-onset cases. Many published studies fail to distinguish between people who had childhood-onset gender dysphoria and have aged into adolescence versus people whose onset was not until adolescence. (Analogously, there are reports failing to distinguish people who had adolescent-onset gender dysphoria and aged into adulthood from adult-onset gender dysphoria.) Studies selecting groups according to their current age instead of their ages of onset produces confounded results, representing unclear mixes according to how many of each type of case wound up in the final

[5]After initial criticism, the publishing journal conducted a reassessment of the article. The article was expanded with additional detail and republished. The relevant results were unchanged. Littman's paper as revised has been widely cited.

sample.

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

140. *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.

141. 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 2019 at 48.)

142. 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 at 51.)

143. 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.)

144. 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.)

145. 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.

146. 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.)

147. 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.

148. 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.

149. 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.)

150. 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.

151. 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.)

152. 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.)

153. 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). (See section XI.) 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.

154. 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.

XI. Mental health profiles differ across adult-, adolescent-, and childhood-onset gender dysphoria.

A. Mental health issues in Adult-Onset Gender Dysphoria.

155. Systematic review of all studies examining mental health issues in transgender adults identified 38 such studies. (Dhejne 2016.) The review indicated that many studies were methodologically weak, but nonetheless consistently found (1) that the average rate of mental health issues among adults is highly elevated both before *and after* transition, (2) but that the average was less elevated among adults who completed transition. It could not be concluded that transition improves mental health, however. Patients were commonly receiving concurrent psychotherapy, introducing a confound (meaning, again, that it cannot be determined whether the change was caused by the transitioning or the mental health treatment). Further, several studies showed more than 40% of patients to become "lost to follow-up." It remains unknowable to what extent the information from the remaining participants accurately reflects the whole population.

B. Mental health issues in Childhood-Onset Gender Dysphoria.

156. Elevated rates of multiple mental health issues among gender dysphoric children are reported throughout the research literature. A formal analysis of children (ages 4–11) undergoing assessment at the Dutch child gender clinic showed that 52% fulfilled criteria for a formal DSM diagnosis of a clinical mental health condition other than Gender Dysphoria. (Wallien 2007 at 1307.) A comparison of the children attending the Canadian versus Dutch child gender dysphoria clinic showed only few differences between them, and a large proportion in both groups were diagnosable with clinically significant mental health issues. Results of standard assessment instruments (Child Behavior Check List, or CBCL) demonstrated that among 6–11-year-olds, 61.7% of the Canadian and 62.1% of the Dutch sample satisfied the diagnostic criteria for one or more mental health conditions other than gender dysphoria. (Cohen-Kettenis 2003 at 46-47.)

157. A systematic review of all studies of Autism Spectrum Disorders (ASDs) and Attention-Deficit Hyperactivity Disorder (ADHD) among children diagnosed with gender dysphoria was recently conducted. (Thrower 2020.) It was able to identify a total of 22 studies examining the prevalence of ASD or ADHD youth with gender dysphoria. Studies reviewing medical records of children and adolescents referred to gender clinics showed 6–26% to have been diagnosed with ASD. (Thrower 2020 at 695.) Moreover, those authors gave specific caution on the "considerable overlap between symptoms of ASD and symptoms of gender variance, exemplified by the subthreshold group which may display symptoms which could be interpreted as either ASD or gender variance. Overlap between symptoms of ASD and symptoms of GD may well confound results." (Thrower 2020 at 703.) The rate of ADHD among children with GD was 8.3–11%. Conversely, data from children (ages 6–18) with Autism Spectrum Disorders (ASDs) show they are more than seven times more likely to have parent-reported "gender variance." (Janssen 2016 at 63.)

158. As shown by the outcomes studies (see Section XIII), there is little reliable evidence that transition improves the mental well-being of children. As shown repeatedly by clinical guidelines from multiple professional associations, mental health issues are expected or required to be resolved *before* undergoing transition. The reasoning behind these conclusions is that children may be expressing gender dysphoria, not because they are experiencing what gender dysphoric adults report, but because they mistake what their experiences indicate or to what they might lead. For example, a child experiencing depression from social isolation might develop the hope—and the unrealistic expectation—that transition will help them fit in, as a member of the other sex.

159. In cases where gender dysphoria is secondary to a different issue, efforts at transition

are aiming at the wrong target and leave the primary issue(s) unaddressed. Given the highly reliable, repeatedly replicated finding that childhood-onset gender dysphoria resolves with puberty for the large majority of children, the evidence indicates that blocking a child's puberty blocks the child's natural maturation that itself would resolve the dysphoria.

C. Mental health issues in Adolescent-Onset Gender Dysphoria (ROGD).

160. The literature varies in the range of gender dysphoric adolescents with co-occurring disorders. In addition to self-reported rates of suicidality (see Section X), clinical assessments reveal elevated rates not only of depression (Holt 2016; Skagerberg 2013; Wallien 2007), but also anxiety disorders, disruptive behavior difficulties, Attention Deficit/Hyperactivity Disorder, Autism Spectrum Disorder, and personality disorders, especially Borderline Personality Disorder (BPD). (Anzani 2020; de Vries 2010; Jacobs 2014; Janssen 2016; May 2016; Strang 2014, 2016; Swedish Socialstyrelsen, Evolution 2020.)

161. Of particular concern in the context of adolescent-onset gender dysphoria is Borderline Personality Disorder (BPD; diagnostic criteria in Table X below). Symptoms of BPD overlap in important respects with symptoms commonly interpreted as signs of gender dysphoria, and it is increasingly hypothesized that very many cases appearing to be adolescent-onset gender dysphoria actually represent cases of BPD. (E.g. Anzani 2020; Zucker 2019.) That is, some people may be misinterpreting their experiencing of the broader "identity disturbance" of symptom Criterion 3 to represent a gender identity issue specifically. Like adolescent-onset gender dysphoria, BPD begins to manifest in adolescence, is three times more common in biological females than males, and occurs in 2–3% of the population, rather than 1-in-5,000 people. (Thus, if even only a portion of people with BPD experienced an identity disturbance, and focused that disturbance on gender identity resulting in transgender identification, they could easily overwhelm the number of genuine

cases of gender dysphoria.)

Table 4. DSM-5-TR Diagnostic Criteria for Borderline Personality Disorder.

> A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:
>
> 1. Frantic efforts to avoid real or imagined abandonment. (Note: Do not include suicidal or self-mutilating behaviour covered in Criterion 5.)
> 2. A pattern of unstable and intense interpersonal relationship characterized by alternating between extremes of idealization and devaluation.
> 3. *Identity disturbance: markedly and persistently unstable self-image or sense of self.*
> 4. Impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating). (Note: Do not include suicidal or self-mutilating behavior covered in Criterion 5.)
> 5. *Recurrent suicidal behaviour, gestures, or threats, or self-mutilating behavior.*
> 6. Affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days).
> 7. Chronic feelings of emptiness.
> 8. Inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights).
> 9. Transient, stress-related paranoid ideation or severe dissociative symptoms.
>
> (Italics added.)

(American Psychiatric Association 2022 at 752-753.)

162. Mistaking cases of BPD for cases of Gender Dysphoria may prevent such youth from receiving the correct mental health services for their condition. A primary cause for concern is symptom Criterion 5: *recurrent suicidality.* (See Section X on suicide and suicidality.) Regarding the provision of mental health care, the distinction between these conditions is crucial: A person with BPD going undiagnosed will not receive the appropriate treatments (the currently most effective of which is Dialectical Behavior Therapy). The problem was not about *gender* identity, but about having an *unstable* identity.

163. Regarding research, there have now been several attempts to document rates of suicidality among gender dysphoric adolescents. The scientific concern presented by BPD is that

it poses a potential confound: samples of gender dysphoric adolescents could appear to have elevated rates of suicidality, not because of the gender dysphoria (or transphobia in society), but because of the number of people with BPD in the sample.

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

164. 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 not 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.

XII. Medicalized transition of gender remains *experimental,* lacking causal evidence of mental health improvement.

A. Criteria distinguishing *'experimental'* from *'established'*.

165. In science, the term "experimental" has a specific technical meaning. Within the scientific method, research studies can be *observational* or *experimental.* Among observational studies, such as surveys, the researchers do not administer any treatment and instead only describe the features of the group observed. Among experimental studies, treatments are actively administered by the researchers, who then compare the treated and untreated groups (or compare a group to itself, before versus after treatment). Also, within a given treatment study, the term "experimental treatment" would be used to distinguish it from the "control treatment" or "treatment-as-usual" being provided to the control group.

166. Outside research studies and within public and legal contexts, the term 'experimental' typically denotes '*unverified by experimental evidence'.* A treatment would continue to be experimental until the demonstration of (1) reliable, clinically meaningful improvement and (2) the reliable estimation of safety risks in randomized, controlled trials (RCTs) or research of equivalent level of evidence. A treatment would remain experimental while its effects, including side effects, remain uninvestigated.

167. Being long-standing, popular, or familiar do not, of themselves, impact whether a treatment is experimental—they suggest opportunities for the experiments to have been done. Clinicians' feelings of self-confidence do not impact status as experimental.

B. International consensus explicitly regards gender transition to be experimental.

168. In England, after a thorough review of the literature and the current practice, Dr. Cass stated that the critical and currently unanswered question "is whether the evidence for the use and

safety of the medication is strong enough as judged by reasonable clinical standards." She recognized that these treatments cannot formally be called "experimental" not because they are proven, but because the experiments needed to test their efficacy and safety have not only not been done, but are not even being attempted. (Cass 2022 at 37.) To address this, Dr. Cass called for "the rapid establishment of the necessary research infrastructure to prospectively enrol young people being considered for hormone treatment into a formal research programme." (Cass Review Letter 2022). In response, in its interim service specification NHS England states that it "will only commission GnRHa [i.e., puberty blockers] in the context of a formal research protocol." (NHS 2022 at 12.)

169. Finland, by law, restricts all assessment and treatment activities for gender dysphoric minors to its two research clinics, Helsinki University Central Hospital and Tampere University Hospital. (COHERE Summary.) Further, after conducting a systematic review of the research, the council responsible for the assessment of public health care services in Finland (COHERE Finland) concluded, "In light of available evidence, gender reassignment of minors is *an experimental practice.*" (COHERE Summary, italics added.)

