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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO

JANE ROE, et al.

Plaintiffs,

v.

RAÚL LABRADOR, in his official capacity as Attorney General of the State of Idaho; et al.

Defendants.

Case No. 1:24-cv-00306-CWD

DECLARATION OF MICHAEL K. LAIDLAW

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I, Michael K. Laidlaw, M.D., hereby declare as follows:

1. I am over the age of eighteen and submit this expert declaration based on my personal knowledge and experience.

2. I am a board-certified endocrinologist. I received my medical degree from the University of Southern California in 2001. I completed my residency in internal medicine at Los Angeles County/University of Southern California Medical Center in 2004. I also completed a fellowship in endocrinology, diabetes and metabolism at Los Angeles County/University of Southern California Medical Center in 2006.

3. The information provided regarding my professional background is detailed in my curriculum vitae. A true and correct copy of my curriculum vitae is attached as Exhibit 1.

4. In my clinical practice as an endocrinologist, I evaluate and treat patients with hormonal and/or gland disorders. Hormone and gland disorders can cause or be associated with psychiatric symptoms, such as depression, anxiety, and other psychiatric symptoms. Therefore, I frequently assess and treat patients demonstrating psychiatric symptoms and determine whether their psychiatric symptoms are being caused by a hormonal issue, gland issue, or something else.

5. I have been retained by Intervenor-Defendants in the above-captioned lawsuit to provide an expert opinion on the efficacy and safety of sex reassignment treatment, including the trustworthiness of proposed standards of care or treatment guidelines promulgated by medical organizations.

6. If called to testify in this matter, I would testify truthfully and based on my expert opinion. The opinions and conclusions I express herein are based on a reasonable degree of scientific certainty.

7. I am being compensated at an hourly rate of $500 per hour plus expenses for my time spent preparing this declaration, and to prepare for and provide testimony in this matter. I am being compensated at an hourly rate of $750 for testimony at depositions or trial. My compensation does not depend on the outcome of this litigation, the opinions I express, or the testimony I may provide.

8. My opinions contained in this report are based on: (1) my clinical experience as an endocrinologist in particular dealing with hormone excess, hormone deficiency, and hormone balance; (2) my clinical experience evaluating individuals who have or have had gender incongruence including a detransitioner; (3) my knowledge of research and studies regarding the

treatment of gender dysphoria, including for minors and adults; and (4) my first-hand personal experience in human research as a physician, having been involved in two studies, one involving magnesium and bone density and the other involving ultrasound use for detecting recurrent thyroid cancer.[1] I frequently review medical studies conducted by others and have experience assessing the strengths and weaknesses of such studies.

9. I was provided with and reviewed the following case-specific materials: the complaint of the plaintiffs, the memorandum of law in support of plaintiffs' motion for a temporary restraining order, the various declarations submitted by the Plaintiffs, the expert declaration submitted by Dr. Ettner, and the full text of Idaho House Bill no. 668.

10. A true and correct copy of my CV is attached to this declaration. In the previous four years, I have provided expert testimony in the following cases: Kayla Lovdahl v Kaiser, Arbitration Case No. 18496 (Cal, filed June 20, 2024); Victor Voe v Thomas Mansfield, No. 1:23-cv-864 (M.D. N. Car., filed June 3, 2024); *A.B. vs. Premera Blue Cross*, No. 2:23-cv-00953-TSZ (W.D. Wash. Filed June 27, 2023); *T.D. v. Wrigley*, No. 08-2023-CV-02189 (N.D. filed Sept. 14, 2023); *Brockman v. Kaiser Foundation Hospitals, Inc.*, No. STK-CV-UMM-2023-0001612 (Cal. Sup. Ct. filed Feb. 22, 2023); *Van Garderen v. State of Montana*, No. DV 2023-0541 (Missoula Cnty. Dist. Ct. filed May 9, 2023); *Koe v. Noggle*, No. 1:23-cv-02904-SEG (N.D. Ga. filed June 29, 2023); *Poe v. Drummond*, No. 23-cv-00177-JFH-SH (N.D. Okla. filed May 2, 2023); *Doe v. Thornbury*, No. 3:23-CV-00230-DJH (W.D. Ky. filed May 3, 2023); *L.W. v. Skrmetti*, No. 3:23-cv-00376 (M.D. Tenn. filed Apr. 20, 2023); *Boe v. Marshall, No. 2:22-cv-184-LCB* (M.D. Ala. filed Apr. 19, 2022); *Dekker v. Marstiller*, No. 4:22-cv-00325-RHMAF (N.D. Fla. filed Sept. 7, 2022); *C.P. v. Blue Cross Blue Shield of Illinois*, No. 3:20-cv-06145-RJB (W.D. Wash. filed Nov. 23, 2020); *Pflag, Inc. v. Abbott*, No. D-1-GN-22-002569 (459th Dist. Ct., Travis Cnty., filed June 8, 2022); *Paoli v. Hudson*, No. 279126 (Cal. Super. Ct. Tulare Cnty. filed June 20, 2019); *Doe v. Snyder*, No. 4:20-cv-00335-SHR (D. Ariz. filed Aug. 6, 2020); *A.M. v. Dr. F.*, No. S2011599,

[1] For the latter study I helped to design an Institutional Review Board ("IRB") approved protocol. Furthermore, I received certification in the required course "Understanding the Fundamentals: Responsibilities and Requirements for the Protection of Human Subjects in Research" at the University of Southern California in 2003.

2021 BCSC 32 (Can.); *A.B. v. C.D.*, [2019] No. E190334 (Can. B.C. Sup. Ct. J.); and *A.B. v. C.D.*, 2020 BCCA 11 (Can.).

11. In my professional opinion, treatment interventions on behalf of children and adults diagnosed with gender dysphoria must be held to the same scientific standards as other medical treatments. These interventions must be optimal, efficacious, and safe. Any treatment which alters biological development in children should be used with extreme caution. Except in the case of a fatal injury or disease, the minor will become an adult and present to the adult physician. The adult physician must be able to have a thorough understanding of any condition which alters the biological development of children and, in the case of the endocrinologist, be knowledgeable about the long-term effects of hormones on the human body, particularly when the hormones are being used in ways that alter development.

12. The following expresses my expert opinion regarding persons who present with a disparity between their biological sex and internal feeling about their gender, specifically with regard to the use of social transition, medications which block normal pubertal development, the applications of hormones of the opposite sex, and surgical procedures that alter the genitalia and/or breasts for those individuals.

I. Background

A. Biological Sex in Contrast to Gender Identity

13. A recognition and understanding of biological sex is critical to my practice as an endocrinologist because the endocrine physiology of men and women, boys and girls, differ.

14. Dr. Ettner states that "There is broad scientific understanding that gender identity is biologically based and a significant body of scientific and medical research that gender dysphoria has a physiological and biological etiology (cause or origin)." (Ettner decl., p. 8) However she provides no evidence of a definitive biological test to confirm the gender identity of an individual.

15. Biological sex is the objective physical condition of having organs and body parts which correspond to a binary sex. There are only two physical sexes, male and female. The male is identified as having organs and tissues such as the penis, testicles and scrotum. The female sex is identified by having organs and tissues such as the labia, vagina, uterus, and ovaries. Biological

sex is easily identified by physical observation such that adults and even young children can identify the biological sex of a newborn baby.

16. It is also noteworthy that the physical organs described above as representing biological sex have a physical genetic correlate. In other words, it is a well-established scientific fact that two X chromosomes identify the cells correlating to a female person, and an X and a Y chromosome correlate to a male person.

17. Gender identity is not a component of sex. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5 TR) states that "sex and sexual refer to the biological indicators of male and female (understood in the context of reproductive capacity), such as in sex chromosomes, gonads, sex hormones, and non-ambiguous internal and external genitalia" (DSM-5 TR, emphasis added). Note that gender identity is not a component of biological sex as defined by the DSM 5.

18. Gender identity in the DSM 5 is defined separately: "Gender identity is a category of social identity and refers to an individual's identification as male, female, or, occasionally, some category other than male or female" (DSM 5-TR). So, we can see that gender identity is not a physical entity but is described as a social identity. It is a subjective identification known only once a patient makes it known. It cannot be identified by any physical means, cannot be confirmed by any outside observer, and can change over time.

19. Gender identity is a psychological concept. It has no correlate in the human body. In the letter to the editor I wrote with my colleagues, we wrote in our critique of the Endocrine Society Guidelines that "[t]here are no laboratory, imaging, or other objective tests to diagnose a 'true transgender' child" (Laidlaw et al., 2019).

20. For example, one cannot do imaging of the human brain to find the gender identity. Likewise, there is no other imaging, laboratory tests, biopsy of tissue, autopsy of the brain, genetic testing, or other biological markers that can identify the gender identity. There is no known gene that maps to gender identity or to gender dysphoria. In other words, there is no objective physical measure to identify either gender identity or gender dysphoria.

21. This is in contrast to endocrine disorders which have a measurable physical change in either hormone levels or gland structure which can be confirmed by physical testing. Therefore, gender dysphoria is a purely psychological phenomenon and not an endocrine disorder. But as my colleagues and I wrote in our letter to the editor, it becomes an endocrine condition through gender affirmative therapy: "Childhood gender dysphoria (GD) is not an endocrine condition, but it

becomes one through iatrogenic puberty blockade (PB) and high-dose cross-sex (HDCS) hormones. The consequences of this gender-affirmative therapy (GAT) are not trivial and include potential sterility, sexual dysfunction, thromboembolic and cardiovascular disease, and malignancy" (Laidlaw et al. 2019).

22. Gender identity is not determined by any known gene or set of genes. If gender identity were to be determined by genes, we would expect that identical twins would profess having the same gender identity nearly 100 percent of the time. This is not the case. In fact, the largest transexual twin study ever conducted included seventy-four pairs of identical twins (Diamond, 2013). They were studied to determine in how many cases both twins would grow up to identify as transgender. In only twenty-one of the seventy-four pairs (28 percent) did both identical twins identify as transgender. This study does not demonstrate "the role of genetics" as the primary factor "in the development of gender dysphoria" as per Dr. Ettner (Ettner decl. p. 8). Rather this study is consistent with the fact that multiple factors play a role in determining gender identity, including psychological and social factors. This study suggests that those factors are more important than any potential genetic contribution. Furthermore, no genetic studies have ever identified a transgender gene or genes.

23. Sex is clearly identified in 99.98% of cases by chromosomal analysis (Sax, 2002). Sex is also clearly recognized at birth in 99.98% of cases (Id.). Therefore, sex is a clear provable objective reality that can be identified through advanced testing such as karyotyping, or simple genital identification at birth by any layperson. The other 0.02% of cases have some disorder of sexual development (DSD). DSDs do not represent an additional sex or sexes, but simply a disorder on the way to binary sex development (Chan et al., 2021).

B. Human Sexual Development

1. Embryologic Development

24. Another confirmation that there are only two biological sexes comes from what is known about embryologic development and fertilization. The biologic development of the human person begins with a gamete from a female termed an ovum or egg and a gamete from a biological male which is termed sperm. The fertilization of the egg by the sperm begins the process of human biological development. The cells of the fertilized ovum then multiply and the person undergoes the incredible changes of embryologic development.

25. It is noteworthy that the male sperm comes from the biological male and the female egg comes from the biological female. There is no other third or fourth or fifth type of gamete that exists to begin the development of the human person. This is consistent with the binary nature of human sex (Alberts et al., 2002).

26. The sex binary of the human embryo is further developed between roughly weeks 8 to 12 of human development. There are two primitive structures present within the developing embryo called the Wolffian duct and Mullerian ducts (Larsen et al., 2003). The Wolffian ducts develop into substructures of the genitalia including the vas deferens and epididymis which belong exclusively to the male sex. For the female, the Mullerian ducts go on to form the uterus, fallopian tubes, cervix and upper one third of the vagina which belong exclusively to the female sex (Id.)

27. Significantly once the male structures are developed from Wolffian ducts, the Mullerian ducts are obliterated. This means that throughout the rest of embryological development the Mullerian ducts will not form into biological female structures. Likewise, in the female, the Wolffian ducts are destroyed by week 12 and will not form male structures at any point in the future (Id.).

28. Thus we can see in very early development that the sex binary is imprinted physically not only in the chromosomes, but also on the very organs that the body produces. Additionally, the potential to develop organs of the opposite sex is eliminated. Thus, in the human being there are only two physical tracts that one may progress along, the one being male and the other being female (Wilson and Bruno, 2022).

2. Pubertal Development

29. As mentioned previously, at the time of birth an infant's sex is easily identified through observation of the genitalia. Corresponding internal structures could also be confirmed through imaging if needed.

30. In early childhood, some low level of sex hormones are produced by the sex glands. The male testes produce testosterone. The female ovaries produce primarily the hormone estrogen. These sex glands remain quiescent for the most part, producing low levels of sex hormones until the time of pubertal development.

31. Puberty is an essential part of human development. Its purpose is to achieve full adult sexual function and reproductive capacity. Puberty is a time of development of the sex organs, body, and brain. There are well known changes in physical characteristics of the male such

as growth of facial hair, deepening of the voice, and increasing size of the testicles and penis. Importantly, the testicles will develop sperm under the influence of testosterone and become capable of ejaculation. Because of these changes, the male will become capable of fertilizing an egg. The inability to produce sperm sufficient to fertilize an egg is termed infertility.

32. For the female, pubertal development includes changes such as breast development, widening of the pelvis, and menstruation. The female will also begin the process of ovulation which is a part of the menstrual cycle and involves the release of an egg or eggs from the ovary. Once the eggs are released in a manner in which they can become fertilized by human sperm then the female is termed fertile. The inability to release ovum that can be fertilized is infertility (Kuohong and Hornstein, 2021).

3. Tanner Stages of Development

33. From a medical perspective it is important to know the stage of pubertal development of the developing adolescent. This can be determined through a physical examination of the body. The female will have changes in breast characteristics and pubic hair development. Similarly, the male will have changes in testicular size and pubic hair development. These findings can be compared to the Tanner staging system which will allow the stage of puberty to be known.

34. Tanner stages are divided into five. Stage 1 is the pre-pubertal state before pubertal development of the child begins. Stage 5 is full adult sexual maturity. Stages 2 through 4 are various phases of pubertal development (Greenspan and Gardner, 2004).

35. Awareness of the Tanner stage of the developing adolescent is also useful to assess for maturation of sex organ development leading to fertility. For girls, the first menstruation (menarche) occurs about two years after Tanner stage 2 and will typically be at Tanner stage 4 or possibly 3 (Emmanuel and Boker, 2022). For males, the first appearance of sperm (spermarche) will typically be Tanner stages 4 (Id.). If puberty is blocked or disrupted before reaching these critical stages, the sex glands will be locked in a premature state and incapable of fertility.

4. Biological Sex Cannot Be Changed

36. Dr. Ettner states that "transition-related medical treatments confirm, rather than 'change,' an individual's sex by aligning primary and secondary sex characteristics with a person's gender identity." (Ettner, par 44).

37. I agree with Dr. Ettner that it is not possible for a person to change from one biological sex to the other. There is no technology that allows a biological male to become a

biological female or vice-versa. However I disagree that one can align their primary sex characteristics with their gender identity. For example, it is not technologically possible to transform sex glands from one to the other. In other words, there are no hormones or other means currently known to change an ovary into a testicle or a testicle into an ovary.

38. Furthermore, as noted earlier, several of the sex specific structures (such as the epididymis of the male or uterus of the female) are produced early in embryological development from around weeks 8 to 12. The primitive ducts which lead to these organs of the opposite sex are obliterated. There is no known way to resuscitate these ducts and continue development of opposite sex structures.