170. Sweden's research on gender transition is conducted at the Karolinska Institutet in Stockholm. In 2015, that facility registered its research on medicalized transition with the U.S. National Institutes for Health (NIH), noting "[H]ormonal treatment includes inhibition of one's own sex hormone production followed by treatment with testosterone or estrogen levels that are normal for the opposite sex. *Seen as experimental model,* this is a process that provides an opportunity to study the sex hormone dependent influences." (Clinicaltrials.gov.) In its policy updates in 2021, Sweden limited medicalized treatments for gender dysphoria in minors to clinical research studies approved by the Swedish national research ethics board ("EPM"). (Medscape

Psychiatry 2021.)

171. Norway reviewed its own national policy on transition in minors in 2023, explicitly concluding such medical procedures to be experimental. (Ukom 2023.)

172. The widely cited Dutch studies were co-conducted by Dr. Thomas Steensma. Despite being an originator and international leader of medicalized transition of gender dysphoric minors, Dr. Steensma stated in an interview in 2021 that he still considers it to be experimental: "Little research has yet been done on the treatment with puberty inhibitors and hormones in young people. That is why it is also *seen as experimental*." Dr. Steensma decried other clinics for "blindly adopting our research" despite the indications that those results may not actually apply: "We don't know whether studies we have done in the past are still applicable to today. Many more children are registering, and also a different type." Steensma opined that "every doctor or psychologist who is involved in transgender care should feel the obligation to do a good pre- and post-test." (Tetelepta 2021.) But few if any are doing so.

C. Claims that medical transition is "medically necessary" are undefined, unsupported, and self-interested.

173. While European health authorities have examined the science and concluded that medical transition for minors remains "experimental" and of unproven benefit, terminology has been distorted in the U.S. because the U.S. lacks a public health care system and the terms "medically necessary" and "experimental" impact health insurance coverage. "Medically necessary" justifies coverage for these procedures; advocates know or fear that the term "experimental" will preclude coverage.

174. WPATH's 2016 statement asserting "medical necessity" was explicitly made in order to facilitate insurance claims, as is clear in their document entitled, "Position Statement on Medical Necessity of Treatment, Sex Reassignment, and Insurance Coverage in the U.S.A." (WPATH

Position Statement.) The AMA released a similar statement supporting insurance coverage for medical transition as a result of being assertedly medically necessary.[6] U.S. medical associations' advocacy corresponds to the financial interests of their members.

175. Moreover, there do not exist a scientific definition or objective criteria of "medically necessary." An analysis published in the *Canadian Medical Association Journal,* however (not pertaining to gender dysphoria or transition), attempted to define 'medically necessary.' (Caulfield 2012.) The article quoted Timothy Caulfield, Research Chair in Health, Law, and Policy at the University of Alberta (Edmonton), Canada: "As for putting great effort into coming up with a tidy, all-encompassing definition of 'medically necessary'—it's probably a waste of time…Given the history of the concept of 'medically necessary' and the numerous failed attempts to define it, a practical, operational and meaningful definition is likely unattainable." (Caulfield at 1771–1772.) According to Mark Stabile, director of the School of Public Policy and Governance and professor of economics and public policy at the Rotman School of Management at the University of Toronto, "Providers of those services will naturally be critical of the decision if they feel that the demand for their services will decline as a result." (Caulfield at 1772.)

D. WPATH repeatedly warns of untested hypotheses, continuing unknowns, and lack of research.

176. The latest (2022) WPATH Standards of Care v8 document avoided the word "experimental" in its guidelines, but instead repeatedly deployed terms and phrases that are synonymous with being experimental: "The criteria in this chapter [on assessment of adults] have been significantly revised from SOC-7 to reduce requirements and unnecessary barriers to care. *It is hoped that future research will explore the effectiveness* of this model." (Coleman 2022 at S33, italics added.)

[6] Available from https://www.ama-assn.org/system/files/2019-03/transgender-coverage-talking-points.pdf

177. The WPATH Standards of Care v8 (Coleman 2022.) indicates the lack of experimental evidence available again and again (italics added):

- "It primarily includes an assessment approach that uses specific criteria that are examined by [a Health Care Provider, or] HCP in close cooperation with a TGD adult and does not include randomized controlled trials or long-term longitudinal research" (at S33.)
- "While there was *limited supportive research,* this recommendation was considered to be good clinical practice as it allows a more reversible experience prior to the irreversible experience of surgery" (at S40.)
- "Due to *the limited research in this area,* clinical guidance is based primarily on individual case studies and the expert opinion of HCPs" (at S41.)
- "While available research shows consistent positive outcomes for the majority of TGD adults who choose to transition…some TGD adults may decompensate or experience a worsened condition following transition. *Little research has been conducted to systematically examine variables that correlate with poor or worsened biological, psychological, or social conditions following transition"* (at S42.)
- "Future research would shed more light on gender identity development if conducted over long periods of time with diverse cohort groups" (at S45.)
- "In addition, elevated scrotal temperatures can be associated with poor sperm characteristics, and genital tucking could theoretically affect spermatogenesis and fertility (Marsh 2019) although *there are no definitive studies evaluating these adverse outcomes.* Further *research is needed to determine the specific benefits and risks* of tucking in youth" (at S54.)
- *"There is no formal research evaluating* how menstrual suppression may impact gender incongruence and/or dysphoria" (at S54-55.)
- "Currently, there are only preliminary results from retrospective studies evaluating transgender adults and the decisions they made when they were young regarding the consequences of medical-affirming treatment on reproductive capacity. It is important not to make assumptions about what future adult goals an adolescent may have" (at S57.)
- *"Only limited empirical research exists* to evaluate such interventions" (at S75.)
- *"Research has not been conclusive* about when in the life span such detransition is most likely to occur, or what percentage of youth will eventually experience gender fluidity and/or a desire to detransition" (at S77.)
- "Research on pitch-lowering surgeries is limited" (at S139.)
- "The number and quality of research studies evaluating pitch-lowering surgeries are currently insufficient" (at S141.)
- "To date, *research on the long-term impact of [Gender Affirming Hormone Treatment*

or] GAHT on cancer risk is limited…We have *insufficient evidence* to estimate the prevalence of cancer of the breast or reproductive organs among TGD populations (Joint et al., 2018.)" (at S144.)

- "Contraceptive *research gaps within this population are profound. No studies have examined* how the use of exogenous androgens (e.g., testosterone) may modify the efficacy or safety profile of hormonal contraceptive methods (e.g., combined estrogen and progestin hormonal contraceptives, progestin-only based contraceptives) or non-hormonal and barrier contraceptive methods" (at S162.)
- "TGD individuals AFAB undergoing abortion still represents a critical gap in research" (at S162.)
- "The effects of current TGD-related medical treatments on sexuality are heterogeneous (Ozer et al., 2022; T'Sjoen et al., 2020), and *there has been little research on the sexuality of TGD adolescents"* (at S163.)
- "While sex-positive approaches to counseling and treatment for sexual difficulties experienced by TGD individuals have been proposed (Fielding, 2021; Jacobson et al., 2019; Richards, 2021), to date *there is insufficient research on the effectiveness of such interventions"* (at S163.)

XIII. There have been 11 cohort studies of puberty blockers and cross-sex hormones in minors. They provide no reliable evidence of effectiveness for improving mental health relative to mental health treatments that lack medical risk.

178. Several studies are cited by plaintiffs' experts and in the media as purporting to show that medical transition in minors brings important improvements in mental health beyond the issues of suicide and suicidality that I have already addressed. In fact, there is no reliable evidence of any such benefit.

179. In this section, I summarize the results of all cohort studies investigating the mental health outcomes of puberty blockers and cross-sex hormones on minors. These include all such studies identified by any of the systematic reviews of effectiveness from England, Sweden, Finland, and WPATH. (Listed in Table 1, *Cohort studies of effectiveness and safety of puberty blockers and cross-sex hormones in minors.*)

180. As enumerated in the following section, all of these studies that reported improved mental health among transitioners were also providing psychotherapy at the same time. (See Section VI on confounding.) None of these studies was able to differentiate which of them was contributing to the improvement.

181. The problem imposed by confounding medicalized transition with psychotherapy is widely recognized. As explicated in the NICE review from England:

> [V]ery little data are reported on how many children and adolescents needed additional mental health support, and for what reasons, or whether additional interventions, and what form and duration (for example drug treatment or counselling) that took. This is a possible confounder for the treatment outcomes in the studies because *changes in critical and important outcomes may be attributable to external care rather than the psychological support or GnRH analogues used in the studies.* (NICE 2020a at 41, italics added.)

Similarly, WPATH's own systematic review noted that "[T]his conclusion is limited by high risk of bias in study designs, small sample sizes, and *confounding with other interventions."* (Baker

2021 at 1, italics added.)

182. The need to disentangle the roles of these two treatments has been largely ignored despite that several issues depend upon them. If medicalized transition does not show mental health improvement superior to that of mental health treatment, it cannot readily be called "medically necessary" for insurance purposes or other institutional needs. Clinicians may be subjecting minors to known and potential (but unstudied) harms without any scientific justification.

183. Moreover, without a control group for comparison (i.e., another group of similar age, sex, and mental health status), these studies are also unable to identify when and if any changes are due to regression to the mean or maturation over time.

A. Of the cohort studies, four found little to no improvement in mental health.

184. Kaltiala, *et al.* (2020) similarly reported that after cross-sex hormone treatment, "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." (Kaltiala 2020 at 213.) They concluded:

> 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. (Kaltiala 2020 at 213.)

185. Cantu, *et al.* (2020) studied 80 youth, 11–18 years of age (average of 15.1 years), measuring patients' levels of anxiety, depression, and suicidality. This sample was 18.75% male-to-female, 72.5% female-to-male, and 8.75% nonbinary, but the report did not include the patients' ages of onset. The study authors compared youth according to those receiving puberty blockers only, cross-sex hormones only, both treatments, or neither. No significant differences in mental health were detected on any of these variables. Of the 27 youth reporting suicidality before

medicalized treatment, 81% continued to report suicidality after medicalized treatment. Remarkably, although the authors reported that "the results of this study suggest that no clinically significant changes in mood symptoms occur" (Cantu 2020 at 199), they did not convey the logical interpretation that transition failed to help these youth. Instead, they emphasized that "findings suggest changes may actually take longer to occur." (Cantu 2020 at 196.)

186. Carmichael, *et al.* (2021) released their findings from the Tavistock and Portman clinic in the U.K. (Carmichael 2021.) Study participants were ages 12–15 (Tanner stage 3 and above for natal males, Tanner stage 2 and above for natal females) and were repeatedly tested before beginning puberty-blocking medications and then every six months thereafter. Cases exhibiting serious mental illnesses (*e.g.*, psychosis, bipolar disorder, anorexia nervosa, severe body-dysmorphic disorder unrelated to gender dysphoria) were excluded. Relative to the time point before beginning puberty suppression, there were *no* significant changes in any psychological measure, from either the patients' or their parents' perspective.

187. Hisle-Gorman, *et al.* (2021) analyzed military families' healthcare data to compare 963 transgender and gender-diverse youth before versus after hormonal treatment, using their non-gender dysphoric siblings as a control group. The study participants included youth undergoing puberty-blocking as well as those undergoing cross-sex hormone treatment, but these subgroups did not differ from each other. Study participants had a mean age of 18 years when beginning hormonal treatments, but their initial clinical contacts and diagnoses occurred at a mean age of 10 years. According to the study, "mental health care visits overall did not significantly change following gender-affirming pharmaceutical care" (Hisle-Gorman 2021 at 1448), yet, "psychotropic medication use *increased*," (Hisle-Gorman 2021 at 1448, italics added.) indicating *deteriorating* mental health.

B. Six of the cohort studies confounded medical treatment with psychotherapy.

188. The initial enthusiasm for medical blocking of puberty followed largely from early reports from the Dutch clinical research team suggesting at least some mental health improvement. (de Vries 2011, 2014.)

189. The Dutch clinical research team followed up a cohort of youth at their clinic undergoing puberty suppression (de Vries 2011), and later cross-sex hormone treatment and surgical sex reassignment (de Vries 2014). The youth improved on several variables upon follow-up as compared to pre-suppression measurement, including depressive symptoms and general functioning. No changes were detected in feelings of anxiety, or anger, or in gender dysphoria itself as a result of puberty suppression. Moreover, natal females suffered *increased* body dissatisfaction both with their secondary sex characteristics and with nonsexual characteristics. (Biggs 2020.)

190. The reports' own authors noted that while it remains possible that the improvement on some variables was due to the puberty blockers, it was also possible that the improvement was due to the mental health support or to natural maturation. The study authors noted this explicitly: "All these factors may have contributed to the psychological well-being of these gender dysphoric adolescents." (de Vries 2011 at 2281.)

191. van der Miesen, et al. (2020) provided an update of the Dutch clinic's sample, reporting continued improvement in transitioners' psychological functioning, but the medical and psychological treatments remained confounded. Also, the authors indicate that the changing demographic and other features among gender dysphoric youth might have caused the treated group to differ from the control group in unknown ways. The study authors expressly noted, "The present study can, therefore, not provide evidence about the direct benefits of puberty suppression

over time and long-term mental health outcomes." (van der Miesen 2020 at 703.)

192. Allen, *et al.* (2019) reported on a sample of 47 youth, ages 13–20, undergoing cross-sex hormone treatment. They reported observing increases in measures of well-being and decreases in measures of suicidality; however, as the authors also noted, "whether a patient is actively receiving psychotherapy" may have been a confounding variable. (Allen 2019.)

193. Becker-Hebley, *et al.* (2021) assessed the quality of life and overall functioning of a sample of German youth both before and after undergoing treatment with GnRHa, CSHT, or both. Excluded from participating were youth with severe psychiatric issues, including suicidality. Of the sample, 79% of the sample participated in psychotherapy at the same time. As the study authors were careful to indicate, "Because this study did not test for statistically significant differences between the four intervention groups or before and after treatment, the findings cannot be generalized to other samples of transgender adolescents." (Becker-Hebly 2021 at 1755.)

194. In Kuper, *et al.* (2020), a multidisciplinary team from Dallas used a battery of mental health tests to assess 148 youth undergoing either puberty-blocking or cross-sex hormone treatment. The tests revealed highly inconsistent results: Most revealed no significant change, some indicated improvement, and some indicated deterioration. Because 144 of the 148 participants were also in treatment with a therapist or counselor (Kuper at 7, Table 4), no conclusions can be drawn regarding the cause of the improvements. Similarly, 47% of the sample were receiving psychiatric medication at the time of their initial assessments, but it was 61% of the sample at the follow-up time: It cannot be known to what extent mental health improvement was associated with transition-related or with psychiatric medication. Importantly, the variables demonstrating deterioration included each of the ones indicating suicidality and self-harm: At follow-up time, the sample showed *higher* levels of suicidal ideation (from 25% to 38%), suicide

attempts (from 2% to 5%), and "non-suicidal self-injury" (from 10% to 17%) (Kuper at 8, Table 5).

195. This evidence of worsening mental health was highly obscured in the Kuper report, however. Rather than provide the standard comparison of pre- and post-treatment rates, Kuper instead listed the post-treatment rates along side the full *lifetime* rates: "Lifetime and follow-up rates were 81% and 39% for suicidal ideation, 16% and 4% for suicide attempt, and 52% and 18% for NSSI, respectively" (p. 1). Rates from over a lifetime are necessarily higher numbers, and putting them where pre-treatment rates normally appear conveys the statistical illusion of a decrease, exactly opposite to the actual pattern.

C. Two found no advantage of medicalization over psychotherapy.

196. Costa, *et al.* (2015) provided preliminary outcomes from a small study conducted with patients of the GIDS clinic in the UK. They compared the psychological functioning of one group of youth receiving psychological support with a second group receiving both psychological support as well as puberty blocking medication (representing an "active comparator" group. See Section III.C.2). The "untreated" group, however, was different from the treated group in another important respect, in that these were the patients who began with such severe psychiatric co-morbidities that they were deemed ineligible to begin puberty blockers until mental health improved. Further, the study suffered a dramatic loss-to-follow-up, with almost two thirds of participants dropping out across just 18 months. (Biggs 2019.) In this preliminary report, both groups improved in psychological functioning over the course of the study, but no statistically significant difference between the groups was detected at any point. (Costa 2015 at 2212, Table 2.) In any event, all these findings have been superseded, however, and are moot. The final outcomes report for this cohort was subsequently published (as Carmichael 2021, above), finding

that neither group actually had experienced any significant improvement at all. (Carmichael 2021.)

197. Achille, *et al.* (2020) at Stony Brook Children's Hospital in New York studied a sample of 95 youth with gender dysphoria, but 45 were lost-to-follow-up within just 12 months, failing to complete follow-up surveys at 6 month and or 1 year. That is, outcomes were available only for the 50 who remained in the study. As well as receiving puberty blocking medications, "Most subjects were followed by mental health professionals. Those that were not were encouraged to see a mental health professional." (Achille 2020 at 2.) Upon follow-up, some incremental improvements were noted; however, after statistically adjusting for psychiatric medication and engagement in counselling, "*most predictors did not reach statistical significance*." (Achille 2020 at 3, italics added.) That is, puberty blockers did not improve mental health any more than did mental health care on its own. More specifically, only one of the 12 predictors reached statistical significance. (Achille 2020 at Table 4.) That is, medicalized transition was not associated with improved mental health beyond improvement associated with the mental health care received. Moreover, the single predictor reaching the threshold for statistical significance is not reliable: the study authors made a methodological error by failing to account for the multiple comparisons it conducted. Had the study applied the standard adjustment for correcting for multiple comparisons, that remaining predictor would also have ceased to be statistically significant.

198. Tordoff, et al. (2022) reported on the mental health of youth (mean age 15.8) as they underwent their first year of puberty blocker or cross-sex hormone treatment. Of the initial 104, 62.5% were receiving psychotherapy at the same time. (Tordoff 2022 at 5 Table 1.) An unknown number of participants were also receiving psychiatric medications, which the report acknowledged as a potential confounding factor. There were 104 participants at the beginning of the study, but by the end, only 65 remained. Importantly, the report failed to indicate its procedures

for assessing the mental health readiness of prospective transitioners, and the results are highly susceptible to selection bias between those deemed eligible for hormones or puberty blockers, and those who were not.

D. One failed to report whether psychotherapy was provided.

199. Chen, *et al.* (2023) reported finding some improvement in some mental health variables associated with the cosmetic changes after two years of cross-sex hormone treatment in a sample of 315 youth (mean age, 16 years). Unlike the other studies, Chen et al. did not report how many participants were receiving psychotherapy or psychiatric medication at the same time as the hormone treatments. It is therefore not possible to assess to what extent any changes were due to hormone treatment versus the potential confounds. Because the study did not include a control group, it is not possible to assert that changes were due to hormone treatment rather than representing regression to the mean. Potential conclusions are also hampered by the large proportion of mental health data that were missing: Of the 315 youth in the sample, analyses could be conducted with only 208–217 (Chen 2023, supp. Material at 12, Table S5). The purported changes in mental health variables were statistically significant, but not clinically meaningful. The depression test used by Chen et al consisted of 21 items, with each item contributing up to 3-points to the total score. For example:

> 0 I do not feel sad.
> 1 I feel sad.
> 2 I am sad all the time and I can't snap out of it.
> 3 I am so sad and unhappy that I can't stand it.

Thus, the total scores range from 0 to 63. Scores 0–13 represent minimal difficulty; 14–19 represent mild depression; 20–28, moderate; and 29–63, severe. The change that Chen et al. found after two years of hormone treatment was from 16.39 to 13.95 (at Table S5). Changes of this size are unlikely to be associated with patients reporting they feel better. Such scores are below the

"minimum clinically important difference". (Button 2015.) Although the report did not include data on co-morbid mental health diagnoses, it noted that two patients receiving cross-hormone treatment died by suicide (representing 0.6% mortality within just two years). (Chen 2023 at 240.)

200. In addition to the incomplete reporting of key aspects of the project and large proportion of missing data, Chen et al appears to have provided only a selected subportion of the information it collected. A knowledgeable journalist investigating transgender issues, Jesse Singal, identified documentation representing the full set of information the Chen et al team planned to collect. I have verified that documentation and have come to the same conclusion. As described by Singal:

> In their study protocol, including a version that they submitted into a preregistration database, the researchers hypothesized that members of this cohort would experience improvement on eight measures, including ones that are just about universally recognized by youth gender researchers as important outcomes, such as gender dysphoria, suicidality, and self-harm. Then, in the published *NEJM* paper, the researchers changed their hypothesis and six of those variables were nowhere to be found. The two remaining—anxiety and depression—moved in a positive direction for trans boys (natal females) but not trans girls (natal males). The researchers reported on three other variables, too, without explaining how they picked them (two improved for trans girls and boys, and one just for trans boys). (Singal 2023.)