39. It is also not possible to produce gametes of the opposite sex. In other words, there is not any known way to induce the testicles to produce eggs. Nor is there any known way to induce the ovaries to produce sperm. Therefore, creating conditions for a biological female to create sperm capable of fertilizing another ovum is impossible. The induction of opposite sex fertility is impossible. It is not possible to create a functional vagina, uterus and fallopian tubes in a natal male. It is not possible to create a functional penis in a natal female that is equivalent to a natal male penis. It is also not technologically possible at this time to change sex chromosomes; these will remain in every cell throughout life.

40. In fact, as I will discuss, gender affirming therapy can lead to infertility, potential sterilization, and a host of negative health consequences.

C. Endocrine Disorders

41. Before discussing gender dysphoria and gender affirmative therapy from the perspective of an endocrinologist, it is helpful to discuss the background of endocrine diseases. This background demonstrates the difference in gender dysphoria, which is a psychological diagnosis, and other conditions treated by endocrinologists, which are physical diagnoses.

42. Endocrinology is the study of glands and hormones. Endocrine disorders can be divided into three main types: those that involve hormone excess, those that involve hormone deficiency, and those that involve structural abnormalities of the glands such as cancers.

43. It is important for the endocrinologist to determine the cause of hormone gland excess or deficiency in order to devise an appropriate treatment plan. The plan will generally be to help bring the hormones back into balance and thus bring the patient back to health.

44. To give an example of hormone excess, hyperthyroidism is a term which means overactivity of the thyroid gland. In this condition excess thyroid hormone is produced by the thyroid gland. This results in various physical and psychological changes for the afflicted patient. Examples of physical changes can include tachycardia or fast heart rate, hand tremors, and weight loss. Examples of psychological symptoms include anxiety, panic attacks, and sometimes even psychosis.

45. An endocrinologist can recognize thyroid hormone excess in part by signs and symptoms but can also confirm the diagnosis with laboratory testing that shows the thyroid hormones to be out of balance. Once this is determined and the degree of excess is known, then treatments can be given to bring these levels back into balance to benefit the patient's health and to prevent other disease effects caused by excess hormone.

46. Dr. Ettner falsely compares type 1 diabetes which is a physical diagnosis to gender dysphoria which is a psychological diagnosis (Ettner decl, par 35), and I will explain why.

47. Insulin is a hormone which regulates blood glucose levels. Both insulin and glucose levels can be measured by laboratory tests (unlike gender dysphoria and gender identity). If there is damage to the pancreas such that insulin levels are very low, then blood glucose levels will rise. If the glucose levels rise to a certain abnormally high level, then this is considered diabetes. In the case of type 1 diabetes, insulin levels are abnormally low and therefore blood glucose levels are abnormally high leading to a variety of signs and symptoms. For example, the patient may have extreme thirst, frequent urination, muscle wasting, and weight loss. They may often experience lethargy and weakness.

48. In this case laboratory tests of glucose and insulin levels can confirm the diagnosis. Once diabetes is confirmed, the patient must be treated with insulin to help restore glucose balance in the body and prevent long-term complications of diabetes. By contrast there is no equivalent hormonal or metabolic deficiency in gender dysphoria that warrants treatment with hormonal medications.

49. To give an example of a structural abnormality, a patient may have a lump on the thyroid gland in the neck. This may be further examined by an imaging test such as an ultrasound. A needle biopsy can be performed so that the cells can be examined under a microscope. A trained medical professional such as a pathologist can then examine the cells to determine if they are

benign or cancerous. In the case of thyroid cancer, a surgical procedure known as a thyroidectomy may be performed to remove the diseased thyroid gland in order to treat the cancer.

50. Noteworthy in the preceding three examples is that all three disease conditions are diagnosed by physical observations. In other words, a laboratory test of a hormone, an imaging test of an organ, or an examination of cells under a microscope—or all three—may be employed in the diagnosis of endocrine disease.

D. Gender Dysphoria is a Psychological Diagnosis

51. Gender dysphoria, on the other hand, is not an endocrine diagnosis. It is a psychological diagnosis. Gender dysphoria is the persistent state of distress that stems from the feeling that one's gender identity does not align with one's physical sex (DSM-5 TR). It is diagnosed purely by psychological methods of behavioral observation and questioning. The criteria for diagnosis is found in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5 TR).

52. As a practicing endocrinologist and scientist, I have made a study of GD and its treatment for two reasons: 1) I want to be sure that my colleagues and I understand the science before we treat any patients with GD; and 2) I am concerned that the medical society that claims to speak for me and other endocrinologists has abandoned scientific principles in endorsing treatments for GD that have questionable scientific support. The opinions expressed in this report are the result of my own experience, studies, education, and review of the scientific literature related to GD.

II. Gender Affirmative Therapy

53. In the section that follows I discuss four interventions (social transition, blocking normal puberty, opposite sex hormones, and surgery) that some physicians are using to treat gender dysphoria. Each intervention can lead to iatrogenic harms to the patient. The term "iatrogenic" is used in medicine to describe harms or newly created medical conditions that are the result of a treatment. These harms will be described in detail below. I speak of these harms because it is important to understand that once a patient begins GAT it is more likely the patient will continue on to surgery (de Vries et al,, 2011; de Vries et al., 2014). Thus, GAT interrupts the natural desistance process and instead places the patient on a lifetime regimen of hormonal and surgical care. A good understanding of these harms is also critical to my practice as an endocrinologist: if I did not understand these harms, I could not advise patients of the risks associated with GAT.

54. There are three general approaches to treating gender dysphoria in minors. (Zucker, 2020). One is psychosocial treatment that helps the young person align their internal sense of gender with their physical sex. Another would be to "watch and wait" and allow time and maturity to help the young person align sex and gender through natural desistance, while providing psychological support and therapy as needed and addressing comorbidities. The third option, which is the focus of that which follows, is referred to as gender affirmative therapy.

55. Gender affirmative therapy of adults and minors consists of psychosocial, medical, and surgical interventions that attempt to psychologically and medically alter the patient so that they come to believe they may become similar to the physical sex which aligns with their gender identity (but not their biological sex) and thereby reduce gender dysphoria. GAT consists of four main parts: 1) social transition, 2) blocking normal puberty or menstruation, 3) high dose opposite sex hormones, and 4) surgery of the genitalia and breasts.

56. The application of this medical therapy to minors[2] is a fairly new intervention and is associated with a number of harms both known and unknown. GAT suffers from a lack of a quality evidence-base, poorly performed studies, and ongoing unethical human experimentation. As discussed below, in my professional opinion as an endocrinologist, no child should be given these treatments.

A. Social transition

57. The first stage of gender affirmative therapy is termed social transition. Social transition is a psychological intervention. The child may be encouraged to adopt the type of clothing and mannerisms or behaviors which are stereotypical of the opposite sex within a culture.

[2] "[T]he US Department of Health and the Food and Drug Administration reference approximate age ranges for these phases of life, which consist of the following: (1) infancy, between birth and 2 years of age; (2) childhood, from 2 to 12 years of age; and (3) adolescence, from 12 to 21 years of age. Additionally, *Bright Futures* guidelines from the American Academy of Pediatrics identify adolescence as 11 to 21 years of age, dividing the group into early (ages 11–14 years), middle (ages 15–17 years), and late (ages 18–21 years) adolescence. The American Academy of Pediatrics has previously published a statement on the age limit of pediatrics in 1988, which was reaffirmed in 2012 and identified the upper age limit as 21 years with a note that exceptions could be made when the pediatrician and family agree to an older age, particularly in the case of a child with special health care needs. Recent research has begun to shed more light on the progression of mental and emotional development as children progress through the adolescent years into young adulthood. It is increasingly clear that the age of 21 years is an arbitrary demarcation line for adolescence because there is increasing evidence that brain development has not reliably reached adult levels of functioning until well into the third decade of life." (Hardin, 2017) (footnotes omitted).

For example, in the United States a boy might wear his hair long and wear dresses to socially transition. A girl may cut her hair short and wear clothes from the boys' section of a department store.

58. Social transition of the child has been noted by an expert researcher in the field of child gender dysphoria, Ken Zucker, to itself be a form of iatrogenic harm (Zucker, 2020). This is because the social transition process may solidify the young person's belief that they are in fact the sex opposite of their biological sex. The 2017 Endocrine Society Guideline states that "[s]ocial transition is associated with the persistence of GD/gender incongruence as a child progresses into adolescence" (Hembree et al., 2017). A recent study also supports the contention that children who undergo social transition are more likely to have their gender dysphoria persist into adolescence. In the 2022 article "Gender Identity 5 Years After Social Transition," which studied 317 socially transitioned youths, the authors found that "most participants were living as binary transgender youth (94.0%)" (Olson et al., 2022).

59. From an endocrine point of view, it is understandable that a child having the outward appearance of the opposite sex would believe that he or she is destined to go through puberty of the opposite sex. At this age, the child likely has only a poor understanding of the internal structures of the body, the function of the sex glands, the role of the sex glands in fertility and so forth.

60. Therefore, it would be quite frightening for a boy who believes he is a girl to be turning into a man with all of the adult features that accompany manhood. Vice versa, the girl who has become convinced that she is a boy will be frightened by the physical changes brought on by womanhood.

61. In fact, it would appear that in the minds of children and adolescents that they are anticipating a sort of disease state in the future by the hormone changes that will occur as a normal and natural part of human development. Until relatively recently in human history, it has not been possible to interfere with puberty through pharmaceutical means.

B. Medications That Block Pubertal Development

1. Background

62. A second stage of gender affirmative therapy may involve blocking normal pubertal development. This may be done with puberty blocking medications (PB) that act directly on the pituitary to cause the endocrine condition known as hypogonadotropic hypogonadism (HH).

63. In order to understand what is occurring in this process, it is helpful to be aware of normal hormone function during pubertal development. There is a small pea-sized gland in the brain called the pituitary. It is sometimes referred to as the "master gland," as it controls the function of several other glands. One key function for our purposes is the control of the sex glands. There are two specific hormones produced by the pituitary referred to as luteinizing hormone (LH) and follicle stimulating hormone (FSH). These are responsible for sex hormone production and fertility. The LH and FSH act as signals to tell the sex glands to begin or to continue their function.

64. In the adult male, the production of LH will cause adult levels of testosterone to be produced by the testicles. In the adult female, the production of LH will cause adult levels of estrogen to be produced by the ovaries.

65. In early childhood, prior to the beginning of puberty, the pituitary function with respect to the sex glands is quiescent. However, during pubertal development LH will signal the testicle to increase testosterone production and this carries the boy through the stages of pubertal development into manhood. Likewise for the female, the interaction of LH with the ovaries increases estrogen production and carries the girl through the stages of development into womanhood.

66. Hypogonadotropic hypogonadism is a medical condition in which the pituitary does not send the hormonal signals (LH and FSH) to the sex glands. Therefore, the sex glands are unable to make their sex specific hormones of testosterone or estrogen.

67. If this condition occurs during puberty, the effect will be to stop pubertal development. This is a disease state which is diagnosed and treated by the endocrinologist.

68. Medications such as GnRH analogues (sometimes called puberty blockers) act on the pituitary gland to lower the pituitary release of LH and FSH levels dramatically. The result is a blockage of the signaling of the pituitary to the testicles or ovaries and therefore underproduction of the sex hormones. This will stop normal menstrual function for the female and halt further pubertal development. For the male this will halt further pubertal development. If the male had already reached spermarche, then production of new sperm will stop.

2. GnRH Agonist Medication Effects Vary by Use Case

69. There are a variety of uses for GnRH agonists. The use and outcome can be very different for different applications.

70. For example, the initial development of the medication called Lupron was for the treatment of prostate cancer, the idea being that blocking pituitary hormones will block the adult male's release of testosterone from the testicles. Since testosterone will promote the growth of prostate cancer, the idea is to lower testosterone levels to a very low amount and therefore prevent the growth and spread of prostate cancer. This is a labeled use of the medication. In other words, there is FDA approval for this use.

71. Another labeled use of GnRH agonist medication is for the treatment of central precocious puberty. In the disease state of central precocious puberty, pituitary signaling is activated at an abnormally young age[3], say age four, to begin pubertal development. In order to halt puberty which has begun at an abnormally early time, a GnRH agonist may be used. Here the action of the medication on the pituitary will disrupt the signaling to the sex glands, stop early sex hormone production, and therefore stop abnormal pubertal development.

72. Then, at a more normal time of pubertal development, say age 11, the medication is stopped and puberty is allowed to proceed. The end result is to restore normal sex gland function and timing of puberty. This is a labeled use for a GnRH agonist medication.

73. What about the use of GnRH analogue medications such as Lupron in gender affirmative therapy? In these cases, we have physiologically normal children who are just beginning puberty or are somewhere in the process of pubertal development. They have healthy pituitary glands and sex organs. However, a puberty blocking medication is administered to stop normal pubertal development.

74. In this case the condition of hypogonadotropic hypogonadism described above (a medical disease) is induced by medication and is an iatrogenic effect of treating the psychological condition of gender dysphoria. GnRH analogue medications have not been FDA approved for this use. The use of GnRH analogue medication for this purpose in adolescents is experimental as there have been no randomized controlled trials for this specific use case.

75. In my opinion, there is not sufficient evidence to conclude that the use of puberty blockers to block natural puberty is safe when administered as part of gender affirming therapy. Nor is there sufficient evidence to conclude that the effects of puberty blockers when used in this manner are reversible.

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[3] "The traditional definition of precocious puberty is the development of secondary sexual characteristics before 8 years of age in girls and 9 years in boys" (Kota and Ejas, 2023).

3. Hypogonadotropic Hypogonadism

76. As described above, hypogonadotropic hypogonadism is a condition in which the pituitary fails to send signals to the gonads thereby preventing the testicle of the male from making testosterone or the ovary of the female from making estrogen.

77. As an endocrinologist I frequently evaluate patients to ascertain if they have the condition of hypogonadotropic hypogonadism. This is done by a laboratory evaluation. If the patient has this condition, I then determine the cause and the proper treatment.

78. The primary hormone of the pituitary which is abnormal in this condition is called luteinizing hormone or LH. In order to diagnose the condition, a laboratory test with reference ranges based on the person's sex and age is used to evaluate the blood sample.

79. For example, figure 1 shows the normal laboratory reference range for LH over the course of a month in an adult pre-menopausal female (0.5-76.3 mIU/mL) (Quest LH, 2023). A very low level of LH (red) with low estrogen levels indicates hypogonadotropic hypogonadism[4].

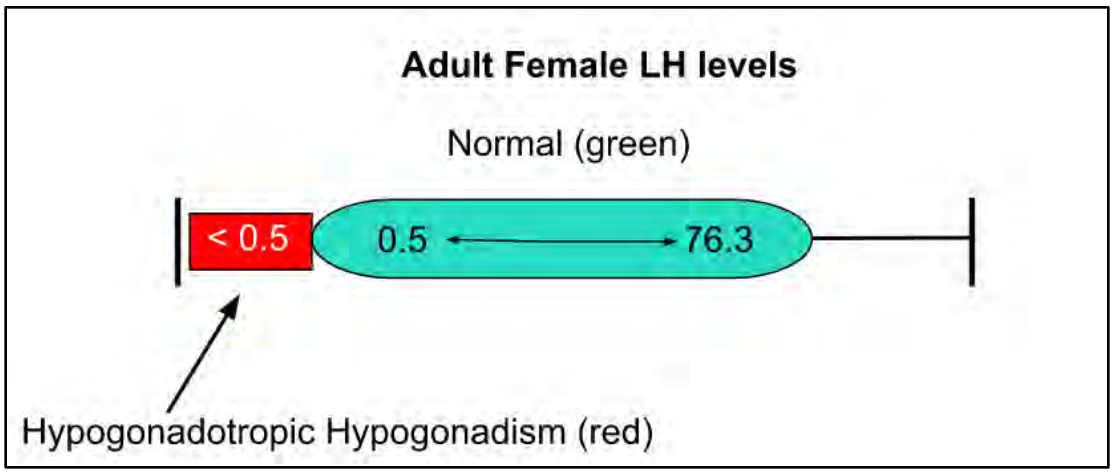

Figure 1.

80. As one can see, in hypogonadotropic hypogonadism the level of LH is below the reference range. In the female, this causes the cessation of estrogen production, and in the male it causes cessation of testosterone production. In adolescents of either sex, this will stop further pubertal development. For females in mid-puberty or beyond, this condition will also stop normal menstrual cycles and ovulation. For the male in mid-puberty or beyond, it will cause the cessation of normal sperm production.

[4] Levels will be similarly low for adolescents, though the normal reference range is different.

81. As an endocrinologist, I would confirm the condition of hypogonadotropic hypogonadism based on laboratory results and then treat this medical condition.

82. What occurs to pituitary hormones and the sex hormones[5] when administering a GnRH analogue medication such as Lupron? The effect is identical to figure 1. Over time, the result of the medication is to cause very low LH levels (red) leading to low sex hormone levels thereby medically inducing the condition of hypogonadotropic hypogonadism.

83. In gender affirmative therapy, the medical condition of hypogonadotropic hypogonadism is being deliberately created by the use of medications called GnRH analogues, one of which is called Lupron.

4. Adverse Health Consequences of Blocking Normal Puberty

a. Infertility

84. There are a number of serious health consequences that occur as the result of blocking normal puberty. The first problem is infertility.

85. GnRHa have profound implications for fertility. The Endocrine Society Guideline recommends beginning puberty blockers as early as Tanner stage 2. As discussed earlier, this is the very beginning of puberty. Fertility development happens later, generally in Tanner stage 4. Thus, if the developing person is blocked at Tanner stage 2 or 3, as advocated by the guidelines, this is prior to the patient becoming fertile. The gonads will remain in an immature, undeveloped state.

86. If the patient remains blocked in an early pubertal stage, then even the addition of opposite sex hormones will not allow for the development of fertility. In fact, high doses of opposite sex hormones may permanently damage the immature sex organs leading to sterilization. Certainly, the removal of the gonads by surgery will ensure sterilization.

87. In a Dutch study by de Vries et al. that included seventy adolescents who took puberty blockers, all seventy decided to go on to hormones of the opposite sex (de Vries, et al. 2011). In a follow-up study by de Vries et al., the overwhelming majority went on to have sex reassignment surgery by either vaginoplasty for males or hysterectomy with ovariectomy for

5 The primary sex hormones being estrogen for females and testosterone for males.

females (de Vries, et al. 2014). These surgeries resulted in sterilization[6]. This is why puberty blockers, rather than being a "pause" to consider aspects of mental health, are instead a pathway towards future sterilizing surgeries and potentially sterilizing hormonal treatments.

88. Even though procedures to preserve fertility are available for patients in late pubertal stages (Tanner 4 and 5), studies show that less than 5% of adolescents in North America receiving GAT even attempt fertility preservation (FP) (Nahata, 2017). Moreover, for those in early pubertal stages (Tanner 2 and 3), "ovarian tissue cryopreservation is still considered experimental in most centers and testicular tissue cryopreservation remains entirely experimental[7]. These experimental forms of FP would be the only options in children [with puberty] blocked prior to spermarche and menarche and are high in cost and limited to specialized centers. Even with FP there is no guarantee of having a child" (Laidlaw, Cretella, et al., 2019).

89. As an example, if a four-year-old child is diagnosed with precocious puberty, the abnormally early puberty may be halted by GnRH analogues (puberty blocking medication). The child will at a later time, say at age 12, have the puberty blocker discontinued and at that point normal pubertal development will be allowed to proceed. Therefore, when the child is no longer taking the medication, he or she will gain natural fertility.

90. In contrast, puberty blocking medication given to minors as a part of GAT occurs during the time for natural puberty—precisely the time that the adolescent person would have otherwise gained reproductive function. The effects of puberty blockers on the adolescent are to prevent sperm production in the male and ovulation in the female, which produces the infertile condition. Importantly, so long as the minor continues PB, he or she will thus remain infertile. And should the patient continue on to opposite sex hormones as part of GAT, then the patient will remain infertile. There is the additional possibility that cytotoxic effects of high dose opposite sex hormones will damage the immature gonads leading to permanent sterility.

b. Sexual Dysfunction

91. Another problem I would expect to find in youths who have HH and puberty stopped at an early stage is sexual dysfunction. The child will continue their chronological age

[6] The surgeries were consequential in another important way. One person who had a vaginoplasty died of post-surgical complications of necrotizing fasciitis which is a rapidly progressive and very severe infection of the soft tissues beneath the skin and which has a high mortality (Id.).

[7] "Once testicular tissue has been cryopreserved, future options for its use may include in vitro maturation or germ cell transplant, which at this time are theoretical in nature" (Klipstein et al., 2020).

progression toward adulthood and yet remain with undeveloped genitalia. This will lead to sexual dysfunction, including potential erectile dysfunction and inability to ejaculate and orgasm for the male. For the female with undeveloped genitalia potential sexual dysfunction may include painful intercourse and impairment of orgasm.

92. An example of the impairment of sexual function caused by stopping puberty in early development was evident in the TLC reality show "I am Jazz". This program documents Jazz Jenning's life experiences as a person with gender incongruence including Jazz's medical care. Jazz had been given puberty blockers at an early pubertal stage. In an episode of the show, Jazz, who was identified as a male at birth, visited the plastic surgeon, Christine McGinn, for a surgical evaluation for genital surgery (TLC, accessed 2022). Dr. McGinn describes her evaluation of Jazz's penis, stating it is "very, very small". In my opinion this very small penis size is consistent with beginning puberty blockers at a very early pubertal stage. Jazz also has a discussion about sexual function with the surgeon. Jazz states: "I haven't experienced any sexual sensation." Regarding orgasm, Jazz says: "I don't know, I haven't experienced it"[8] In my opinion, these descriptions are consistent with the type of sexual dysfunction that one would expect from early blockade of normal puberty.

c. Negative Effects of Hypogonadotropic Hypogonadism on Bone Density

93. Puberty is a time of rapid bone development. This time period is critical in attaining what we call peak bone density or the maximum bone density that one will acquire in their lifetime (Elhakeem, 2019).

94. Any abnormal lowering of sex hormones occurring during this critical time will stop the rapid accumulation of bone and therefore lower ultimate adult bone density. If a person does not achieve peak bone density, they would be expected to be at future risk for osteoporosis and the potential for debilitating spine and hip fractures as adults. Hip fractures for the older patient very significantly increase the risk of major morbidity and death (Bentler, 2009). Allowing a "pause" in puberty for any period of time can lead to an inability to attain peak bone density.

95. DEXA scans are used to evaluate changes in bone density and to help evaluate risk for future fractures. In my practice I order and interpret DEXA scans for this purpose.

[8] Jazz's age is somewhere in the mid-teens during this episode.

96. The Z-score of a DEXA scan is used to compare a patient's bone density to the same population based on age and sex. For example, a person who has a bone density similar to the average of the population would be at the 50th percentile. Those who have greater relative bone density would be above the 50th percentile. Those who have lower bone density would have a Z score below the 50th percentile.

97. Puberty blockers used in adolescence to cause HH will inhibit the normal accrual of bone density. This can be evaluated by DEXA scan. In a study in the UK, 44 patients aged 12-15 with gender dysphoria were given puberty blockers and tests of bone density were done at baseline, 12 months, 24 months and 36 months (Carmichael, 2021).

98. Figure 2 shows the Z-scores of the average age matched population percentile which is 50%. It shows the average baseline (before puberty blockers) Z-score percentile for the study participants. It also shows the bone density percentile at 12, 24, and 36 months. One can see that the average baseline z score was about 32% compared to peers of similar age and sex. At 12 months this had decreased to about 15%, and by 24 months it had declined further to about 5% compared to their peers and remained at this low level.

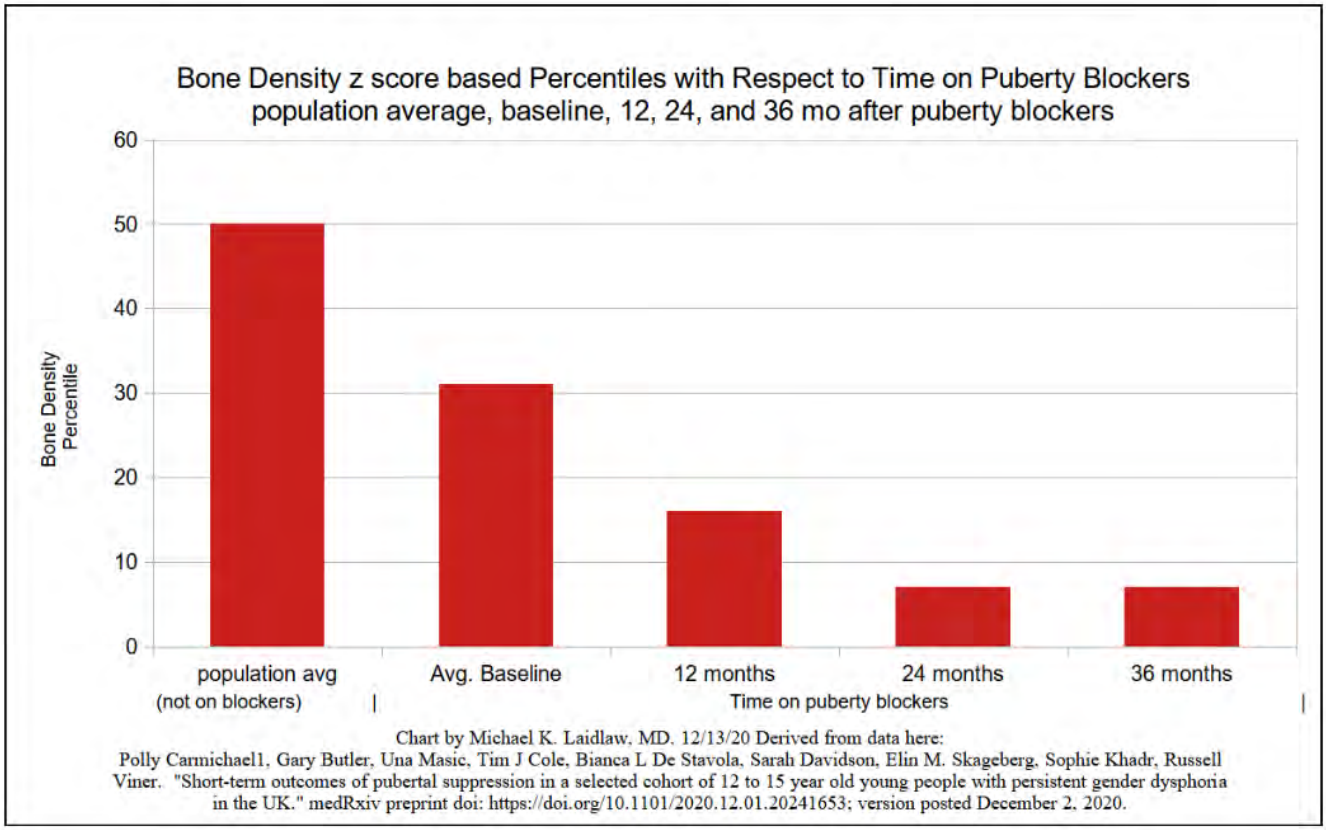

Figure 2

99. This is the same pattern of diminishing bone density compared to their peers that one would see in hypogonadotropic hypogonadism due to a pituitary injury. However, in these cases hypogonadotropic hypogonadism was caused by GnRH analogues (puberty blocking medication) that lead to greatly diminished bone density compared to their peers of the same age.

100. In natal females, hypogonadotropic hypogonadism leads to amenorrhea, meaning the absence of menstrual periods. Amenorrhea is detrimental to bone health: "In addition to this[9] important long-term consequence of amenorrhea, other problems, such as premature bone demineralization or inadequate bone formation, are likely to put amenorrheic women at high risk for osteoporosis and fracture" (Santoro, 2011) (emphasis added).

101. Another consideration is the effects of HH in adolescents and late teens on the maturation of the human brain. It is known that adolescence is a crucial time of neurodevelopment and that puberty plays "a critical role in these neurodevelopmental processes" (Baxendale, 2024). Furthermore, "sex hormones including estrogen, progesterone, and testosterone can influence the development and maturation of the adolescent brain." (Arain, 2013). It is also known that the "suppression of puberty impacts brain structure and the development of social and cognitive functions in mammals, the effects are complex and often sex specific." (Baxendale, 2024) Therefore, there are unknown, but likely negative, consequences to blocking normal puberty with respect to brain development.

d. Psychosocial Development

102. A third major problem with blocking normal puberty involves psychosocial development. Adolescence is a critical time of physical, mental, and emotional changes for the adolescent. It is important that they develop socially in conjunction with their peers.

103. While I am not a psychologist, I am familiar with and rely upon the literature in this area for the rationale of the treatment of precocious puberty[10]. It is generally accepted in endocrinology that there are psychological benefits to adolescents who go through puberty around the same time as their peers, and this is why puberty blockers (GnRH analogues) in central

[9] "This" refers to cardiovascular disease: "Diagnosis and treatment of amenorrheic states is of increasing clinical importance because lifetime menstrual irregularities are known to be predictive of subsequent CVD in women."

[10] "The other concern often used as a rationale for treatment is negative psychosocial consequences of precocious puberty, particularly in girls" (Eugster, 2019, emphasis added).

precocious puberty are sometimes used to delay a child's abnormally early pubertal development to a more age-appropriate time.

104. The development of the adolescent along with their peers is also well recognized in the psychological literature: "For decades, scholars have pointed to peer relationships as one of the most important features of adolescence." (Brown, 2009). If one is left behind for several years under the impression that they are awaiting opposite sex puberty, they will miss important opportunities for socialization and psychological development. Psychosocial development will be necessarily stunted as they are not developing with their peers. This is a permanent harm as the time cannot be regained.

105. Aside from the multiple serious problems that are iatrogenically acquired by blocking normal puberty, there appear to be independent risks of the puberty blocking medication themselves. For example, one can read the labeling of a common puberty blocking medication called Lupron Depot-Ped and find under psychiatric disorders: "emotional lability, such as crying, irritability, impatience, anger, and aggression. Depression, including rare reports of suicidal ideation and attempt. Many, but not all, of these patients had a history of psychiatric illness or other comorbidities with an increased risk of depression" (Lupron, 2022). This is particularly concerning given the high rate of psychiatric comorbidity with gender dysphoria (Kaltiala-Heino, 2015).

C. Opposite Sex Hormones

106. The third stage of gender affirmative therapy involves using hormones of the opposite sex (also called cross sex hormones) at high doses to attempt to create secondary sex characteristics in the person's body.

107. Dr. Ettner states that "[t]ransgender women who have undergone gender-affirming orchiectomy or other gender-affirming genital surgeries resulting in removal of the testicles, must receive consistent gender-affirming hormone therapy at the appropriate therapeutic levels to avoid adverse health effects" (Ettner decl, par 42). However I will show that both natal males and females suffer a multitude of adverse health effects and risks by taking cross sex hormones as part of GAT.

108. In GAT, what is termed "cross sex hormones" is the use of hormones of the opposite sex to attempt to create secondary sex characteristics. To do so, very high doses of these hormones are administered. When hormone levels climb above normal levels they are termed supraphysiologic.

1. Testosterone

109. Testosterone is an anabolic steroid of high potency. It is classified as a Schedule 3 controlled substance by the DEA: "Substances in this schedule have a potential for abuse less than substances in Schedules I or II and abuse may lead to moderate or low physical dependence or high psychological dependence" (DEA, 2022). A licensed physician with a valid DEA registration is required to prescribe testosterone.