201. This appears to represent "cherry-picking" of the findings being reported, rather than a comprehensive reporting on the complete set of evidence. Further, Chen et al. failed to balance the concrete and strikingly high rate of *completed* suicide among their sample against the very incremental mental health changes they claim, even though the ethical and clinical importance of those suicides is obvious.

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

202. As I have explained, any conclusion about safety requires knowledge about and balancing of both risks and benefits.

203. In concluding that safety has not been established (see Section V above), national health authorities, authors of systematic reviews, and researchers have identified a number of harms which are either known to result from administration of puberty blockers and cross-sex hormones to children and adolescents, or can be reasonably anticipated but have not been sufficiently studied to reach any conclusion as to the likelihood or severity of harm.

204. When applying research regarding harms to clinical policy, several considerations need to be included: (1) The harms of medicalized transition of gender does or may differ between male-to-female and female-to-male cases, differ between ages of transition, and differ according to age-of-onset of the gender dysphoria. Evidence and conclusions about harms (and safety) cannot be generalized or extrapolated across such cases. (2) The evidence has strongly shown that after social transition of gender, minors are much more likely than otherwise to undergo medicalized transition of gender. Thus, the appropriate assessment of the risk:benefit ratio for social transition must include the increased risks posed by the medicalized path to which it is likely to lead. (3) The evidence has shown strongly that youth who undergo puberty blocking are highly likely to undergo cross-sex hormone treatment. Thus, the appropriate risk:benefit evaluation must also consider its potential implications over the full lifespan.

205. Systematic reviews of the evidence have identified fewer than 10 studies investigating potential harms of medicalized transition of minors at all, (NICE 2020a at 6.) and most of these have been limited to bone and skeletal health. As concluded by the NICE systematic review, “A key limitation to identifying the effectiveness and safety of GnRH analogues for children and

adolescents with gender dysphoria is the lack of reliable comparative studies." (NICE 2020a at 40.) With that said, numerous harms are either known, or reasonably anticipated by respected health authorities but thus far unmeasured.

A. Sterilization without proven fertility preservation options.

206. Clinical guidelines for the medical transition of gender among children include the need to caution and counsel patients and parents about what are euphemistically called "options for fertility preservation." (e.g., Endocrine Society Guidelines, Hembree 2017 at 3872.) For children who are placed on puberty blockers at Tanner Stage 2, however, because most continue onto cross-sex hormones once they begin a medicalized approach to their dysphoria, no viable fertility preservation options exist. The decision to undergo medicalized transition also represents the decision never to have biological children of one's own.

207. For the large new population of young people who are first being put on puberty blockers and/or cross-sex hormones at a somewhat later stage of puberty, no studies at all have been done of when, whether, or with what probability either males or females can achieve healthy fertility if they later regret their transition decision and cease taking puberty blockers and/or cross-sex hormones. Much less has this been studied as a function of the stage of development at which they began puberty blockers and/or cross-sex hormones, and how long their gonads were subjected to cross-sex hormones.

B. Permanent loss of capacity for breast-feeding in adulthood.

208. While the removal of the breasts of a biological female adolescent or young adult may be cosmetically revised, it is functionally irreversible; even if the person later regrets and detransitions before or during adulthood, breast-feeding a child will never be possible. To the adolescent determined to transition, this may seem no cost at all. To the future adult mother, it may

be a very severe harm indeed.

C. Lifetime lack of orgasm and sexual function.

209. There has not been systematic investigation of the effects on adult sexuality among people medically transitioned at an early stage of puberty. Notably, Dr. Marci Bowers, current President of WPATH, and surgeon with substantial experience conducting penis-to-vagina operations, opined, "If you've never had an orgasm pre-surgery, and then your puberty's blocked, it's very difficult to achieve that afterwards…I consider that a big problem, actually. It's kind of an overlooked problem that in our 'informed consent' of children undergoing puberty blockers, we've in some respects overlooked that a little bit." (Shrier 2021.) In my opinion as a psychologist and sex and couple's therapist, this represents a large potential harm to future relationships and mental health to "overlook," and must be taken into consideration in any serious risk:benefit analysis of "safety."

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

210. 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.)

211. 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.)

212. 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.)

213. 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.

214. 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. (See Section XV.)

E. Substantially delayed puberty is associated with medical harms.

215. 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.)

F. Elevated risk of Parkinsonism in adult females.

216. Epidemiological research has shown adult, non-transsexual women who undergo surgical removal of both ovaries to have substantially elevated odds of developing parkinsonism, including Parkinson's Disease, relative to age-matched women randomly selected from the local population in an on-going epidemiological study. (Rocca 2022.) The effect was greater among younger women, showing 7–8 times greater odds among women under 43. The observed delay between removal of ovaries and the onset of parkinsonism was 26.5 years. Whether chemically suppressing the ovaries of a biological female via puberty blockers during adolescence followed by cross-sex hormones will cause a similar increase in parkinsonism, or when, remains unknown.

G. Reduced bone density.

217. 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.[7] (Twohey & Jewett 2022.)

218. 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.

219. 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 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.

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

220. 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.)

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

221. 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.)

222. 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).[8] The warning label on Lupron reads that "Psychiatric events have been reported in patients…such as crying, irritability, impatience, anger and aggression."

223. 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 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

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

ratio for "safety" against the undemonstrated benefits claimed for hormonal interventions, these observed harms should not be ignored.

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

224. 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.)

225. 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).

226. 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).

XV. Assertions that puberty blockers act only as a "fully reversible" "pause button" are not supported by scientific evidence.

227. Plaintiffs' experts, along with many advocates and organizations, have boldly asserted that the administration of puberty blockers to adolescents is "fully reversible." The assertion is not consistent with or supported by any objective assessment of the existing science. Although withdrawal of the medication will allow the pubertal process to resume, that is very far from establishing that the impact of that interruption of natural development is "fully reversible." The evidence is not that the person's life will proceed as if the medical intervention never happened, as the popularized phrase suggests. Rather, the evidence repeatedly indicates that stopping a healthy child's natural onset of puberty imposes multiple substantial harms, risks, or opportunity costs.

228. First, as I have previously mentioned (Section IV.D), it is scientifically invalid to extrapolate results from using puberty blockers to prevent precocious puberty by delaying the pubertal process to its normal age range, to using them to *prevent* normally occurring healthy puberty, merely assuming the effects and side-effects will be the same. The two are very different populations and very different uses.

229. Second, not all the effects of GnRHa's in otherwise healthy children are known: It is therefore not possible to assess whether all effects are reversed or to what extent. Indeed, within the scientific method, it is never possible to demonstrate that any intervention is "fully reversible." In science, it always remains possible for future evidence to identify an effect that does not reverse. To assert that all the effects of GnRHa's are fully reversible is to assert that all its effects have been investigated and checked for reversibility, which is false.

230. Third, and more concretely, I have reviewed above a large number of medical and developmental risks which multiple responsible voices have associated with administration of

puberty blockers to adolescents, and which are either established by studies or have not been shown not to exist. In the face of this knowledge and lack of knowledge, it is scientifically unsupported and irresponsible to assert that this use of puberty blockers is "fully reversible" and "just a pause."

231. Here, I identify additional psycho-social developmental impacts of delaying healthy, naturally-occurring puberty which are likely to be irreversible, but have not been meaningfully studied.

A. Stopping puberty does not stop time: Patients' peers continue to develop and mature, with patients falling increasingly behind.

232. Initiating puberty blockers at Tanner Stage 2 (at the very first signs of puberty, typically ages 9 or 10) holds the child in a prepubescent state, while their peer group and classmates continue to grow. By the time many patients begin cross-sex hormone treatment, their peers will have completed puberty and progressed far into adolescence. Puberty may become unblocked, but these children have irreversibly lost the opportunity and experience of developing with their peers and must instead do so alone.

233. Being a "late bloomer," indeed among the latest possible bloomers, has psychological consequences of its own. Having the body and mind of a prepubescent child while one's friends have grown into physically mature sixteen-year-olds is extreme. Despite being a teenager chronologically, remaining prepubescent both physically and mentally while the lives of one's peers have advanced to teenagers' interests only increases the isolation of children already reporting social distress. There does not exist a means of distinguishing how much of any improvement in mental health that might be observed across these years in a particular study is simply the result of finally undergoing at least some pubertal development and finally catching up with one's peers in at least some parameters.

234. Concretely, undergoing puberty much later than one's peers (as a result of naturally

occurring rather than medically induced conditions) has been associated with poorer psychosocial functioning and lesser educational achievement. (Koerselman & Pekkarinen 2018.) Whether this holds true when the late puberty is the result of puberty blockers has not been studied.

B. Blocking puberty blocks the awareness of sexuality and sexual orientation that can play an important role in the individual's understanding of gender identity.

235. As demonstrated unanimously by the cohort studies of prepubescent children with gender dysphoria, the great majority cease to feel gender dysphoric during the course of puberty. (Section IX.B.) Studies also find that many such children subsequently identify as gay or lesbian, providing a potential alternative source and understanding of their atypical childhood gender interests. But for all children, blocking puberty necessarily blocks the onset of adult sexual interest, sexual arousal, and sexual response which are part of "the usual process of sexual orientation and gender identity development." (Cass 2022 at 38.) That is, blocking the experience of sexual feelings and development blocks normal phenomena that enable the young person to understand sexuality and sexual orientation, as distinct from gender identity. As Dr. Cass summarized:

> We do not fully understand the role of adolescent sex hormones in driving the development of both sexuality and gender identity through the early teen years, so by extension we cannot be sure about the impact of stopping these hormone surges on psychosexual and gender maturation. We therefore have no way of knowing whether, rather than buying time to make a decision, puberty blockers may disrupt that decision-making process. (Cass Review Letter 2022 at 5.)

Thus, contrary to the hypothesis that providing time might permit more considered understanding and decision-making, the prevention of puberty blocks the awareness of a central factor that may well influence that understanding.