110. I prescribe testosterone to men for testosterone deficiency. The state of testosterone deficiency can cause various problems including problems of mood, sexual function, libido, and bone density. Prescription testosterone is given to correct the abnormally low levels and bring them back into balance. The dose of testosterone must be carefully considered and monitored to avoid excess levels in the male as there are a number of serious concerns when prescribing testosterone. The use of high dose testosterone in females is experimental.

111. Contrast the FDA approved use of testosterone in males versus its experimental use females. Testosterone is FDA approved for use in adult men as well as the pediatric male population aged 12 and older (Actavis, 2018). There is no FDA approved usage of testosterone for women or pediatric aged females.[11] The prescribing indications for adult males and pediatric males are identical and are to treat the conditions of low testosterone caused by either primary hypogonadism or secondary hypogonadism (Id.). The intent of testosterone for women and pediatric aged females in GAT is to cause severe hyperandrogenism. In this case the purpose, effects, and ultimate outcome of the FDA approved usage of testosterone for males versus the experimental use for females in GAT are very different. Therefore, the low-quality evidence guidelines of the Endocrine Society/WPATH are not an acceptable substitute for proper scientific studies including randomized controlled trials (Malone et al., 2021; Hembree et al., 2017).

112. Regarding the potential for abuse, the labeling for testosterone reads: "Testosterone has been subject to abuse, typically at doses higher than recommended for the approved indication...Anabolic androgenic steroid abuse can lead to serious cardiovascular and psychiatric adverse reactions...Abuse and misuse of testosterone are seen in male and female adults and adolescents...There have been reports of misuse by men taking higher doses of legally obtained

[11] "Testosterone Cypionate Injection, USP is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone" (Actavis, 2018, emphasis added).

testosterone than prescribed and continuing testosterone despite adverse events or against medical advice." (Actavis Pharma, 2018, emphasis added)

113. Adverse events with respect to the nervous system include: "Increased or decreased libido, headache, anxiety, depression, and generalized paresthesia." (Actavis Pharm, 2018)

114. With regard to ultimate height, "[t]he following adverse reactions have been reported in male and female adolescents: premature closure of bony epiphyses with termination of growth" (Actavis Pharma, Inc., 2018). What this means is that testosterone applied to the adolescent will cause premature closure of the growth plates, stopping further gains in height in the growing individual, and ultimately making the person shorter than they otherwise would have been.

115. With respect to the cardiovascular system of men using ordinary doses, "Long-term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy in men" (Actavis Pharma, 2018). No clinical safety trials have been performed for women or adolescent girls to my knowledge.

116. "There have been postmarketing reports of venous thromboembolic events [blood clots], including deep vein thrombosis (DVT) [blood clot of the extremity such as the leg] and pulmonary embolism (PE) [blood clot of the lung which may be deadly], in patients using testosterone products, such as testosterone cypionate" (Actavis Pharma, 2018).

117. A published study of adverse drug reactions (ADRs) as part of gender affirming hormone therapies in France states that "[o]ur data show a previously unreported, non-negligible proportion of cases indicating cardiovascular ADRs in transgender men younger than 40 years… In transgender men taking testosterone enanthate, all reported ADRs were cardiovascular events, with pulmonary embolism in 50% of cases" (Yelehe et al., 2022).

118. There are also serious concerns regarding liver dysfunction: "Prolonged use of high doses of androgens ... has been associated with development of hepatic adenomas [benign tumors], hepatocellular carcinoma [cancer], and peliosis hepatis [generation of blood-filled cavities in the liver that may rupture] —all potentially life-threatening complications" (Actavis Pharma, 2018).

a. Hyperandrogenism

119. Hyperandrogenism is a medical condition of elevated blood androgens such as testosterone. As an endocrinologist I frequently evaluate patients to determine if they have the

condition of hyperandrogenism. Hyperandrogenism in the female or male is harmful and can lead to various maladies.

120. In order to diagnose hyperandrogenism, a laboratory blood test of testosterone is done. In hyperandrogenism, one will find testosterone levels elevated above the reference range.

121. For example, for females aged 18 or older, the normal reference range is 2-45 ng/dL (Quest testosterone, 2023).[12] However, in female disease conditions these levels can be much higher. Levels above this normal reference range are considered hyperandrogenism (figure 3).

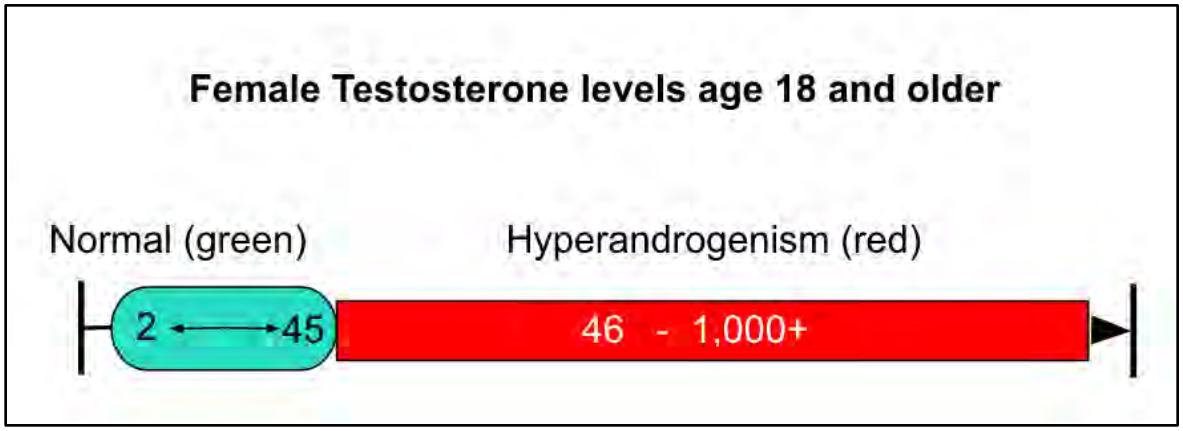

Figure 3

122. For example, in polycystic ovarian syndrome levels may range from 50 to 150 ng/dL.

123. I frequently diagnose and treat the hyperandrogen condition called polycystic ovarian syndrome (PCOS). These patients have elevated testosterone levels. These levels are mildly to moderately elevated and may range from 50-150. Hyperandrogenism found in PCOS has been associated with insulin resistance (Dunaif, 1989), metabolic syndrome (Apridonidze, 2005) and diabetes (Joham, 2014).

124. I also evaluate patients to rule out rare androgen producing tumors that generate very high levels of testosterone. These rare endocrine tumors can cause severely elevated testosterone levels in the 300-1000 range. Once the cause of a hyperandrogen condition is identified, treatments may be put in place to help bring the testosterone levels down to the normal reference range.

[12] For females aged 11-17 the reference range is <= 40 and below this age group, the range is even lower.

125. Recommendations from the Endocrine Society's clinical guidelines related to GAT are to ultimately raise female levels of testosterone to 320 to 1000 ng/dL[13] which is on the same order as dangerous endocrine tumors for women as described above (Hembree, 2017). A simple calculation shows this level for the adult may be anywhere from 6 to 100 times higher than native female testosterone levels. In doing so they are inducing severe hyperandrogenism. These extraordinarily high levels of testosterone are associated with multiple risks to the physical and mental health of the patient.

126. The following chart shows testosterone levels in the normal adult female range (blue), PCOS (gray), endocrine tumors (red), and gender affirmative therapy (orange) as part of female to male (FtM) transition (figure 4).

[13] In the Endocrine Society's Guidelines there is no grading of evidence for the rationale of using such high supraphysiologic doses of opposite sex hormones for the female or male. There seems to be an underlying assumption that because the person believes to be the opposite sex then they acquire the sex specific laboratory ranges of the opposite sex. "The root cause of this flaw in thinking about diagnostic ranges was exemplified in a response letter by Rosenthal et al claiming that gender identity determines the ideal physiologic range of cross-sex hormone levels (5). Thus, a psychological construct, the 'gender identity', is imagined to affect physical reality and change a person's sex-specific laboratory reference ranges. This is clearly not the case, otherwise there would be no serious complications of high-dose androgen treatment in transgender males" (Laidlaw et al., 2021).

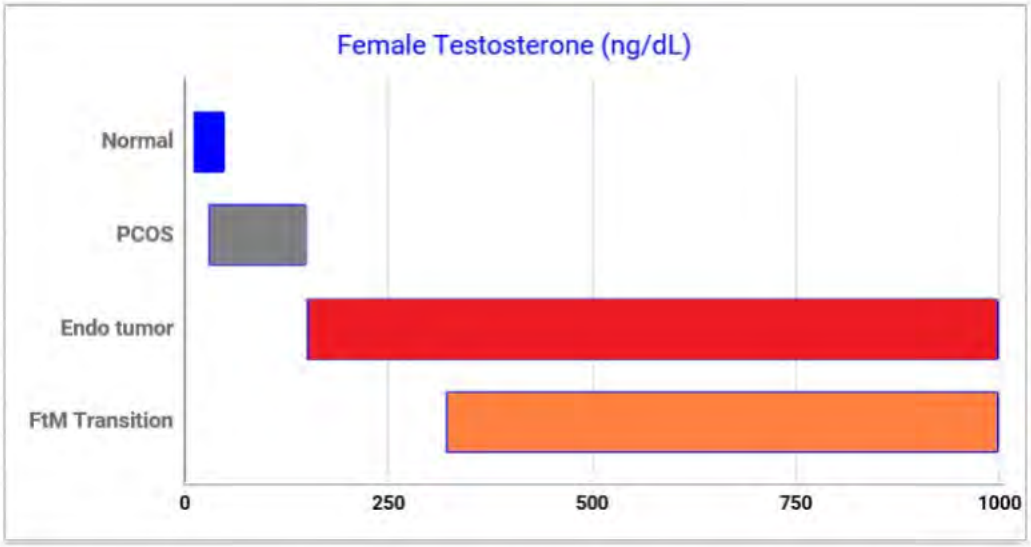

Image by Michael K Laidlaw. MD. Approximate total testosterone in ng/dL based on laboratory, etc. FtM transition from 2017 Endo Society Guidelines on Gender Dysphoria. With PCOS testosterone levels may be as high as 150. With endocrine tumors testosterone may be in the 150-1000 range. The recommendations of the Endocrine Society/WPATH are to bring levels into the 300-1000 range which is 6-100 times higher than normal endogenous adult female levels.

Figure 4.

b. Medical Problems Related to Hyperandrogenism

127. With respect to cardiovascular risk, "[s]tudies of transgender males taking testosterone have shown up to a nearly 5-fold increased risk of myocardial infarction relative to females not receiving testosterone" (Laidlaw et al.,2021; Alzahrani et al., 2019).

128. Permanent physical effects of testosterone therapy involve irreversible changes to the vocal cords. Abnormal amounts of hair growth which may occur on the face, chest, abdomen, back and other areas is known as hirsutism. Should the female eventually regret her decision to take testosterone, this body hair can be very difficult to remove. Male pattern balding of the scalp may also occur. I would expect these changes to occur to the plaintiffs taking testosterone to induce hyperandrogenism. Common sense suggests that changes of voice and hair growth could be psychologically troubling should a patient decide to detransition and attempt to reintegrate into society as female.

129. Changes to the genitourinary system due to hyperandrogenism include polycystic ovaries, clitoromegaly and atrophy of the lining of the uterus and vagina (Hembree, 2017). The breasts have been shown to have an increase in fibrous breast tissue and a decrease in normal glandular tissue (Grynberg et al., 2010). Potential cancer risks from high dose testosterone include

ovarian and breast cancer (Hembree, 2017). I would expect some or all of these effects and risks to occur to the plaintiffs taking testosterone to induce hyperandrogenism.

130. The long-term effects of starting an adolescent on puberty blockers in early puberty (Tanner stage 2 or 3) and then adding opposite sex hormones on ultimate sterility are unknown in the sense that we do not have studies showing precisely what happens, but based on what we do know, it seems safe to say that opposite sex hormones are likely cytotoxic to the immature gonads.

131. Dr. Ettner states with respect to psychological benefits of opposite sex hormones that she has "observed clinically the many psychological and physiological benefits of hormone therapy" and that "[i]ndividuals experience a previously unknown level of well-being when receiving hormonal treatment, and improvement is observable in virtually every area of a patient's life." (Ettner, par 43) She also reports that "[d]epression, anxiety, suicidality and self-harm are often significantly reduced, or entirely eliminated." (Id.) However the evidence paints a different picture.

132. The closest biological model to the administration of high dose androgens such as testosterone is found in anabolic steroid abuse. According to research, anabolic steroid abuse[14] has been shown to predispose individuals towards mood disorders, psychosis, and psychiatric disorders. The "most prominent psychiatric features associated with AAS [anabolic androgenic steroids, i.e., testosterone] abuse are manic-like presentations defined by irritability, aggressiveness, euphoria, grandiose beliefs, hyperactivity, and reckless or dangerous behavior. Other psychiatric presentations include the development of acute psychoses, exacerbation of tics and depression, and the development of acute confusional/delirious states" (Hall, 2005). Moreover, "[s]tudies... of medium steroid use (between 300 and 1000 mg/week of any AAS) and high use (more than 1000 mg/week of any AAS) have demonstrated that 23% of subjects using these doses of steroids met the DSM-III-R criteria for a major mood syndrome (mania, hypomania, and major depression) and that 3.4% — 12% developed psychotic symptoms" (Hall, 2005).

133. In an observational study of the Food and Drug Administration's Event Reporting system database for people using opposite sex hormones for the purpose of gender transition a "striking 88% were categorized as serious ADRs [adverse drug reactions]" (Gomez-Lumbreras and Villa-Zapata, 2024). Of natal females taking testosterone for transition, they found that "a

[14] Anabolic steroid abuse involves the deliberate creation of hyperandrogenism in the body as a result of high doses of testosterone or other androgens.

substantial portion of the reports were deemed serious (72, 87.8%), with 2 deaths (2.4%) and 25 hospitalizations (30.5%)". These serious findings of harm underscore the dangers of high dose testosterone used for the purpose of gender transition. With respect to psychological effects, adverse reactions included anxiety, depression, affect lability, euphoric mood, self-destructive behavior, anger, aggression, anti-social behavior, and homicidal ideation. Additionally, there were reports of suicide attempts, suicidal behavior and ideation, dissociation, and emotional disorder and distress. In my opinion, these adverse mental health findings of natal females on supraphysiologic doses of testosterone are consistent with the next closest biological model, which is anabolic steroid abuse.

c. Erythrocytosis as a Result of Hyperandrogenism

134. I regularly monitor patients who are receiving testosterone to evaluate for erythrocytosis. Erythrocytosis is a condition of high red blood cell counts. Prolonged hyperandrogenism such as occurs with the use of testosterone at supraphysiologic levels can cause erythrocytosis.

135. Males and females have different reference ranges for red blood cells (measured as hematocrit). For example, the normal range of hematocrit for females over age 18 is 35.0-45.0% and males 38.5-50.0% (Quest Hematocrit, 2023). Levels above this range signify erythrocytosis (see figure 5).

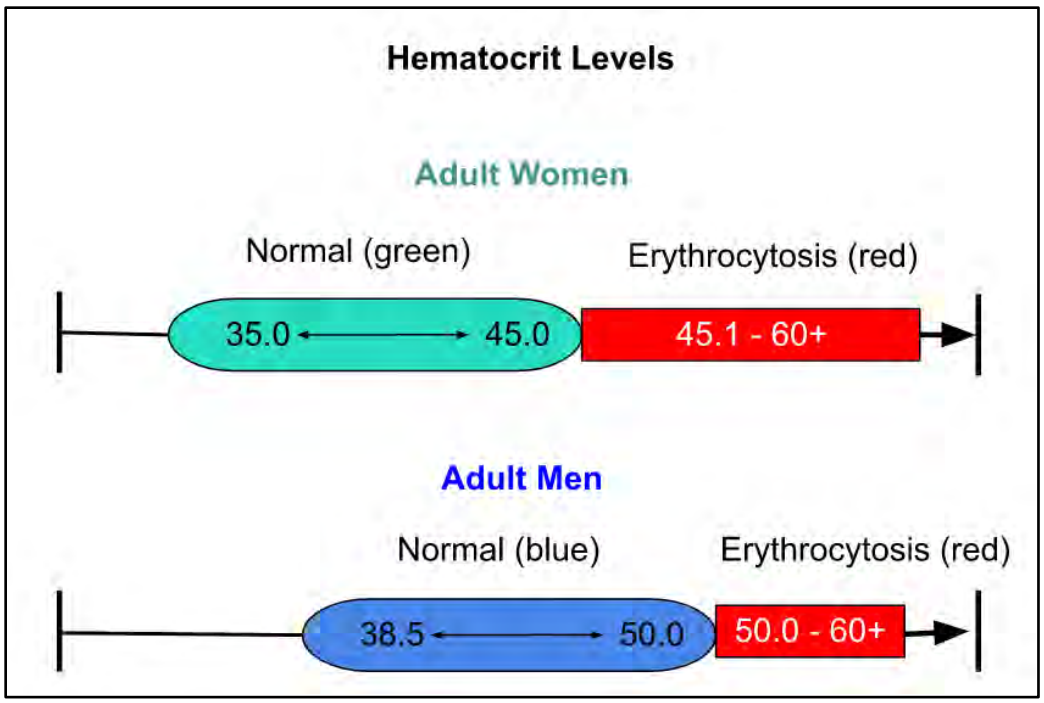

Figure 5.

136. As one can see, there is an overlap in the ranges of males and females such that levels between 45.1 and 50 are considered normal for the male. However, for the female these levels are considered erythroctyotic. Levels above 50 for the male are considered erythrocytosis and for the female severe erythrocytosis.

137. The Madsen study was a "20-year follow-up study in [1,073] adult trans men who started testosterone therapy and had monitoring of hematocrit at our center" (Madsen, 2021). In this study, 24% of trans men had hematocrit levels 50% at some time which would be considered severe erythrocytosis. Unfortunately, they did not examine the hematocrit range of 45-50. However, one would presume that this would occur in at least the same percentage or higher as those who had developed severe erythrocytosis.

138. Any level of erythrocytosis in young women has been shown to be an independent risk factor for cardiovascular disease, coronary heart disease and death due to both (Gagnon, 1994).

2. Estrogen

139. Estrogen is the primary sex hormone of the female. Prescription estrogen may be used if a woman has low estrogen levels due to premature failure of her ovaries. Estrogen is prescribed to bring these levels back into a normal range for the patient's age. Another labeled use

of estrogen is to treat menopausal symptoms. The use of estrogen to treat pediatric age males is experimental.

140. Hyperestrogenemia is a condition of elevated blood estrogens such as estradiol. I regularly evaluate patients for hyperestrogenemia in my practice. Hyperestrogenemia in the male is harmful and can lead to various maladies.

141. In order to diagnose hyperestrogenemia, a laboratory blood test of estrogen is performed. In hyperestrogenemia, one will find estrogen levels elevated above the reference range. For example, in an adult male the normal estrogen reference range is 60-190 pg/mL (Quest Estrogen, 2023). Levels above this range are consistent with hyperestrogenemia. See figure 6.

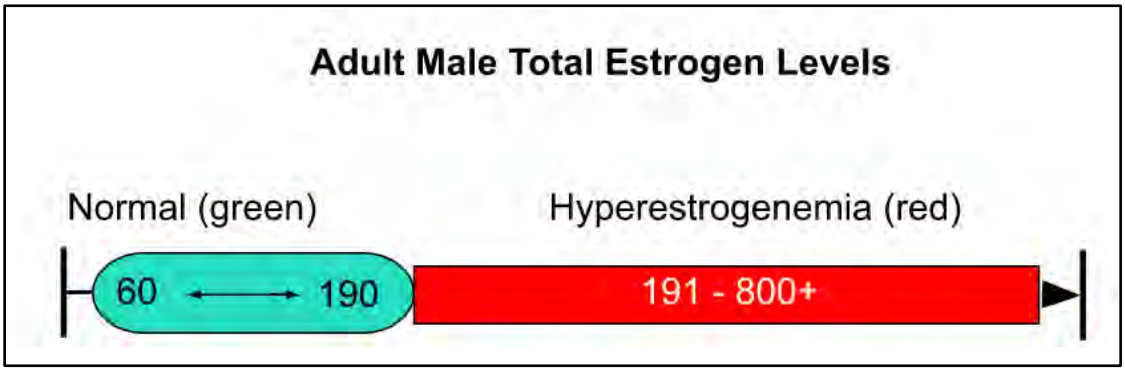

Figure 6.

142. There are medical conditions which can result in hyperestrogenemia. For example, "[t]he concentration of estrogen in cirrhotic patients is thought to increase by fourfold compared to individuals without cirrhosis" (Pagadala, 2023). Certain rare tumors for example of the adrenal gland can result in estrogen levels 3 to 10-fold higher than normal (Cavlan, 2010).

143. In gender affirmative therapy, the medical condition of hyperestrogenemia is being deliberately, medically induced by the off-label use of high doses of estrogen. The Endocrine Society guideline for treating gender dysphoria recommends raising estradiol levels to 2 to 43 times above the normal range.[15] The high doses are used in an attempt to primarily affect an increase of male breast tissue development known as gynecomastia. Gynecomastia is the abnormal growth of breast tissue in the male. I evaluate and treat patients with gynecomastia. I have prescribed medication and have referred patients for surgery for this condition.

[15] Estradiol is a type of estrogen. The Endocrine Society Guideline recommends raising estradiol levels to 100-200 pg/mL (Hembree, 2017). The normal adult male estradiol range is 7.7-42.6 pg/mL (Labcorp Estradiol, 2023).

144. Other changes of secondary sex characteristics may develop because of hyperestrogenemia such as softening of the skin and changes in fat deposition and muscle development.

145. Long-term consequences of hyperestrogenemia include increased risk of myocardial infarction and death due to cardiovascular disease (Irwig, 2018). Also "[t]here is strong evidence that estrogen therapy for trans women increases their risk for venous thromboembolism[16] over 5 fold" (Irwig, 2018).

146. Breast cancer is a relatively uncommon problem of the male. However, the risk of a male developing breast cancer has been shown to be 46 times higher with high dose estrogen (Christel et al., 2019).

147. Sexual dysfunction, including decreased sexual desire and decreased spontaneous erections, is another adverse effect of hyperestrogenemia (Hembree, 2017).

D. Surgeries

148. The fourth stage of gender affirmative therapy is surgical alterations of the body of various kinds in an attempt to somehow mimic features of the opposite sex. Although endocrinologists do not typically perform surgery, we do refer patients for surgeries and need to be aware of the risks, benefits, complications, and long-term outcomes.

149. Individual surgical procedures can be a complex topic. It is helpful to first step back and consider conceptually what any surgery can and cannot accomplish.

150. In its basic form surgery is subtractive. In other words, a portion of tissue, an organ, or organs are removed in order to restore health. For example, a diseased gallbladder may be surgically removed to help the patient get back to wellness. An infected appendix may be surgically removed to prevent worsening infection or even death. In both of these cases an unhealthy body part is surgically removed in order to restore health.

151. In some cases a diseased tissue or organ is removed so that a foreign replacement part may be substituted for an unhealthy organ or tissue. For example, a diseased heart valve may be replaced with a pig valve or a prosthetic heart valve. Another example is a failed liver may be replaced by liver transplant.

[16] Venous thromboembolism is a blood clot that develops in a deep vein and "can cause serious illness, disability, and in some cases, death" (CDC, 2022).

152. Though modern surgical techniques and procedures are astounding, there are very noteworthy limitations. Importantly, surgery cannot de novo create new organs. If a person's kidneys fail, the surgeon has no scientific method for creating a new set of kidneys that can be implanted or grown within the patient. This conceptual background is helpful when considering various gender affirming surgeries.

153. There are a variety of gender affirming surgeries for females. These may include mastectomies, metoidioplasty, and phalloplasty.

1. Mastectomy

154. Mastectomies are the surgical removal of the breasts. The procedure is used in GAT in an attempt to make the chest appear more masculine. The surgery results in a permanent loss of the ability to breastfeed and significant scarring of 7 to 10 inches. The scars are prone to widening and thickening due to the stresses of breathing and arm movement. Other potential complications include the loss of normal nipple sensation and difficulties with wound healing (American Cancer Society, 2022).

155. It is important to note that this operation cannot be reversed. The female will never regain healthy breasts capable of producing milk to feed a child (Mayo Clinic, Top Surgery, 2022).

156. Another important consideration is that compared to the removal of an unhealthy gallbladder or appendix, in the case of gender dysphoria the breasts are perfectly healthy and there is no organic disease process such as a cancer warranting their removal.

2. GAT Surgeries on the Male

157. GAT surgeries for the male include removal of the testicles alone to permanently lower testosterone levels. This is by nature a sterilizing procedure. Further surgeries may be done in an attempt to create a pseudo-vagina; that procedure is called vaginoplasty. In this procedure, the penis is surgically opened and the erectile tissue is removed. The skin is then closed and inverted into a newly created cavity in order to simulate a vagina. A dilator must be placed in the new cavity for some time so that it does not naturally close.

158. Potential surgical complications may include urethral strictures, infection, prolapse, fistulas and injury to the sensory nerves with partial or complete loss of erotic sensation (Mayo Clinic, Feminizing Surgery, 2022).

3. GAT Surgeries of the Female Pelvis and Genitalia

159. Other types of surgery for females include those of the genitalia and reproductive tract. For example, the ovaries, uterus, fallopian tubes, cervix and the vagina may be surgically removed. Removal of the ovaries results in sterilization.

160. Importantly, removing female body parts does not produce a male. Rather, the female has had sex-specific organs permanently destroyed with no hope of replacement, while remaining biologically female.

161. There have also been attempts to create a pseudo-penis. This procedure is known as phalloplasty. It is not possible to de novo create a new human penis. Instead, a roll of skin and subcutaneous tissue is removed from one area of the body, say the thigh or the forearm, and transplanted to the pelvis. An attempt is made to extend the urethra or urinary tract for urination through the structure. This transplanted tissue lacks the structures inherent in the male penis which allow for erection, therefore erectile devices such as rods or inflatable devices are placed within the tube of transplanted tissue in order to simulate erection (Hembree, 2017). The labia may also be expanded to create a simulated scrotum containing prosthetic objects to provide the appearance of testicles.

162. Complications may include urinary stricture, problems with blood supply to the transplanted roll of tissue, large scarring to the forearm or thigh, infections including peritonitis, and possible injury to the sensory nerve of the clitoris (Mayo Clinic, Masculinizing Surgery, 2022). A recent systematic review and meta-analysis of 1731 patients who underwent phalloplasty found very high rates of complications (76.5%) including a urethral fistula rate of 34.1% and urethral stricture rate of 25.4% (Wang, 2022).

III. The Lack of Evidence Supporting Gender-Affirming Therapy

163. There is not a medical consensus supporting the use of puberty blockers and cross-sex hormones for the treatment of gender dysphoria. In my opinion, there is insufficient evidence to conclude that any benefit of such treatment would outweigh the harm, particularly given the evidence of a rapid rise in cases of youth gender dysphoria, the high rates of coexisting mental health comorbidities, and naturally high rates of desistance.

A. The Endocrine Society and WPATH

164. Clinical guidelines promoting GAT have been produced by medical organizations such as the Endocrine Society and social-political advocacy groups like WPATH. Dr. Ettner is a

longstanding WPATH member including having been "a Fellow, Diplomate, and [having] served on the Board of Directors from 2001 to 2005" as well as starting on the Executive Committee of WPATH as Secretary on Oct. 13, 2017 (James, 2024; WPATH Providers, 2024). Dr Ettner is also "an author of the WPATH Standards of Care Version 8" (SOC 8) (Ettner decl, par 7). Dr. Ettner frequently relies on and refers to recommendations from the SOC 8 throughout her declaration.

1. WPATH

a.WPATH is an Advocacy Organization Primarily for Promoting Social and Political Activism

165. WPATH has functioned primarily as an advocacy organization for promoting social and political activism rather than as a strictly scientific organization. Unlike a scientific organization that must allow for internal debate to clarify issues of uncertainty, WPATH has actively sought to stymie such debate. As an example, Dr. Kenneth Zucker, whom I cited earlier, is a psychologist who led the Child Youth and Family Gender Clinic in Toronto, which was "one of the most well-known clinics in the world for children and adolescents with gender dysphoria." (Singal, 2016). He also led the group which wrote the DSM's gender dysphoria section. (*Id.*)

166. Dr. Zucker has been a longstanding member of WPATH. In fact, his work was cited 15 times in the 2012 WPATH Standards of Care 7. (Bazelon, 2022). Dr. Zucker discovered over the course of nearly forty years of clinical research "that most young children who came to his clinic stopped identifying as another gender as they got older." (*Id.*).

167. Dr. Zucker was invited to speak to the USPATH's 2017 inaugural conference. During his presentation, protestors disrupted his talk and made demands of WPATH. "That evening, at a meeting with the conference leaders, a group of advocates led by transgender women of color read aloud a statement in which they said the 'entire institution of WPATH' was 'violently exclusionary' because it 'remains grounded in 'cis-normativity and trans exclusion.' The group asked for cancellation of Zucker's appearance on a second upcoming panel. Jamison Green, a trans rights activist and former president of WPATH, said the board agreed to the demand. 'We are very, very sorry,' he said." (Bazelon, 2022).

168. As an example of WPATH's one-sided political advocacy, consider also the recent inflammatory message by WPATH president Marci Bowers, MD in a letter to members. Writing about laws that seek to protect vulnerable minors from experimental procedures, Bowers wrote: "Ultimately, what terrifies conservatives most is that gender diversity is a force of nature that can no longer be contained by religious conscription or enforcement of a gender binary." Bowers concluded: "Anti-trans legislation needs to be fought with every voice, every thought, every inclination by all who know it. We need to make anti-trans legislation a losing political issue." (Bowers 2023). These statements are social-political advocacy statements and rallying cries, not scientific arguments. They reduce any disagreement or concern regarding the safety and efficacy of GAT for minors to "anti-trans" religious-based bigotry, and they leave no space for those who are concerned that, based on current scientific knowledge, the risks of GAT for minors outweigh their known benefits. In my experience, these statements are sadly indicative of WPATH's primary role as a political and social advocacy organization, not a scientific one.

b. WPATH SOC 8

169. As for WPATH's Standards of Care 8 (SOC 8), these were published Sep. 6, 2022 (Coleman et al., 2022). However, there are multiple serious problems with this document such that any clinician who follows its recommendations puts his or her patients at great risk as I will explain.

170. WPATH has made claims about the nature of evidence in their SOC 8 document. In their FAQ document, they state that "[t]his version [8] of the Standards of Care uses an enhanced evidence-based approach to include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and possible harms of alternative care options." (WPATH FAQ, 2024).

171. The lead author of SOC 8, Eli Coleman, claims, "WPATH followed a rigorous, multi-year process and was based on the best available scientific evidence and weighing all risks and benefits to arrive at the recommendations in our Standards of Care 8 guidelines...WPATH stands behind our process and conclusions." (Bowers, 2023).