236. Because puberty blockers prevent prepubescent children from developing any understanding of sexual arousal and sexual relationships, such children are necessarily incapable of providing informed consent. There does not exist—indeed, there cannot exist—an age-

appropriate way to equip a child who has not gone through puberty to make an informed decision about age-inappropriate issues, such as their future sex life, choices of sexual partners, sex-bonded relationships including marriage, and sacrificing ever experiencing orgasm.

C. Blocking puberty may block development of adult decision-making capacity.

237. As I have explained above, there are reasons to fear that use of puberty blockers may have permanent negative effects on brain development. That long-term risk aside, blocking puberty nevertheless threatens to prevent the child from growing towards adult decision-making capability during precisely the years in which he or she is being asked to make life-altering decisions about gender identity, gender presentation and cross-sex hormones. Pubertal brain development includes pervasive change in structural and functional connectivity (Chen 2020), re-balancing its capabilities between the acquisition of skills and knowledge and their application. Foremost among these are acquiring the abilities to control impulsivity and engage in rational and long-term decision-making (Crone & Steinbeis 2017), in association with development of a brain region called the "prefrontal cortex," and similarly acquiring the capacity to process adult social interaction, in association with the development of a network of brain areas (Kilford 2016), collectively called the "social brain." To understand medicalized transition of gender and its known and unknown consequences is one of the most complicated questions that a young person today could face, and a prepubescent brain is not equipped to process that information rationally, objectively, and with a whole lifetime rather than immediate desires and social pressures in mind.

D. Time spent on puberty blockers poses significant opportunity costs.

238. One of the primary, if not the foremost, justifications for medically transitioning children and adolescents is to reduce the psychological distress they report. That hypothesis interprets these children's psychological concerns (e.g., anxiety and depression) to gender

dysphoria and/or external sources (e.g., transphobia). As I have noted here previously, however, many gender dysphoric children and adolescents suffer from multiple other mental health issues. In several studies of minors on puberty blockers, a substantial portion of the subjects do not report ongoing psychological care. If years spent on puberty blockers in the hopes that that will relieve distress distract from systematic efforts to directly address comorbidities through psychotherapy, then it diverts the minors from treatment which exhibits substantial evidence of effectiveness for improving mental health and lacks the multiple and significant side-effects of puberty blockers.

XVI. Assessments of clinical guidelines, standards, and position statements.

239. Several sets of recommendations have been offered regarding the clinical treatment of people with gender dysphoria. In this section, I comment on these protocols or recommendations individually.

A. The Dutch Protocol (aka Dutch Approach).

240. The Netherlands' child gender identity clinic in Amsterdam associated with the Vrije University (VU) was one of the international leaders in the use of hormonal interventions to treat gender dysphoria in minors. Researchers associated with that clinic have generated a large portion of the seminal research literature in the field. Key early publications from that group spelled out criteria and procedures that are collectively referred to as the "Dutch Protocol," and this approach has been widely influential internationally.

241. The purpose of the protocol was to compromise conflicting desires and considerations including: clients' initial wishes upon assessment; the long-established and repeated observation that those wishes will change in the majority of (but not in all) childhood cases; and that cosmetic aspects of medical transition are perceived to be better when they occur earlier rather than later in pubertal development.

242. The VU team summarized and explicated their approach in their paper, *Clinical management of gender dysphoria in children and adolescents: The Dutch Approach*. (de Vries & Cohen-Kettenis 2012.) Key components of the Dutch Approach are:

- no social transition at all considered before age 12 (watchful waiting period),
- no puberty blockers considered before age 12,
- cross-sex hormones considered only after age 16, and
- resolution of mental health issues before any transition.

243. For youth under age 12, "the general recommendation is watchful waiting and carefully

observing how gender dysphoria develops in the first stages of puberty." (de Vries & Cohen-Kettenis 2012 at 301.)

244. The age cut-offs of the Dutch Approach were not based on any research demonstrating their superiority over other potential age cut-offs. Rather, they were chosen to correspond to the ages of consent to medical procedures under Dutch law. Nevertheless, whatever the original rationale, the data from this clinic simply contain no information about the safety or efficacy of employing these measures at younger ages.

245. The authors of the Dutch Approach repeatedly and consistently emphasize the need for extensive mental health assessment, including clinical interviews, formal psychological testing with validated psychometric instruments, and multiple sessions with the child and the child's parents.

246. Within the Dutch Approach, there is no social transition before age twelve. That is, social affirmation of the new gender may not begin until age 12—as desistance is less likely to occur past that age. "Watchful Waiting" refers to a child's developmental period up to that age. Watchful waiting does not mean do nothing but passively observe the child. Rather, such children and families typically present with substantial distress involving both gender and non-gender issues, and it is during the watchful waiting period that a child (and other family members as appropriate) would undergo therapy, resolving other issues which may be exacerbating psychological stress or dysphoria. As noted by the Dutch clinic, "[T]he adolescents in this study received extensive family or other social support [and they] were all regularly seen by one of the clinic's psychologists or psychiatrists." (de Vries 2011 at 2281.) One is actively treating the person, while carefully "watching" the dysphoria.

247. The use of hormonal interventions described in the Dutch Protocol, while markedly

more conservative than today's practice in many U.S. clinics, has recently been criticized in detail in a peer-reviewed article as unjustified by reliable evidence (Biggs 2022; Levine 2023; Levine 2022). Certainly, the published research evidence base concerning safety and efficacy available to the VU clinicians is and was no greater than the global evidence base that the NICE review recently labelled as uniformly of "very low quality."

248. Because clinical practices are often justified by alluding to the Dutch Protocol, however, it is important to be aware of the limitations on the use of hormones and puberty blockers specified by the Dutch Protocol and listed above (and thus the limits of the clinical evidence published out of the VU clinic) which are regularly ignored by clinicians in the U.S.

B. World Professional Association for Transgender Health (WPATH).

249. The WPATH standards of care have been lauded as long-established and high quality procedures. This does not reflect any objective assessment, however. The previous WPATH standards (version 7) were subjected to standardized evaluation, the Appraisal of Guidelines for Research and Evaluation ("AGREE II") method. (Dahlen 2021.) That assessment concluded "[t]ransition-related [clinical practice guidelines] tended to lack methodological rigour and rely on patchier, lower-quality primary research." (Dahlen 2021 at 6.) The WPATH guidelines were not merely given low scores, but received unanimous ratings of "Do not recommend." (Dahlen 2021 at 7.)

250. Immediately after the release of the current (2023) version of WPATH's standards (version 8), WPATH fundamentally altered it by removing from it minimum ages previously required for undergoing social or medical transition of gender. (WPATH Correction 2022.) This is despite the fact that age is the central component to young people's emerging understanding of their sexual identities through social identity formation, pubertal development, and the onset of

sexual interest. The removal of age restrictions was not based on any research evidence at all—WPATH provided no reference to any study as justification, and the WPATH leadership have been explicit in indicating that the change was intended to prevent clinical care providers from legal liability for physicians rejecting those minimums. The implementation of such fundamental and dramatic changes, in the complete absence of any supporting science whatsoever, negates entirely any claim that WPATH represents evidence-based or empirically-supported treatment. As explicated herein, on Table 1, the systematic review on which WPATH based its standards for minors included exactly one study on puberty blockers and three studies on cross-sex hormones. All other references represent cherry-picked citations of studies rejected by its own systematic process. Moreover, even among the four studies in WPATH's review, three were rejected by the Swedish review, due to the low quality of the science they contained.

C. Endocrine Society (ES).

251. As I have noted, in preparing its guidelines the Endocrine Society did not conduct systematic reviews of evidence relating to efficacy of any hormonal intervention in children or adolescents, and instead conducted reviews on only two safety-related endpoints.

252. Although outside the professional expertise of endocrinologists, mental health issues were also addressed by the Endocrine Society, repeating the need to handle such issues before engaging in transition, "In cases in which severe psychopathology, circumstances, or both seriously interfere with the diagnostic work or make satisfactory treatment unlikely, clinicians should assist the adolescent in managing these other issues." (Hembree 2017 at 3877.) This ordering—to address mental health issues before embarking on transition—avoids relying on the unproven belief that transition will solve such issues.

253. The Endocrine Society did not endorse any affirmation-only approach. The guidelines

were neutral with regard to social transitions before puberty, instead advising that such decisions be made only under clinical supervision: "We advise that decisions regarding the social transition of prepubertal youth are made with the assistance of a mental health professional or similarly experienced professional." (Hembree 2017 at 3870.)

254. The Endocrine Society guidelines make explicit that, after gathering information from adolescent clients seeking medical interventions and their parents, the clinician "provides correct information to prevent unrealistically high expectations [and] assesses whether medical interventions may result in unfavorable psychological and social outcomes." (Hembree 2017 at 3877.)

255. The 2017 update of the Endocrine Society's guidelines added a disclaimer not previous appearing:

> The guidelines cannot guarantee any specific outcome, nor do they establish a standard of care….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 3895-3896.)

256. The Endocrine Society guidelines do not rely on any systematic review of evidence of *efficacy* of any form of treatment for gender dysphoria. The Dahlen et al. team also subjected these guidelines to review according to the AGREE II criteria, and two out of three independent reviewers concluded that they should *not* be used clinically. (Dahlen 2021 at 7.)

D. American Academy of Pediatrics (AAP).

257. A "Policy Statement" issued by the American Academy of Pediatrics (AAP) in 2018, but on its face declared to represent exclusively the work of one author who alone is "accountable for all aspects of the work," is unique among the major medical associations in being the only one to endorse an affirmation-on-demand policy, including social transition before puberty without

any watchful waiting period. (Rafferty 2018.) Although changes in recommendations can obviously be appropriate in response to new research evidence, the AAP identified no such new evidence to justify a radical departure from the "therapy first" approach of the Dutch Protocol. Rather, the research studies AAP cited in support of its policy simply did not say what AAP claimed they did. In fact, the references that AAP cited as the basis of their policy instead outright contradicted that policy, repeatedly endorsing watchful waiting. (Cantor 2019.) Moreover, of all the outcomes research published, the AAP policy cited *one*, and that without mentioning the outcome data it contained. (Cantor 2019.)

258. Immediately following the publication of the AAP policy, I conducted a point-by-point fact-check of the claims it asserted and the references it cited in support. I submitted that to the *Journal of Sex & Marital Therapy*, a well-known research journal of my field, where it underwent blind peer review and was published. I append that article as part of this report. *See* Appendix 2. A great deal of published attention ensued; however, the AAP has yet to respond to the errors I demonstrated its policy contained. Writing for *The Economist* about the use of puberty blockers, Helen Joyce asked AAP directly, "Has the AAP responded to Dr Cantor? If not, have you any response now?" The AAP Media Relations Manager, Lisa Black, responded: "We do not have anyone available for comment."

XVII. Assessment of plaintiffs' experts' reports.

259. In the body of my report above I have addressed the nature and strength of the scientific evidence concerning the primary scientific issues raised in the expert reports of Plaintiffs' experts. Here, I add a few remarks directed to specific evidentiary or logical defects in the opinions offered by specific experts.

A. Antommaria

260. Dr. Antommaria argues first that "Gender-affirming medical care is supported by evidence of its safety and efficacy," repeatedly citing as his evidence the Endocrine Society which "uses a rigorous method to develop its clinical practice guidelines." (Antommaria Report at 4−5.) Although Dr. Antommaria outlined what those methods entailed for other issues, Dr. Antommaria failed to indicate that those methods were not applied for this one: Puberty blockers were not included in the Endocrine Society's commissioned systematic reviews at all, nor did the Endocrine Society's systematic reviews look at mental health effects of either puberty blockers or cross-sex hormones. Their review was limited only to selected physiological effects of cross-sex hormones. Moreover, the wording of the Endocrine Society review leaves ambiguous whether minors were included at all or if the review was limited to adults. Dr. Antommaria added to the Endocrine Society review a single-blind study (Burinkul 2021), which pertained to adults only, not children.

261. Dr. Antommaria argues next that low quality evidence can sometimes be sufficient for clinical recommendations. In so doing, Dr. Antommaria makes the logical error of confusing what is "necessary" with what is "sufficient." Where the Endocrine Society indicates that a multidisciplinary team is necessary for recommendations, Dr. Antommaria insinuates having such a team is sufficient for making such decisions—even in the absence of meaningful evidence as to either risks or benefits. As I have detailed above, multiple respected international health authorities

or advisory bodies disagree, deeming the available evidence *insufficient* on which to base clinical recommendations for the use of hormonal interventions in children and adolescents. (Section V.) In actuality, the Endocrine Society included no review of outcomes at all, made no claims about potential success, and even denies responsibility for outcomes. (See Section XVI.C.)

262. The only research study Dr. Antommaria cites here is de Vries, *et al.*, 2014: That study provided both psychotherapy and medicalized transition at the same time, making it impossible to know which one led to the report mental health improvements. (See section XIII.B.)

263. Dr. Antommaria next claims that it would even be unethical to conduct an RCT of medicalized transition. Each of the reasons he gave, however, is incorrect. He indicated "clinical equipoise must exist." (Antommaria Report at 15)—that there must exist genuine uncertainty about which procedure is superior, whereas he and the colleagues he surrounds himself with feel entirely certain. Dr. Antommaria is incorrect about this ethical principle: According to bioethicist Benjamin Freedman, the originator of the concept of clinical equipoise, writing in the *New England Journal of Medicine*, "The requirement is satisfied if there is genuine uncertainty within *the expert medical community*—not necessarily on the part of the individual investigator—about the preferred treatment." (Freedman 1987.) The international expert medical community is indeed highly uncertain, as thoroughly documented both herein and in the international medical press, such as the British Medical Journal's recent article: *Gender Dysphoria in youth people is rising and so is professional disagreement.* (Block 2023.)

264. Moreover, it is Dr. Antommaria's certainty (and that of whomever else he feels he is entitled to speak for) that is unjustified. As already documented herein, nonmedicalized treatments have already shown benefits indistinguishable from those from medicalized transition.

265. Dr. Antommaria writes that RCTs would be unethical also because medicalized

transition could not be compared with a non-pharmacological or placebo treatment. Both claims are incorrect. The routine and ethical alternative procedure in clinical science is to use what is called an "active comparator," as was spelled out in the NICE reviews from England. (NICE 2020a at 40; NICE 2020b at 47.) In such an RCT, participants would be randomly assigned into a psychotherapy-only group or a psychotherapy + medicalization group.

266. Dr. Antommaria's other argument against RCTs is his belief that "A randomized trial is unlikely to enroll enough participants." (Antommaria Report at 16.) That belief is also baseless. Healthcare systems of *entire countries* throughout Europe are limiting *all* medicalized transition of minors to research studies.

267. Dr. Antommaria next relies on WPATH, asserting that it "conducted selected systematic reviews of the literature." (The WPATH review is published as Baker, *et al.,* 2021.) Missing from Dr. Antommaria's report was that WPATH did not include any safety-related data in minors, either of puberty blockers or of cross-sex hormones in their systematic review. (Section IV.B.) Also, as I have noted above, WPATH did not even attempt any review with respect to outcomes of hormonal interventions in adolescents.

268. Dr. Antommaria's only reference to the international systematic reviews (indeed, the only such reference by any of the plaintiffs' experts) is the single paragraph, beginning on page 18, indicating that the reviews "do not make treatment recommendations" and therefore do not actually contradict the WPATH and Endocrine Society recommendations. Dr. Antommaria is either confused or intentionally dodging the regular practice and relevant recommendations. The routine procedure for establishing evidence-based practice is a two-step process, the first being the conduct of the systematic review, and the second being its integration with financial, political, and other constraints to yield the recommendations themselves. For example, the UK conducted

reviews (released under NICE) which were then incorporated into recommendations (released under Cass). WPATH conducted a review (released as Baker *et al,* 2021), which was allegedly incorporated into their guidelines (released under Coleman *et al,* 2022). What Dr. Antommaria is alleging to be a mismatch between "the Endocrine Society's and WPATH's clinical practice guidelines and recent European documents" (Antommaria Report at 18), is merely Dr. Antommaria's own failure to compare reviews with reviews and guidelines with guidelines. I have reviewed the actual recommendations from European health authorities and advisory commissions above.

269. Dr. Antommaria writes, "None of the documents recommend criminalizing gender-affirming medical care as does VCAP." (Antommaria Report at 19.) The means by which a state or other government implements research results and protects citizens from harm is a political rather than a scientific or clinical question, and I can offer no expert opinion. (See section I.C.) I am, however, a citizen of two countries (Canada and the United States), working within the very different health care systems of each. From that experience, I can observe that countries with centralized public health care systems (such as Canada and European nations), have direct control over what treatments are or are not administered within those nations, while the decentralized and often private health care system of the U.S. must rely on different mechanisms of control.

270. In his next argument, Dr. Antommaria contests the results of the entire set of cohort studies, all of which found that most pre-pubescent children with gender dysphoria cease to feel dysphoric by puberty. Against these eleven studies, Dr. Antommaria cited a single study, Wiepjes, *et al.,* 2018, but misrepresented its contents: Dr. Antommaria attributed to Wiepjes that "individuals who fulfill the criteria for gender-affirming medical care generally continue in their gender identity." (Antommaria Report at 22.) Dr. Antommaria's application of the word

"individuals" hides from the court that Wiepjes' conclusion applied to the adults while *the reverse was true for the children:* Wiepjes included 5,433 adults age 18 or older and 548 children under age 12. (Wiepjes 2018 at Table 1.) Of the adults, 69.9% went on to medicalized treatment, whereas only 40.3% of the children did. Dr. Antommaria's choice of the ambiguous word "individuals" misleads the court, erroneously applying the results from adults to the children, declaring to the court the very opposite of what Wiepjes actually showed. In any case, as I have reviewed above, a phalanx of respected voices in the field, including the Endocrine Society, disagree with Dr. Antommaria and instead agree with my reading that the cohort studies do support the conclusion that a large majority of prepubertal children who suffer from gender dysphoria will desist. (Section IX.B.)

271. Dr. Antommaria's only other argument is that cohort studies of children "have substantial limitations" (Antommaria Report at 22.) citing a single commentary as support, Newhook, *et al.,* 2018. As detailed herein (Section IX.B), Temple Newhook, *et al.* criticized four studies of prepubescent children with gender dysphoria for using (in Temple Newhook's view) overly broad diagnostic criteria. I have detailed above a number of reasons why Temple Newhook's criticism is invalid, and that article has been additionally rebutted in a peer-reviewed paper. (Zucker 2018, *The Myth of Persistence*.) Moreover, Dr. Antommaria's argument introduces an additional error by insinuating that all of the relevant cohort studies used the same criteria as the four studies that Temple Newhook contested, but failed to inform the court that the other seven studies, using different criteria, came to exactly the same conclusion as the four. (See Section IX.B.) That is, Dr. Antommaria's invocation of Temple Newhook's argument cannot contradict the unanimous finding. The international systematic reviews also expressed the conclusion I provided herein and not that of Temple Newhook.

272. Dr. Antommaria's insinuation that gender dysphoria persists in most children also conflicts with the conclusion of the Endocrine Society, which Dr. Antommaria otherwise repeatedly accepts as authoritative. According to the Endocrine Society:

> Combining all outcome studies to date, the GD/gender incongruence of a *minority* of prepubertal children appears to persist in adolescence….In adolescence, a significant number of these desisters identify as homosexual or bisexual. (Hembree 2017 at 3876, italics added.)

273. Dr. Antommaria indicates that watchful waiting applies only to prepubescent children, insinuating that adolescent-onset cases differ, are unlikely to desist, and therefore do not require a watchful waiting period. That insinuation is incorrect: There do not exist cohort (or superior level) research studies on adolescent-onset cases. There are no meaningful data regarding persistence and desistance for this large, new population. It is not knowable whether their outcomes will resemble those of adult-onset cases (despite differing on all objective variables), or will resemble those of childhood-onset cases (despite also differing from theirs), or will show altogether different outcomes.

274. As detailed herein, all the international health care systems that have conducted or commissioned systematic reviews concluded medicalized transition to be *experimental*. (See Section V.) Dr. Antommaria denies that consensus, arguing that "The clinical use of puberty blockers and gender affirming hormones treatment is not experimental" because "the goal of clinical practice is to benefit individual patients" rather than "to contribute to generalizable knowledge." (Antommaria Report at 23.)[9] Dr. Antommaria's argument is mere word-play: He swaps the common use of "experimental" meaning "untested" with the technical use of

[9] Dr. Antommaria also contested the word "new;" however, newness is not a criterion in science or its assessment. Moreover, that *cross-sex* hormones were used for transition in 1966 does not disconfirm that using *puberty blockers* is new, and their use *in adults* does not disconfirm their use *in minors* being new. In this context, "new" clearly refers to whether there has been sufficient time undergoing sufficient examination for a treatment's effects to be reliably predicted.