172. Admiral Rachel Levine, a highly positioned and influential, politically appointed administrator within HHS, serving as assistant secretary of health, has made numerous statements attesting to the purported validity, importance, and scientific integrity of WPATH's guidelines.

173. With respect to how the SOC 8 was generated, Admiral Levine stated that "[r]ather than relying on a few cherry-picked reports to make a political argument, WPATH assesses the full state of the science and provides substantive, rigorously analyzed, peer-reviewed recommendations to the medical community on how best to care for patients who are transgender or gender non-binary." (Levine, 2022).

174. With respect to the SOC 8's recommendations, Admiral Levine stated that "[t]here is nothing one-sided about their approach." Admiral Levine claimed that: 1) "It is founded on a vast body of medical literature." 2) "It is free of any agenda other than to ensure that medical decisions are informed by science." 3) "This is the way medicine is supposed to be practiced, and it is the way doctors are supposed to care for their patients." (*Id*.)

175. Admiral Levine has stated that "we need to lead with real data and compassion rather than slander and stigmatization" (ADM Rachel Levine, Twitter/X @HHS_ASH Jul 19-2022), and I agree. Ironically, however, Dr Levine has also implied that criticism of GAT is "politicized" and shows "the spirit of intolerance and discrimination," and that "it is unconscionable that evidence-based care is being politicized." (ADM Rachel Levine, Twitter/X @HHS_ASH Feb 24-2022).

176. Additionally, Dr. Levine has made statements seeming to imply that suicides or potential suicides of gender dysphoric youth are somehow related to legitimate criticisms of GAT. Levine stated: "The language of medicine and science is being used to drive people to suicide. The mantle of concern for children is being claimed to destroy children's lives." (ADM Rachel Levine, Twitter/X @HHS_ASH Apr 30-2022).

177. The current president of WPATH, Marci Bowers, stated that any criticism of the SOC 8 is by nature an assault on minority groups, women, religious organizations, and humanity itself, stating: "An attack on trans care is an attack on women. It is an attack on black people,

brown people, and Asian people. It is an attack on Jewish, Muslim, Hindi, Sikh, and true Christian communities. It is an attack on diversity and all of the ideals that diversity holds. It is an attack on us all." (Bowers, 2023).

178. Given that Admiral Levine is a highly influential member of HHS whose opinions and recommendations affect millions of American's lives, and that Admiral Levine has relied on WPATH to form judgements about what constitutes the best treatment for children and adolescents with gender dysphoria, physicians and the public at large should expect that these opinions and recommendations are based on a very high level of intellectual and ethical integrity and a thorough knowledge of the subject matter.

179. Accordingly, I investigated the claims of both WPATH and Dr. Levine based on what is known about the SOC 8 document. I relied on the published SOC 8 document and its correction, as well as the claims and opinions of the creators of WPATH. The ultimate goal for everyone should be to provide minor patients with the best evidence-based care for their health and welfare, both now and into the future.

180. The SOC 8 is a document of consensus produced by a narrow, ideologically homogenous group of experts and stakeholders who have two primary aims: 1) ensure the reimbursement of Gender Affirmative Therapy (GAT) related medical visits, medications, surgeries, and procedures; and 2) protect clinicians and others involved in GAT from liability.

181. As a practicing endocrinologist, I use clinical guidelines to help determine the proper diagnosis and care of individual patients. However, it is incumbent upon me as a physician specialist to assess the validity, evidence base, and methodology used to generate such guidelines.

182. The first concern I had when SOC 8 was published was what methodology did WPATH use to generate the guidelines. What were the specific steps involved taken to produce the recommendations?[17]

[17] I went through an identical process with Endocrine Society guidelines of 2017. My coauthors and I wrote about our serious concerns in a letter to the editor of the Endocrine Society's flagship Journal, JCEM, in 2019. (Laidlaw, Van Meter, et al., 2019).

183. WPATH's Standards of Care 8 document claims that the authors used two types of processes to make recommendations. One was the Delphi technique or method and the second was the GRADE system or method. (Coleman et al, 2022, p. S247) These are two different processes for generating recommendations and are not intended to be used together.

i. Delphi

184. First let's examine the Delphi technique. The Delphi technique is a method of generating recommendations based on expert consensus. This technique was developed in the 1950s by the Rand Corporation to use a panel of experts to "forecast the effect of technology on warfare." (Rand Corporation, 2024). The process involves selecting a group of experts and posing a series of questions. (McGeary, 2009). The experts then submit answers anonymously. The answers are collated and ranked and these statements are voted upon. This process of voting and ranking may go through two to four or more iterations. At that point, a consensus statement is produced based on the highest ranked choice. This technique has also been used in many other disciplines including healthcare but is not without criticism.

185. It is important to understand that this technique is not evidence based, but solely consensus based. Recommendations are generated solely based on expert opinion without evidentiary support. In fact, "[in] health sciences, the Delphi technique is primarily used by researchers when the available knowledge is incomplete or subject to uncertainty and other methods that provide higher levels of evidence cannot be used. The aim is to collect expert-based judgments and often to use them to identify consensus." (Niederberger et al., 2020). Additionally, "[i]n intervention research in health sciences, surveys of experts are considered subordinate to evidence-based methods because they do not take account of any reliable findings on observed cause-effect relationships." (*Id*.)

186. One problem that can occur when employing the Delphi method is selection bias with respect to the composition of expert groups because there is no standard of how to compose an expert group. (*Id*.) It stands to reason that a narrow selection of experts with similar opinions makes for biased recommendations. This is exactly what happened with the WPATH SOC 8's Delphi process. Lead author Eli Coleman stated, "We had 119 experts from around the world" involved in producing SOC 8. (Bowers,

2023). However, all of the expert developers of SOC 8 were members of WPATH. In fact, with respect to the criteria used for the selection of the Co-chairs on the SOC 8 Revision committee and Chapter Leads, one had to be a "[l]ongstanding WPATH Full Member in good standing" and a "[w]ell recognized advocate for WPATH and the SOC." (WPATH Revision Committee, accessed 2024). A chapter Workgroup Member had to be a "WPATH Full Member in good standing." (*Id*.)

187. The Delphi technique has also been criticized from a sociological perspective because it raises "questions about [the recommendations'] validity, the dominance of possible thought collectives, and the reproduction of possible power structures." (Niederberger et al., 2020). Because of a collective group bias, another problem is "possibly failing to take new impetus and scientific findings sufficiently into account" (*Id.*)

188. If WPATH authors were more open to the public, explicitly describing that they used the Delphi technique to gather a consensus within their own narrowly defined group and also admitting that they used the Delphi technique because "the available knowledge is incomplete" and "subject to uncertainty," and "other methods that provide higher levels of evidence" could not be used, then clinicians could use this honest admission to understand they are reading a highly biased document of opinions. WPATH did not do that.

ii. GRADE

189. The SOC 8 developers used a second system for generating recommendations known as GRADE—"Grading of Recommendations, Assessment, Development, and Evaluations." In the GRADE system, a clinical question is asked and then evidence is systematically gathered using a specific method for conducting a systematic literature review. The evidence is then weighed and assigned one of four values: very low, low, moderate, or high. (Guyatt et al., 2011). These values are sometimes represented as +, ++, +++, and ++++, respectively. After the evidence is graded, then a recommendation may be made for or against a particular medical intervention. This is classified as either a "strong" or "weak" recommendation. (*Id*.)

190. The lead author of SOC 8, Eli Coleman stated, "[we] used a consensus-based approach (Delphi) involving all committee members to arrive at our conclusions and then graded the strength of our recommendations."[18] (Bowers, 2023)

191. Coleman and WPATH claim to have used a process adapted from the GRADE framework in SOC 8. (Coleman et al., 2022, s250). But, among other issues, they failed to incorporate the quintessential GRADE component in their final published document, which is to show the graded values pertaining to quality of evidence for each recommendation.

192. This intentional omission of the ranking of the quality of evidence in the final versions of SOC 8 and other failures to use GRADE properly were highlighted in the British Journal of Medicine: "WPATH's recommendations lack a grading system to indicate the quality of the evidence—one of several deficiencies." (Block, 2023). The article goes on to highlight further criticisms by one of the developers of GRADE, Dr. Gordon Guyatt: "Both Guyatt and Helfand noted that a trustworthy guideline would be transparent about all commissioned systematic reviews: how many were done and what the results were. But Helfand remarked that neither was made clear in the WPATH guidelines and also noted several instances in which the strength of evidence presented to justify a recommendation was 'at odds with what their own systematic reviewers found.'" (*Id*.)

193. This pattern of removing crucial aspects of the guidelines and ignoring systematic reviews of evidence because they were detrimental to the advocacy role of WPATH is a pattern in the development of the SOC 8. It shows that the goal of SOC 8 was not to present guidelines with a transparent view of the evidence so that clinicians can make decisions for their patients who have questions about their gender identity; rather, it was a way to ensure medical necessity so that

[18] ""Once the statements passed the Delphi process, chapter members graded each statement using a process adapted from the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework. This a transparent framework for developing and presenting summaries of evidence and provides a systematic approach for making clinical practice recommendations (Guyatt et al., 2011). . . .The statements were classified as:

- Strong recommendations ("we recommend") are for those interventions/therapy/strategies where:
  - the evidence is of high quality. . . .
- Weak recommendations ("we suggest") are for those interventions/therapy/strategies where:
  - there are weaknesses in the evidence base""

(Coleman et al., 2022, s250).

medications and procedures can be paid for and to protect clinicians from liability—as I discuss below.

194. In my opinion, the aberrant use of GRADE could easily confuse users of SOC 8 into believing that the SOC 8 authors made recommendations to patients based on high-quality evidence, when in fact the evidence the quality of evidence was never made known.

195. Dr. Guyatt, the GRADE co-developer, expressly warned against the misuse or modification of GRADE in this way: "Some organizations have used modified versions of the GRADE approach. We recommend against such modifications because the elements of the GRADE process are interlinked because modifications may confuse some users of evidence summaries and guidelines, and because such changes compromise the goal of a single system with which clinicians, policy makers, and patients can become familiar." (Guyatt et al., 2011) (emphasis mine).

196. To conclude this section about methods, I do not believe the GRADE system was used in any meaningful way other than as an attempt to imply that the SOC 8 has strong evidence for many of its recommendations. Had the SOC 8 simply relied on the Delphi method alone, it would be clear that the recommendations were made solely or primarily on the basis of the opinions of WPATH's homogenous group of experts rather than a systematic review of the evidence of outcomes. WPATH evaded that honesty. The end result can easily confuse readers that "strong" recommendations are necessarily linked with high-quality evidence and "weak" recommendations with low quality evidence. And the all-important ranking of the actual evidence is missing from the SOC 8 text, rendering it impossible for clinicians and other users to understand how the SOC 8 arrived at its conclusions. (Coleman et al., 2022, p. S250). In my opinion, this muddled, non-transparent, and sloppy approach to generating recommendations only serves to confuse users of the SOC 8 into thinking that the WPATH recommendations are based on a robust evidentiary foundation when that is not the case.

iii. Ethical Considerations and Fertility

197. While it is self-evident that children and adolescents do not have the maturity,

knowledge, and life experience to truly understand fertility or parenthood, the published SOC 8 pays little attention to this as an ethical concern

198. SOC 8 does not include a chapter specifically on ethics with accompanying ethics statements that had, at minimum, been through their biased Delphi process. The published SOC 8 does have a subsection in the "Adolescents" chapter titled "Ethical and human rights perspectives." However, concern about the ethics of puberty blockers and fertility is nowhere to be found. Rather, there is a focus on how *natural* puberty may have "harmful effects." (Colemen et al., p. S48). This contention about the alleged harmful effects of natural puberty has no accompanying grading of evidence.

199. There is also a statement in the chapter prioritizing autonomy of the young person to receive GAT: "From a human rights perspective, considering gender diversity as a normal and expected variation within the broader diversity of the human experience, it is an adolescent's right to participate in their own decision-making process about their health and lives, including access to gender health services (Amnesty International, 2020)." (*Id*.)

200. There is no grading of evidence for this assertion, and the opinion is not based on a journal of medicine or ethics, but rather a human rights organization's press release about puberty blockers.[19] This statement ignores young people's limited knowledge, judgement, maturity, and life experiences with which to make decisions about impairments to fertility, sexual function and breast feeding that occur with GAT.

201. Yet in an educational session titled "Foundations in Gender Affirming Hormone Therapy: Adults and Adolescents," WPATH member Dr. Daniel Metzger, replied to a question about fertility concerns when blocking puberty at the earliest stage like this:

> I think that's the hardest part of what I do, because, of course, it is not in what is in the mind of a 13-year old, or 15-year old, or even a 17-year old... kids have zero idea about their fertility, right?

[19] The press release is a joint statement of Amnesty International UK and an organization called ""Liberty"" commenting on the UK"s High Court ruling about puberty blockers: ""Joint statement following High Court ruling that children under 16 are unlikely to be able to give informed consent to undergo treatment with puberty-blocking drug."" Amnesty International UK, Dec. 2020, https://www.amnesty.org.uk/press-releases/amnesty-international-uk-and-liberty-joint-statement-puberty-blockers.

(Brock 2024 embedded video, 00:45).

202. This reveals that at least some WPATH members are aware of the ethical problems associated with youth fertility, however these are not sufficiently addressed in SOC 8.

203. With respect to natal females who have puberty blocked, take testosterone, and then attempt fertility by pausing GAT, Dr. Metzger states: "So, you can freeze eggs and then later use them but that's still a very early kind of technology that's quite expensive." (*Id*. at 02:30) With respect to natal females who have puberty blocked, Dr. Metzger states that the closest analogy relates to cancer treatment: "You know, a little bit of what we know is from, like, little girls who get cancer, right? […].I don't, I don't think that lots is known about that still, for a, say a 10-year-old assigned female. I don't think we know." (*Id*. at 02:45)

iv. Bone

1. I have discussed the problems with youths acquiring optimal bone density during natural puberty when progression is blocker by medication and the subsequent increased risk for osteoporosis earlier in my report (see section "Negative Effects of Hypogonadotropic Hypogonadism on Bone Density**"**).

2. Dr. Metzger echoed this problem in the same educational presentation referenced earlier. He said: "Normally puberty is the time of putting the calcium into your piggy bank. This is how I explain it to families. You've got a piggy bank for your calcium and you better get it all in by 25 because at 25 you're going to live off that piggy bank." He continued:

> The puberty blockers slow that calcium accrual back into the bones quite a bit, back to the prepubertal level. We do know that even if you look at people now age 22, if you've done all of this and you've gone off and then you go back on the hormones' that you want to have, you have not caught up by age 22. Which is about the time you need to fill up your piggy bank. This is a concern that not everybody is getting their piggy bank completely filled up with calcium.

(Brock, 2024)

v. SOC 8's Use of Studies Associated with Youth Suicides

204. One study author, WPATH member and President-elect of USPATH[20] Johanna Olson-Kennedy, was referenced nearly a dozen times in the SOC 8 for her work with GAT in adolescents. In an interview with PBS news hour, Olson-Kennedy related that "[w]ithout support and [gender affirmative] treatment,...trans kids are a risk for almost everything: depression, self harm, substance abuse, homelessness, HIV and suicide." (PBS News Hour, 2016) (emphasis mine). Elsewhere, Olson-Kennedy described GAT treatments, including hormones and surgeries, like this: "Many of my patients have described the opportunity [to undergo GAT] to align their physical body with their gender as life-saving." (Olson-Kennedy Expert Affidavit, Loe v. Texas, Para. 61) (emphasis mine). In an expert report she stated, "The denial of gender-affirming care, on the other hand, is harmful to transgender people. It exacerbates their dysphoria and may cause anxiety, depression, and suicidality, among other harms." (Olson-Kennedy report, Van Garderen v. MT, Para. 75) (emphasis mine).

205. I have grave concerns about this author's claims in part because of her unethical study involving adolescents, as young as age 13 and 14, receiving mastectomies for gender dysphoria.[21] Mastectomy surgery is an irreversible procedure after which the patient is unable to regain the ability to breast feed. In my professional opinion, minors lack the maturity, life experience, and capacity of good judgment for truly informed consent for this life altering procedure.

206. My colleague and I wrote a letter to the Inspector General of Health & Human Services in 2019 recommending an investigation of Olson-Kennedy's mastectomy study. Among the many concerns we described, we stated, "it would seem that the authors were anxious to get a study published in the literature in order to insure that surgeons would be reimbursed for the

[20] USPATH Board of Directors, https://www.wpath.org/uspath.

[21] The study is titled ""Chest Reconstruction and Chest Dysphoria in Transmasculine Minors and Young Adults Comparisons of Nonsurgical and Postsurgical Cohorts"" (Olson-Kennedy, 2018). There are a number of serious problems with this study. First, the term "chest dysphoria" is a creation of the study authors and is not found as a diagnosis or even referenced in the DSM-5. Second, the "chest dysphoria scale" is a measuring tool created by the authors, but which the authors state "is not yet validated." (Id., p. 435). Third, the mastectomies were performed on girls as young as 13 and 14 years old, who necessarily lacked the maturity and capacity of good judgment for truly informed consent for this life altering procedure. For this reason, in my professional opinion, the research and surgeries performed were flawed and unethical.

resection of the healthy breasts of minor girls." (A true and correct copy of our November 15, 2019 letter to the Office of Inspector General, U.S. Department of Health & Human Services is attached hereto as **Exhibit 2**) This compulsion to help ensure medical necessity for reimbursements is a theme in the creation of the SOC 8, as I will describe later. Note also that the mastectomy study was published in 2018. The SOC 8's original minimum age for mastectomy (before deleting the age minimums, as I will also later discuss) was 15. So even compared to the majority of experts who developed the SOC 8, Olson-Kennedy was more extreme with respect to being willing to advise performing irreversible surgeries on minors.

207. I am also deeply concerned because of Olson-Kennedy's multi-year, NIH funded study involving youths taking opposite sex hormones. In a 2017 progress report to NIH, Olson-Kennedy disclosed that she and her team of researchers reduced the age-minimum criteria for youths taking opposite sex hormones as part of the study from thirteen to eight. (A true and correct copy of the Impact of Early Medical Treatment in Transgender Youth progress reports is attached hereto as **Exhibit 3**). Reducing the age minimum so that children as young as eight years old could be included in the study to take opposite sex hormones and undergo irreversible bodily changes is an indicator of the extreme nature of Olson-Kennedy's research.

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

In order to completely capture the impact on all youth undergoing treatment with GnRH agonists, recruitment will be expanded to include those youth in Tanner 4 of development. In addition, the minimum age for the cross-sex hormone cohort inclusion criteria was decreased from 13 to 8 to ensure that a potential participant who could be eligible for cross-sex hormones based on Tanner Staging would not be excluded due to age alone. The Principal Investigators assert that this will not impact the data analysis and results of the research study.

(*Id.*, Page 44)

208. Another indicator came in 2023, when, contrary to Olson-Kennedy's claims that GAT is "life-saving," her team disclosed in the New England Journal of Medicine that two deaths by suicide were associated with the study. (Chen at al., 2023).

209. Two preliminary articles about this study are a part of the evidence base of SOC 8.[22] Stunningly, rather than describe important medical information related to these deaths in the

[22] They are referenced in SOC 8 as:

published study so that fatalities could be understood and prevented, the authors chose to conclude that GAT improved psychosocial functioning. (*Id.*)

210. One wonders how this allegedly "lifesaving" treatment can be associated with two deaths in a study population of only a few hundred young people. Nevertheless, an NBC News headline from January 2023 claimed, "Hormone therapy improves mental health for transgender youths, a new study finds." (NBC News, 2023). Medpage Today's headline claimed: "Gender-Affirming Hormones Boost Mental Health for Transgender Youth." (Medpage Today, 2023). It appears that Olson-Kennedy's attempt to "flip the script" has led to confusion in the public by making headlines that high-dose hormones improved overall mental health when two youths actually died.

211. Because of the powerful effects of high doses of opposite sex hormones on the human mind (as seen in studies of anabolic steroid abuse), including by inducing problems with mood disorders and even psychosis, it is of the utmost importance that any deaths that occur in a GAT study receive a thorough medical investigation. (See section II.C.1.b) For example, one should expect to know the age and sex of the patients, blood levels of hormones both preceding and after death, psychotropic medications taken (if any), other psychiatric treatments and hospitalizations, other medical and psychiatric history, and to review autopsy reports.

212. My colleagues and I wrote a letter about this study as well in 2019 to the Office for Human Research Protections of the Department of Health and Human Service. (A true and correct copy of my April 5, 2019 letter to Jerry Menikoff, M.D. with the Kelsey Coalition is attached hereto as **Exhibit 4**). In our letter we concluded, "Because this study poses irreversible medical harms (including infertility) to children, we request an immediate moratorium and investigation." (*Id.*)

Olson-Kennedy, J., Chan, Y.-M., Garofalo, R., Spack, N., Chen, D., Clark, L., Ehrensaft, D., Hidalgo, M., Tishelman, A., & Rosenthal, S. (2019). Impact of early medical treatment for transgender youth: Protocol for the longitudinal, observational Trans Youth Care Study. JMIR Research Protocols, 8(7), e14434. https://doi.org/10. 2196/14434

And Chen, D., Abrams, M., Clark, L., Ehrensaft, D., Tishelman, A. C., Chan, Y.-M., Garofalo, R., Olson-Kennedy, J., Rosenthal, S. M., & Hidalgo, M. A. (2021). Psychosocial characteristics of transgender youth seeking gender-affirming medical treatment: Baseline findings from the trans youth care study. Journal of Adolescent Health, 68(6), 1104–1111. https://doi.org/10.1016/j. jadohealth.2020.07.033.

213. Unfortunately, our concerns were dismissed. In a response letter from Diana W. Bianchi, M.D., Director of the NIH's National Institute of Child Health and Human Development, she wrote: "Notably, these research participants and their parents sought and obtained the hormonal therapies independent of the protocol. Therefore, termination of the protocol would not end the treatments; rather, it would only end the compilation of data needed to advance scientific understanding of the risks and likely outcomes of those treatments." (A true and correct copy of the response to our April 5, 20119 letter is attached hereto as **Exhibit 5**). Furthermore, as part of the rationale for the HHS's decision, Dr. Bianchi looked to the Endocrine Society Guideline (ESG) of 2017 (of which nine out of ten authors of the Endocrine Society Guideline were members of WPATH or worked on WPATH's scientific committees)[23] as supporting their determination not to issue a moratorium. She stated that "[p]hysicians at the funded academic centers follow current guidelines for the therapy of trans gender youth," (*Id*.) and referenced the 2017 ESG as apparently a justification for continuing the unethical study. This was in spite of the fact that the ESG stated in its disclaimer that their "guidelines cannot guarantee any specific outcome, nor do they establish a standard of care." (Hembree et al, 2017, p. 3895).

214. Part of the problem with the response letter from Dr. Bianchi is that she and HHS have wrongly separated the gathering of the study participants' data from the underlying treatments. Dr. Bianchi wrote, "Notably, these research participants and their parents sought and obtained the hormonal therapies independent of the protocol. Therefore, termination of the protocol would not end the treatments; rather, it would only end the compilation of data needed to advance scientific understanding of the risks and likely outcomes of those treatments." (**Exhibit 5**). Dr. Bianchi makes a distinction without a difference. It is simply not possible to gather research data without study participants. The NIH is culpable of funding unethical research by virtue of the fact the research gathers data from the unethical treatments of minors.

215. The first principle of the Nuremberg code, a document pertaining to the ethical

[23] See additional information in my May 19, 2023 report Section III.A.2.

principles of human research, states, "The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision." (Shuster, 1997).

216. I contend that the underlying treatments in Olson-Kennedy's study are unethical due to the minor participants being unable to give proper informed consent or assent for health risks such as infertility and death because of their age and immaturity. The parents also cannot provide informed consent on behalf of their children as they have often been coerced by the fear that their child might be suicidal (as per Olson-Kennedy) without such treatment. Neither the child nor the parents "have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision" because of the dearth of available long-term evidence (or even basic animal studies) with respect to the hormonal and surgical treatments. It follows that if the underlying treatments are unethical, then the gathering of data from such a study is also unethical. Therefore, the NIH has funded and continues to fund unethical research with respect to this study.

217. I remain deeply concerned that high dose hormones may have contributed to the deaths of these two youths. There appears to be an unwillingness on the part of HHS to investigate the ethical and potential legal problems with this study further or to intervene to prevent further medical harms.

218. To summarize, in my opinion, the SOC 8 has relied on unethical research in which permanent harms have occurred to minors who were not of sufficient age to consent or assent to the body and mind-altering medications and medical procedures that are an integral part of GAT. The research, rather than proving with long term data that GAT is safe for minors, instead raises serious concerns about the possibility of lifelong regret due to irreversible procedures, and the

possibility of mental health deterioration and death associated with high dose opposite sex hormones.

vi. Medical Necessity

219. In general, any medication, office visit or surgical procedure in the United States needs to be paid for in some manner, and these costs may be substantial. Payers may include insurance companies, government agencies, individuals, or some combination of the three. Particularly for GAT, medications such as puberty blockers or surgical procedures can be very costly. Insurance companies follow a concept called "medical necessity" to determine if a particular medication or procedure has a sufficient benefit to risk ratio compared to the cost in order to justify their coverage. Government entities make similar evaluations.

220. Generally, to establish medical necessity, there must be sufficient published medical research ensuring scientific validity with respect to safety and efficacy. (Institute of Medicine, 2012) Clinical guidelines may assist insurers and government agencies to know which medications and procedures provide the highest benefit to cost ratio with the minimum risks. As healthcare funds are not infinite, crucial decisions need to be made with respect to coverage.

221. Naturally, the production of clinical guidelines could be slanted and biased in such a way as to convince insurance companies and government entities that particular medications and procedures should be covered. In my opinion, a review of chapter 2 of SOC 8 support this being the case.

222. The published statement reads: "2.1- We recommend health care systems should provide medically necessary gender-affirming health care for transgender and gender diverse people." (Coleman et al., 2023). Note again that, according to WPATH's methods, any statement beginning with "We recommend" is supposed to be backed by strong evidence. However, as in the rest of SOC 8, no grading of evidence was provided. In spite of this reluctance to provide evidence, a fairly comprehensive list of possible procedures and medical treatments for GAT are included in the published chapter: "Medically necessary gender-affirming interventions are discussed in SOC-8. These include but are not limited to":

> hysterectomy +/- bilateral salpingo-oophorectomy; bilateral mastectomy, chest reconstruction or feminizing mammoplasty, nipple resizing or placement of breast prostheses; genital reconstruction, for example, phalloplasty and metoidioplasty, scrotoplasty, and penile and testicular prostheses, penectomy, orchiectomy, vaginoplasty, and vulvoplasty; hair removal from the face, body, and genital areas for gender affirmation or as part of a preoperative preparation process; gender-affirming facial surgery and body contouring; voice therapy and/or surgery; as well as puberty blocking medication and gender-affirming hormones; counseling or psychotherapeutic treatment as appropriate for the patient and based on a review of the patient's individual circumstances and needs.

(Coleman et al., 2022, s18). This blanket statement is obviously unscientific. In one fell swoop, the vast majority of types of procedures and medical treatments in GAT were given a strong recommendation without regard to supporting evidence and without regard for the age of the persons receiving such treatments.

223. This appears to be a blatant attempt to ensure that every type of medication or procedure that WPATH proposed would be covered by private and government health plans or by socialized health systems outside of the United States.

vii. On the Removal of Age Minimums for GAT Treatment for Minors

224. The single most telling act on the part of leadership of the WPATH Standards of Care 8 that shows that prioritizing advocacy efforts with respect to medical necessity, minimizing litigation, and advancing their political cause over ensuring the health and safety of minors was the last-minute decision to remove the age minimums for medications and surgeries for minors receiving GAT.

225. In a correction to the SOC 8, recommendations for minimum age of opposite sex hormones were removed (Correction IJTH, 2022).[24] Nearly all recommendations for minimum age of surgery were also removed, meaning a minor of any age could be referred for nearly any of

[24] The correction notice has since been removed from the International Journal of Transgender Health. (Statement of Removal (2022), International Journal of Transgender Health, 23:sup1, S259, DOI: 10.1080/26895269.2022.2125695.)

the GAT surgeries listed previously (*Id.*)[25]

226. The correction reads: "On page S258, the following text was removed: 'The following are suggested minimal ages when considering the factors unique to the adolescent treatment time frame for gender-affirming medical and surgical treatment for adolescents, who fulfil all of the other criteria listed above. – Hormonal treatment: 14 years – Chest masculinization: 15 years – Breast augmentation, Facial Surgery: 16 years – Metoidioplasty, Orchiectomy, Vaginoplasty, – Hysterectomy, Fronto-orbital remodeling: 17 years – Phalloplasty: 18 years" (WPATH SOC 8 Correction, p. S261).

227. Of great concern is that the minimum age recommendations were deleted in contradiction to the recommendation of their own expert consensus: "On page S66, the following text was removed: 'Age recommendations for irreversible surgical procedures were determined by a review of existing literature and the expert consensus of mental health providers, medical providers, and surgeons highly experienced in providing care to TGD adolescents.'" (WPATH SOC 8 Correction, p. S260) (emphasis mine).

228. Naturally, to remove age limits for hormones and surgeries which have life-altering physical consequences should be done with the primary goal of obtaining the best possible health outcome for each patient. This should also be done with solid research and long-term studies justifying these treatments for young, developing persons.

229. However, WPATH's own statements show that liability and politics were their primary motivations. According to SOC 8 author Dr. Tishleman, the changes were made in order to help ensure that doctors would not be liable for malpractice suits if they deviated from their new standards. (Davis, 2022). Additionally, WPATH's president said that to "propose" surgeries at newly set lower age recommendations would necessitate a "better political climate." (Ghorayshi, 2022).

[25] The authors left one caution about phalloplasty surgery in the published text: ""Given the complexity of phalloplasty, and current high rates of complications in comparison to other gender-affirming surgical treatments, it is not recommended this surgery be considered in youth under 18 at this time."" (Coleman et al., 2022, p. S66)

230. Modifying the SOC 8 to put it in the best possible light belies lead author Eli Coleman's claim that SOC 8 "uses an enhanced evidence-based approach to include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and possible harms of alternative care options." (WPATH FAQ).

231. **viii. WPATH's Chapter on the Eunuch Gender Identity Invalidates Gender Identity as a Biological Property**

232. Another concerning component of SOC 8 is a new chapter regarding eunuchs that gives recommendations for how to induce hypogonadism in men who have the eunuch "gender identity"[26] by either orchiectomy (testicle removal) or chemical castration such as with GnRH analogues (Coleman et al., 2022).[27] The notion that there is a "eunuch gender identity" further invalidates gender identity as a serious biological property of human beings: "Many eunuch individuals see their status as eunuch as their distinct gender identity with no other gender or transgender affiliation." (Coleman et al., 2022, p. S88)

ix. Conclusion about WPATH's SOC 8

233. For at least the reasons above, in my professional opinion the SOC 8 do not represent high-quality, evidence-based medical guidelines, but are instead a prime example of activist-based recommendations for this condition. I believe that WPATH SOC 8 represent a grave and immediate danger to minors, young adults, and adults. Their guidelines should not be followed by any physician, mental health care provider, or other medical professional.