"experimental" meaning "currently enrolled in a clinical trial". That is, Dr. Antommaria's argument is that, so long as the physician doesn't plan on recording and reporting the results, then prescribing the drug doesn't count as an "experiment"—even if the safety and effectiveness of the drug is utterly unproven—so the drug itself does not count as experimental. Under Dr. Antommaria's faulty logic, every treatment could avoid ever being called "experimental" so long as no one ever performed the experiment to test it. In fact, the quoted health authorities largely use the word in the sense "unproven," while calling for researchers to undertake the well-designed experiments which have not yet been done.

275. Dr. Antommaria's defence of using off-label, non-FDA-approved uses of drugs is entirely peripheral. Treatment safety and effectiveness do not have a one-to-one correspondence with FDA-approval. The fact that some other drugs are used widely and safely for some other off-label indications does not imply in the least that off-label use of this drug (puberty blockers) for this use (preventing normal, healthy puberty in children) is safe.

276. Dr. Antommaria argues that "VCAP's legislative findings do not provide a sufficient basis for singling out the provision of gender-affirming medical care to adolescents with gender dysphoria." (Antommaria Report at 30.) However inadvertently, Dr. Antommaria actually provides exactly that basis himself in his next paragraph: These medical procedures are permitted to treat problems that are "*medically verifiable."* (Antommaria Report at 31.) Both of Dr. Antommaria's examples (central precocious puberty and complete androgen insensitivity syndrome) are indeed medically verifiable with objective testing, and the medication is applied to bring the patient within healthy norms. By contrast, gender dysphoria is entirely subjective, ascertained by self-report only, with no means of objective verification possible, and the medication is applied precisely to take the patient *outside* of healthy norms.

277. Standards for clinical practice comprise multiple, mutually reinforcing principles and procedures. This overlap can sometimes permit some flexibility in some circumstances where the other principles with high reliability can compensate, such as allowing some reports of pain and sensations when diagnosing a physical disease before prescribing a short-acting and low-risk medication. Dr. Antommaria's recommendations for medicalized transition, however, entail the simultaneous removal of multiple overlapping protections, leaving no meaningful protection at all. Dr. Antommaria is accepting, at face-value only, purely subjective reports, of a diagnosis with no objective evidence of validity, offering long-term and life-long physical intervention, on the basis of the lowest possible quality evidence, despite all objective counterevidence, and without first exhausting the safer and less invasive alternatives.

B. Janssen

278. Dr. Janssen indicates he was deposed as an expert witness by the plaintiffs in BPJ v WV Board of Education. I testified as an expert witness for the defense in that case.

279. Dr. Janssen's report does not provide the science of medicalized transition of minors. I could find no citation or mention of any of the systematic reviews of the topic, whether from an international health care system or a professional guild. Dr. Janssen cited a vanishingly small set of highly cherry-picked publications (ten in total), which do not reflect the state of the science.

280. Four of Dr. Janssen's ten citations represent self- (and/or parent-) report surveys (*i.e.*, Durwood, *et al.,* 2017; Olson, *et al.,* 2016; Turban, *et al.,* 2020a, 2020b). Surveys do not have the scientific rigour to qualify as medical evidence and are rejected by all systematic reviews as insufficient. (See Section IV.A.)

281. Two of Dr. Janssen's citations do not pertain to gender dysphoria at all (i.e., Costello, *et al.,* 2003; Wilens, *et al.,* 2002). Dr. Janssen cites these as general support of the general idea

that adolescents with one mental health diagnosis are likely to have others. That much is true. Dr. Janssen does not, however, include that the pattern of mental illnesses among gender dysphoric youth are different from the pattern of mental illnesses of other adolescents. Dr. Janssen also fails to take his own argument to its parsimonious conclusion: It is because adolescents are experiencing many mental health concerns that Adolescent-Onset Gender Dysphoria may represent simply another of those concerns, amenable to mental health treatment, like those other concerns.

282. Dr. Janssen cites de Vries, *et al.,* 2014, claiming it showed, not only that transition improves mental health, but also that transition is the only treatment that does. Dr. Janssen's claim is untrue and contradicts the study's own authors, who noted "the positive results may also be attributable to supportive parents, open-minded peers, and the social and financial support (treatment is covered by health insurance) that gender dysphoric individuals can receive in the Netherlands." Also, the participants in this study were receiving not only medicalized services, but also psychotherapy, which can also have caused the mental health improvements. (See section III.B.) Despite his bold claim, it is not scientifically possible for Dr. Janssen (or anyone else) to know whether mental health improvement came from the mental health treatment or medicalization.

283. Moreover, Dr. de Vries continues to express the very opposite of what Dr. Janssen attributed to her: Writing in 2023, she repeated that "rigorous longitudinal outcomes studies that provide evidence about whether this approach [hormonal interventions in minors] is effective and safe are needed" and that "Future studies that compare outcomes with different care models are needed." (de Vries 2023 at 276.)

284. Dr. Janssen similarly cited Chen, *et al.,* 2023, to support his claim that "gender transition can—and often does—alleviate co-occurring mental health issues" (Janssen Declaration

at 9.) Yet, the Chen study cannot support that claim either: Chen, *et al.* did not disclose whether the youth in their study were receiving mental health treatment and whether that was responsible for the improvements they reported finding. It does not "compare outcomes with different care models" as Dr. de Vries emphasized were needed. Without that information, it is again impossible for Dr. Janssen to know what he claims to know.

285. Dr. Janssen claims that "well-established research demonstrates the effectiveness of treatment for gender dysphoria in adolescence," citing Turban, *et al.,* 2018. Dr. Janssen's claim misrepresents that source. What Turban, *et al.,* 2018, actually said was that such treatment "has been evaluated in two studies on the same cohort of Dutch adolescents," explicitly warning that "the results come from only one clinic and concern a highly selected sample...Whether the same positive results can be expected for the larger number of adolescents that are treated at clinics that vary in their approach to gender variant adolescence *has yet to be determined."* (Turban 2018 at 640, italics added.) Additionally, the Turban citation in turn cites de Vries, *et al.,* 2014, which I have discussed above. I note also that of the 10 publications Dr. Janssen cites, three were written by the same author (i.e., Turban, 2017, 2020a, 2020b), signalling the cherry-picked nature of the sources Dr. Janssen has chosen to cite.

C. Ladinsky

286. Dr. Ladinsky's report does not provide a complete or accurate account of the relevant research literature, repeatedly citing the three U.S.-based association policies and not any of the systematic reviews available. There was no citation to any other source behind any other claim from page 5 to page 19. Citation numbers 2 through 17 are all to those same documents, which are already evaluated in the present report. The few other sources cited fail to support Dr. Ladinsky's claims.

287. Dr. Ladinsky attributed to Spack, *et al*. (2012) that suicidality and other poor outcomes would result from gender dysphoria "if left untreated," insinuating that "untreated" meant not permitted medical transition. In actuality, Spack, *et al.* (2012) was unambiguous:

> Gender dysphoric children who do not receive *counseling* have a high risk of behavioural and emotional problems and psychiatric diagnoses." (at 422.)

Spack (2013) warned:

> Mental health intervention should persist for the long term, *even after surgery, as patients continue to be at mental health risk, including for suicide.* While the causes of suicide are multifactorial, the possibility cannot be ruled out that some patients unrealistically believe that surgery(ies) solves their psychological distress. (at 484.)

288. Dr. Ladinsky claims of Alabama's law that "If the law goes into effect, based on my expert opinion, it will cause serious harms to my patients as well as other transgender youth throughout Alabama." (Ladinsky Declaration at 17.) Dr. Ladinsky cites no evidence, analysis, or methodology justifying that conclusion or any indication of engaging in any scientific process or applying any criteria that an expert would use to come to such a conclusion.

289. Dr. Ladinsky indicates having reviewed the declarations previously submitted for the present case by me and by other experts for the state. The only point of mine contested by Dr. Ladinsky was my claim that:

> [I]in the absence of long-term follow-up, it cannot be known what proportions come to regret having transitioned and then detransition. Because only a minority of gender dysphoric children persist in feeling gender dysphoric in the first place, "transition-on-demand" increases the probability of unnecessary transition and unnecessary medical risks. (Cantor Declaration, Preliminary Injunction Hearing, ¶43.)

Dr. Ladinsky's only counter-argument is to say that she herself does not permit transition-on-demand in her patients. Whatever Dr. Ladinsky's own practices are and whatever her views of what constitutes adequate investigation may be, reports of the failures of gender clinics to employ meaningful gatekeeping are emerging throughout the Western world. Moreover, it remains true

that Dr. Ladinsky cannot know the long-term outcomes of patients after they have left her care.

290. Dr. Ladinsky emphasizes that "Suicidality is of particular concern" if medicalizing hormones are not provided to minors, citing three articles, Wiepjes, *et al* (2018), de Vries*, et al* (2014), and Turban, *et al* (2020). Dr. Ladinsky is mistaken. Wiepjes, *et al* (2018) contains no information on suicide or suicidality—neither word appears in the document at all. Similarly, de Vries, *et al,* 2014, reported no evidence on suicidality, providing results only on general psychological well-being. Turban, *et al* (2020) reported on a survey in which a high proportion of survey-takers reported suicidality at some time in their life, but provided no evidence whether that rate was due to gender identity or to any of other mental health issues, such as Borderline Personality Disorder, which are highly overrepresented in samples of gender dysphoric youth. (See section XI.C.)

D. McNamara

291. Dr. McNamara indicates that she bases the validity of her argument on the standards of the National Academy of Medicine, as applied by WPATH and the Endocrine Society. Her claim is demonstrably incorrect. According to the document Dr. McNamara cited from the Academy, clinical practice guidelines "are informed by a systematic review of evidence and an assessment of the benefits and costs of alternative care options." (Institute of Medicine, Clinical Practice Guidelines, 2011 at 4.) As documented here already, the Endocrine Society did not include any review of puberty blockers or cross-sex hormones in minors, and WPATH's review did not include the safety of any treatment in minors, instead expressly allowing clinical opinion to substitute for valid experimental evidence. (See Section XVI; Block, Gender Dysphoria 2023.) The several European health care systems did, however, conduct such reviews and concluded the very opposite to Dr. McNamara.

292. Dr. McNamara repeatedly employs circular reasoning. Her report repeatedly refers to medicalized transition as "essential" or "established," based on the *absence* of compelling evidence of harm or inefficacy. As already noted, the absence of evidence is not evidence of the absence of, in this case, harm. Her logic is entirely counter to the scientific method. Whether medicalized transition is essential is the very question being assessed. The claim cannot be simply asserted or assumed until proven otherwise. The scientific procedure for investigating such issues is called "null hypothesis testing." Differences, including clinical improvements, are assumed to be zero until proven otherwise.

293. Dr. McNamara, like Dr. Antommaria, misrepresents or misunderstands the role of RCTs in clinical science, arguing that RCTs cannot be conducted because study participants would become aware of whether they were in the treatment group or the control group. (That is, participants could not be masked or "blinded.") Their error is that studies do not need to be masked to be an RCT: for example, as reported in *The Lancet,* 40% of RCTs published in PubMed during a study period were not, in fact, masked. (Chan & Atman 2005 at 1160.) Although masked RCTs can be superior to non-masked RCTs, the impossibility of masking in certain contexts does not authorize clinicians or clinical scientists simply to skip RCTs altogether and proceed with confidence as if they had been completed and the treatment demonstrated to be successful—which they have not. (See also Section III.C on masked, placebo-controlled research designs.)

294. Dr. McNamara claims that the international medical consensus supports medicalized transition of gender in minors. She cited no source for that claim. As thoroughly documented herein, all international health care systems conducting systematic reviews have in recent years come to exactly the opposite conclusion. Moreover, Dr. McNamara's language is ambiguous. Her words "supports treatment of gender dysphoria" are entirely consistent with using psychotherapy

to alleviate gender dysphoria *without* medicalized transition, which more accurately reflects international consensus.

295. Dr. McNamara claims, "Defendants' experts have previously asserted that essential medical treatment for gender dysphoria causes suicide; however, no study has found a worsening of various mental health measures among recipients of essential medical treatment for gender dysphoria." (McNamara Report at 11.) Regarding her first sentence, I have made no such statement. Dr. McNamara's second sentence is demonstrably incorrect. The Kuper, *et al.* (2020) cohort study (see Section V.C) reported the suicidality of an adolescent sample before and after hormone treatment. Table 5 of that study (Kuper at 8) showed suicidal ideation to be 25% before and 38% after treatment, suicidal attempts to be 2% before and 5% after, and non-suicidal self-harm to have been 10% before and 17% after. For reasons already outlined herein, Kuper's data cannot establish causation, but indeed show decreases in mental health, thus calling for caution and further research rather than suggesting such treatment to be "safe" for these children.

296. Dr. McNamara's dismissal of the systematic review of Dhejne is counter to both clinical ethics and clinical science. It is true that the Dhejne review pertained to adults rather than adolescents, and it is possible that transitioned adolescents might show a pattern opposite of what transitioned adults do. Because it remains substantially unstudied and unknown on what features adolescent cases might resemble adult cases (or prepubescent cases), evidence about the experiences and outcomes among adults after transition cannot be dismissed as irrelevant to the risk:benefit equation for adolescents. Because suicidality is elevated among adults, it is at least plausible that it will also be higher among adolescents. Both research ethics and medical ethics require that this possibility be thoroughly investigated and ruled out with high quality evidence rather than assume the opposite to be true. The combination of the Dhejne evidence from adults

and the Kuper evidence from adolescents together provide strong reason to apply every possible caution before proceeding.

E. Shumer

297. Dr. Shumer indicates that he testified as an expert witness for the plaintiffs in Roe, *et al* v Utah High School Activities Association, *et al.* I testified as an expert witness for the defense in that case, which is currently in process.

298. I have already addressed the substance of most of Dr. Shumer's mistaken assertions regarding the science relevant to hormonal and surgical interventions in minors as a treatment for gender dysphoria. Here, I address a few remaining points from his report.

299. Dr. Shumer faults VCAP Finding 1 because its "description of sex fails to include gender identity, which is an essential medical component of sex for every person" (Shumer Report at 27); however, the VCAP description is correct. In his report, Dr. Shumer conveys a definition of sex which not only is incorrect, but also contradicts the very document he cited as his source of that definition. Dr. Shumer wrote:

> Sex is comprised of several components, including, among others, internal reproductive organs, external genitalia, chromosomes, hormones, *gender identity,* and secondary sex characteristics. (Shumer Report at 6, italics added.)

He attributed that definition to:

> Institute of Medicine. The health of lesbian, gay, bisexual, and transgender people: building a foundation for better understanding. Washington, DC: The National Academic Press; 2011.

In direct contradiction with Dr. Shumer's claim, Institute of Medicine does not, in fact, include gender identity in its definition of sex. Its definition is:

> To discuss the context surrounding the health of LGBT populations, the committee has adopted working definitions for a number of key terms. *Sex* is understood here as a biological construct, referring to the genetic, hormonal, anatomical, and physiological characteristics on whose basis one is labeled at birth as either male or female. (Institute of Medicine, Health, 2011 at 25, italics original.)

That is, the Institute of Medicine—just like Alabama—explicitly limited sex to biological, objective features, as I have defined it in the present declaration. The major clinical associations also limit the definition of sex to objective features, also excluding gender identity (see Section VII.A), again in direct opposition to Dr. Shumer's claim.

300. Dr. Shumer claims that attempting to change a person's understanding of their gender identity "has been found to be both harmful and ineffective" (Shumer Report at 8), on the basis of the evidence in two articles based on a 2015 survey. Dr. Shumer's interpretation of those articles is invalid, however: It is not possible for a survey to demonstrate that anything is either harmful or ineffective. These are both causal claims that surveys are not capable of demonstrating. (See Section III.F.) Not only is there no study that has found that relying on psychotherapy and counseling support for a child or adolescent who suffers from gender dysphoria leads to worse outcomes than does hormonal intervention whether with or without psychotherapy, but also the studies that have compared these treatments failed to find superiority of medicalized transition (See Section XIII.)

301. 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.

302. Dr. Shumer claims, "gender identity, like other components of sex, has a strong biological foundation" (Shumer Report at 9), but again misrepresents the sources he cited. The

research has shown statistically significant differences associated with *sexual orientation,* not gender identity. Although Dr. Shumer cited Heylens, *et al.* (2012) to claim that there are "genetic underpinnings to gender identity development," Dr. Shumer did not, however, share the rest of Heylens' observation, noting this confounding: "In all the cases reported to be concordant for GID [i.e., 'match on gender identity'] there was also concordance for sexual orientation." (Heylens 2012 at 755.) The Endocrine Society guidelines similarly noted the association with sexual orientation. Contrary to Shumer's claim of a "strong" biological foundation, the Endocrine Society emphasized that whatever hypotheses may currently be in play, *no* genetic marker (or other physical marker) enabling verification of transgender status has been identified. (Hembree 2017 at 3875.) Shumer cites no evidence of any biological or other objective marker (let alone a "strong" one) able to identify transgender identity.

303. Dr. Shumer's comparison of gender identity with congenital adrenal hyperplasia (CAH) is invalid. CAH is a biological disorder with objective features that can be objectively detected, entirely unlike gender dysphoria, which remains entirely subjective with no objective means of verification or falsification.

304. Dr. Shumer's "rationale for medical treatment of gender dysphoria in adolescents" (Shumer Report at 11–12) is invalid. He cites five "studies demonstrating positive results of gender-affirming care" (Shumer Report at 11.); however, none of these studies uses a design capable of demonstrating causality. In contrast with Dr. Shumer's (mis)use of causal language, none of these studies is able to distinguish changes due to medicalized transition from changes due to the psychotherapy that the patients were receiving at the same time. (See Section IV.C.)

305. Dr. Shumer repeatedly employs strong terms in describing his opinions; however, these represent only vague and rhetorical terms without scientific definition. For examples, there are no

objective criteria for concluding: when clinician's assessment of a patient has developed "a deep understanding" (Shumer Report at 14); which patients represent "appropriately selected patients" (at 24); which of conflicting clinicians are "highly trained" (at 28); what constitutes a "skillful elicitation of a patient's experience" (at 28); when an assessment represents a "comprehensive evaluation" (at 30); who has been "carefully evaluated" (at 34); or, outside of any systematic review, what still constitutes "robust research" (at 15).

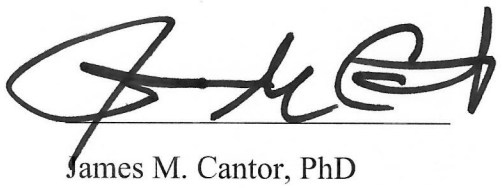
306. Dr. Shumer refers to the WPATH standards of care as "based on the best available science." (Shumer Report at 16.) As I have detailed above, the WPATH SOC does not satisfy the definition of "evidence-based medicine," and extensively ignores "the best available science." (Section XVI.B.)

307. Dr. Shumer asserts separately that "withdrawal of hormones in adulthood often is successful in achieving fertility when it is desired." (Shumer Report at 25.) He does not cite sources that support "often," and does not cite any study that demonstrates achievement of healthy fertility for subjects whose natural puberty was blocked and who then received cross-sex hormones for an extended period of years, as is the course of treatment for gender dysphoric children that Dr. Shumer commends. That is, Dr. Shumer's report addresses the very limited evidence of the effects of using only one or the other of these medications, but fails to include the effects of their combination.

308. Dr. Shumer faults VCAP Finding 12, claiming that "GnRHa is used when it is determined that the progression of puberty would cause significant harm to the adolescent." (Shumer Report at 33.) It is not possible to make such a prediction for any patient—the existing evidence is only correlational, not causal. Dr. Shumer claims, "The benefit of treatment is not unproven or poorly studied." (Shumer Report at 33.) That claim contradicts the conclusion of all

systematic reviews of GnRHa safety. The evidence Dr. Shumer cites as support for his claim are the WPATH and Endocrine Society guidelines; however, neither association included GnRHa safety in their systematic reviews.

Dated: 19 May 2023



James M. Cantor, PhD

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LIST OF APPENDICES

Appendix 1

Curriculum Vita

Appendix 2

Cantor, J. M. (2020). Transgender and gender diverse children and adolescents: Fact-checking of AAP policy. *Journal of Sex & Marital Therapy, 46,* 307–313. doi: 10.1080/0092623X.2019.1698481