2. Endocrine Society

234. In 2017 the Endocrine Society published its guideline titled the "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical

[26] The notion that there is a ""eunuch gender identity"" further invalidates the gender identity as a serious biological property of human beings: ""Many eunuch individuals see their status as eunuch as their distinct gender identity with no other gender or transgender affiliation"" (Coleman et al., 2022, p. S88).

[27] ""Treatment options for eunuchs to consider include:
- Hormone suppression to explore the effects of androgen deficiency for eunuch individuals wishing to become asexual, nonsexual, or androgynous;
- Orchiectomy [testicle removal] to stop testicular production of testosterone;
- Orchiectomy with or without penectomy to alter their body to match their self-image;
- Orchiectomy followed by hormone replacement with testosterone or estrogen."" (*Id.*)

Practice Guideline". It is notable that the Endocrine Society never claimed that its guideline should be considered a standard of care. In fact, quite the opposite. The Endocrine Society states that its "guidelines cannot guarantee any specific outcome, nor do they establish a standard of care" (Hembree et al, 2017, p. 3895, emphasis added).

235. It is also notable that nine out of ten authors of the Endocrine Society Guideline were members of WPATH or worked on WPATH's scientific committees. According to WPATH's website, seven of those nine had at some time been in WPATH leadership, including the WPATH presidency and board of directors.

236. With respect to the Endocrine Society's guideline, the quality of evidence for the treatment of adolescents is rated "very low-quality evidence" and "low quality evidence". "The quality of evidence for [puberty blocking agents] is noted to be low. In fact, all of the evidence in the guidelines with regard to treating children/adolescents by [gender affirmative therapy] is low to very low because of the absence of proper studies" (Laidlaw et al., 2019).

237. Unlike some other recommendations for adolescent GAT, the Endocrine Society's guideline does not include any grading of the quality of evidence specifically for their justification of laboratory ranges of testosterone or estrogen or for adolescent mastectomy or other surgeries.

238. Endocrinologists William Malone and Paul Hruz and other colleagues have written critically of the Endocrine Society's guideline: "Unlike standards of care, which should be authoritative, unbiased consensus positions designed to produce optimal outcomes, practice guidelines are suggestions or recommendations to improve care that, depending on their sponsor, may be biased. In addition, the ES claim of effectiveness of these interventions is at odds with several systematic reviews, including a recent Cochrane review of evidence, and a now corrected population-based study that found no evidence that hormones or surgery improve long-term psychological well-being. Lastly, the claim of relative safety of these interventions ignores the growing body of evidence of adverse effects on bone growth, cardiovascular health, and fertility, as well as transition regret" (Malone et al., 2021) (footnotes omitted).

239. In June of 2022, the Endocrine Society published "Enhancing the Trustworthiness of the Endocrine Society's Clinical Practice Guidelines" (McCartney et al., 2022). It wrote: "In an effort to enhance the trustworthiness of its clinical practice guidelines, the Endocrine Society has recently adopted new policies and more rigorous methodologies for its guideline program." (Id.) The document relates that in 2019, the ECRI Guidelines Trust "asked the Society for permission

to include its guidelines in the ECRI Guidelines Trust database". However, after an evaluation by ECRI, the guideline related to osteoporosis "was the only guideline for which all recommendations were based on verifiable systematic evidence review with explicit descriptions of search strategy, study selection, and evidence summaries" (Id.). It follows that the recommendations from the ESG 2017 on Gender Dysphoria/Gender Incongruence were not all recommendations "based on verifiable systematic evidence review with explicit descriptions of search strategy, study selection, and evidence summaries." Furthermore, these ESG 2017 were highly subject to conflicts of interest. Nine out of the ten authors were members or worked on the scientific committees of the advocacy group WPATH. Additionally, WPATH was a cosponsoring organization of the 2017 Guideline. The "Enhancing Trustworthiness" article recommends the opposite composition of authors for guidelines: "A majority (>50%) of non-Chair GDP members must be free of relevant C/DOI [conflict/duality of interest]" (McCartney et al., 2022).

240. Further problems with the Endocrine Society's guideline are highlighted in a recent BMJ Investigation article. It reads: "Guyatt, who co-developed GRADE, found 'serious problems' with the Endocrine Society guidelines, noting that the systematic reviews didn't look at the effect of the interventions on gender dysphoria itself, arguably 'the most important outcome.' He also noted that the Endocrine Society had at times paired strong recommendations—phrased as 'we recommend'—with weak evidence. In the adolescent section, the weaker phrasing 'we suggest' is used for pubertal hormone suppression when children 'first exhibit physical changes of puberty'; however, the stronger phrasing is used to 'recommend' GnRHa treatment. 'GRADE discourages strong recommendations with low or very low-quality evidence except under very specific circumstances,' Guyatt told the BMJ. Those exceptions are 'very few and far between'" (Block, 2023).

241. It is clear that with respect to the subject of gender dysphoria, the Endocrine Society has acted as a vassal organization of WPATH's social-political advocacy group rather than an independent medical society generating its own scientific opinions. In my opinion, the Endocrine Society's guidelines do not provide a standard of care that any physician should follow.

B. Flawed Studies Based on the Problematic 2015 US Transgender Survey

242. There is much additional evidence that questions the long-term benefits of opposite sex hormones and gender reassignment surgery and in fact suggests serious harms.

243. D'Angelo et al. have written about the 2015 USTS survey as part of the criticism of another flawed study in the journal Pediatrics by Jack Turban in 2020 titled "Pubertal Suppression for Transgender Youth and Risk of Suicidal Ideation" (Turban, 2020). They write in their critique of the USTS that it is "a convenience sampling, a methodology which generates low-quality, unreliable data. Specifically, the participants were recruited through transgender advocacy organizations and subjects were asked to 'pledge' to promote the survey among friends and family. This recruiting method yielded a large but highly skewed sample…Their analysis is compromised by serious methodological flaws, including the use of a biased data sample, reliance on survey questions with poor validity, and the omission of a key control variable, namely subjects' baseline mental health status" (D'Angelo et al., 2021) (footnotes omitted). They also state that "[s]tigmatizing non-'affirmative' psychotherapy for GD [gender dysphoria] as 'conversion' will reduce access to treatment alternatives for patients seeking non-biomedical solutions to their distress") (Id.).

244. Other published studies of GAT have been shown to have serious errors. For example, a major correction was issued by the American Journal of Psychiatry. The authors and editors of a 2020 study, titled "Reduction in mental health treatment utilization among transgender individuals after gender-affirming surgeries: a total population study" (Bränström study, 2020) retracted their original primary conclusion. Letters to the editor by twelve authors including myself led to a reanalysis of the data and a corrected conclusion stating that in fact the data showed no improvement in mental health for transgender identified individuals after surgical treatment nor was there improvement with opposite sex hormones ("Correction", 2020; Van Mol et al., 2020).

245. The initial reports of this study claimed that the authors found treatment benefits with surgery, and this was shared widely in the media. For example, ABC News posted an article titled "Transgender surgery linked with better long-term mental health, study shows" (Weitzer, 2019). An NBC news/Reuters headline reads: "Sex-reassignment surgery yields long-term mental health benefits, study finds" (Reuters, 2019).

246. However, after twelve authors from around the world (including our team) investigated the study in detail, a number of serious errors were exposed leading to a retraction (Kalin, 2020; Anckarsäter et al., 2020).

247. In our letter to the editor, which I co-wrote with former Chairman of Psychiatry at Johns Hopkins Medical School, Paul McHugh, MD, we noted key missing evidence in the original

Branstrom report when compared to the previous body of knowledge yielded from the Swedish Dhejne study. We wrote that "[t]he study supports only weak conclusions about psychiatric medication usage and nothing decisive about suicidality. In overlooking so much available data, this study lacks the evidence to support its pro gender-affirmation surgery conclusion" (Van Mol, Laidlaw, et al., 2020).

248. In another letter, Professor Mikael Landen wrote that "the authors miss the one conclusion that can be drawn: that the perioperative transition period seems to be associated with high risk for suicide attempt. Future research should use properly designed observational studies to answer the important question as to whether gender-affirming treatment affects psychiatric outcomes" (Landen, 2020).

249. In another letter to the editor, psychiatrist David Curtis noted that "[t]he study confirms the strong association between psychiatric morbidity and the experience of incongruity between gender identity and biological sex. However, the Branstrom study does not demonstrate that either hormonal treatment or surgery has any effect on this morbidity. It seems that the main message of this article is that the incidence of mental health problems and suicide attempts is especially high in the year after the completion of gender-affirming surgery" (Curtis, 2020).

250. In yet another critical letter, Dr. Agnes Wold stated that "[w]hether these factors involve a causal relationship (i.e., that surgery actually worsens the poor mental health in individuals with gender dysphoria) cannot be determined from such a study. Nevertheless, the data presented in the article do not support the conclusion that such surgery is beneficial to mental health in individuals with gender dysphoria" (Wold, 2020).

D. High Rates of Completed Suicide and Psychiatric Complications in GAT

251. Dr. Ettner stated that "[d]epression, anxiety, suicidality and self-harm are often significantly reduced, or entirely eliminated [by GAT]." (emphasis mine) (Ettner decl, par 43) She also references a dated 2001 study claiming: "'The vast majority of studies addressing outcome have provided convincing evidence for the benefit of [gender-affirming] surgery in carefully selected cases.' Landen (2001)." She also claims that "abrupt withdrawal of hormones or lack of initiation of hormone therapy" may lead to suicidality. (Ettner decl., par 62)

252. However the data tell a different story. The most comprehensive study of GAT of its kind is from Sweden in 2011[28]. The authors examined data over a 30-year time period (Dhejne, 2011). The Dhejne team made extensive use of numerous Swedish database registries and examined data from 324 patients in Sweden over 30 years who had taken opposite sex hormones and had undergone sex reassignment surgery. They used population controls matched by birth year, birth sex, and reassigned sex. When followed out beyond ten years, the sex-reassigned group had nineteen times the rate of completed suicides and nearly three times the rate of all-cause mortality and inpatient psychiatric care compared to the general population of Sweden.

253. The study published by Chen and Olson-Kennedy et al. in 2023 confirms the inherent danger of gender affirmative therapy found in the Dhejne study. The New England Journal of Medicine published "Psychosocial Functioning in Transgender Youth after 2 Years of Hormones," for which Dr. Johanna Olson-Kennedy is the principal investigator (Chen, Olson-Kennedy, et al., 2023). This arm of her study included 315 adolescents aged 12 to 20 years old who were taking high dose hormones of the opposite sex. The study was not randomized and had no control group. The authors report that 2 out 315 subjects died by suicide. The authors also report "The most common adverse event was suicidal ideation" in 11 subjects.

254. The death by suicide of 2 out of 315 subjects equates to approximately 317 suicide deaths per 100,000 patient-years. If we compare this figure to that of the UK's largest gender identity service, Tavistock, the "annual suicide rate is calculated as 13 per 100,000" patient-years (Biggs, 2021). The death-by-suicide rate was approximately 24 times higher in Dr. Olson-Kennedy's study compared to the much larger Tavistock Clinic. In fact, Professor Biggs reports that two of the four suicide deaths from the Tavistock data were of patients who were on the waiting list and "would not have obtained treatment" (Id.). This strongly suggests that the use of high dose opposite sex hormones in Dr. Olson-Kennedy's study was associated with a much higher death rate. NIH produced the consent forms related to this study pursuant to a FOIA request my colleague submitted. I have reviewed them and provided them to counsel for the Intervenor-Defendants. Unfortunately, of the many side effects of hormone therapy listed on the study's consent forms, death by suicide (or by any cause) is not listed and was not disclosed to participants.

[28] Dr. Ettner failed to cite this important study from Sweden published in 2011. Instead she cited an earlier less comprehensive study from Sweden published in 2001.

255. Unfortunately, unlike the Dhejne study, the Olson-Kennedy study provides little other useful data about outcomes such as psychiatric hospitalizations, suicide attempts, or rates of comorbid psychiatric illness. These facts would be useful to know to determine how high-dose opposite hormones and gender affirmative therapy affect overall health and their association with death by suicide. All of the data collected to date in Dr. Olson-Kennedy's publicly funded study "The Impact of Early Medical Treatment in Transgender Youth" should be released to the public so that other researchers and clinicians can determine how puberty blockers, opposite sex hormones, and mastectomy surgeries affect adolescent physical and mental health.

256. While it is true that patients suffering from gender dysphoria have higher rates of suicidal ideation and completed suicide than the general population, studies have not shown that providing hormones reduces rates of suicide, and in fact those interventions may be associated with increased rates.

E. An Increase in Cases of Gender Dysphoria

257. Gender Dysphoria has been a relatively rare condition in children and adolescents. However there have been very significant increases in referrals for this condition noted around the globe.

258. For example, in the UK, "The number of referrals to GIDS [Gender Identity Development Service] has increased very significantly in recent years. In 2009, 97 children and young people were referred. In 2018 that number was 2519" (Bell v Tavistock Judgment, 2020). There is evidence that this increase may be in part due to social contagion and fueled by social media/internet use (Littman, 2018).

259. The French National Academy of Medicine wrote recently: "Parents addressing their children's questions about transgender identity or associated distress should remain vigilant regarding the addictive role of excessive engagement with social media, which is both harmful to the psychological development of young people and is responsible for a very significant part of the growing sense of gender incongruence" (SEGM, 2022).

260. In "a study of the Finnish gender identity service, '75% of adolescents [assessed] had been or were currently undergoing child and adolescent psychiatric treatment for reasons other than gender dysphoria' (Kaltiala-Heino, 2015). In fact, '68% had their first contact with psychiatric services due to other reasons than gender identity issues.' The same study also showed that 26% percent had an autistic spectrum disorder and that a disproportionate number of females (87%)

were presenting to the gender clinics compared to the past" (Laidlaw in gdworkinggroup.org, 2018).

F. Desistance

261. Desistance is a term indicating that the child, adolescent, or adult who initially presented with gender incongruence has come to experience a realignment of their internal sense of gender and their physical body. "Children with [gender dysphoria] will outgrow this condition in 61% to 98% of cases by adulthood. There is currently no way to predict who will desist and who will remain dysphoric" (Laidlaw et al., 2019; Ristori & Steensma, 2016).

262. Because there is no physical marker to diagnose gender dysphoria, and because it is not possible to predict which child or adolescent will desist, it is not possible to know which young person will remain transgender identified as adults. Also, because the rate of desistance is so high, gender affirmative therapy will necessarily cause serious and irreversible harm to many children and adolescents who would naturally outgrow the condition if not affirmed.

263. Puberty, which pertains to the physical development of the reproductive tract, breasts, and associated secondary sex characteristics, can begin as early as age 8 in girls and age 9 in boys. The studies which have examined desistance involved adolescents and children aged twelve and under. For example, table 1 in Ristori and Steensma 2016 shows multiple studies involving minors. For the three most recent—Singh (2012), Wallien & Cohen-Kettenis (2008), and Drummond et al. (2008)—these involved age ranges from 3 to 12 years old[29]. The desistance rate varied from 61 to 88%. Since the upper age was twelve this would include children in the age range of 8-12 years old, many of whom were already adolescents going through puberty based on

[29] "This study provided information on the natural histories of 25 girls with gender identity disorder (GID). Standardized assessment data in childhood (mean age, 8.88 years; range, 3-12 years)" (Drummond et al., 2008). "We studied 77 children who had been referred in childhood to our clinic because of gender dysphoria (59 boys, 18 girls; mean age 8.4 years, age range 5-12 years)" (Wallien et al., 2008). "Standardized assessment data in childhood (mean age, 7.49 years; range, 3–12 years) and at follow-up (mean age, 20.58 years; range, 13–39 years) were used to evaluate gender identity and sexual orientation outcome. At follow-up, 17 participants (12.2%) were judged to have persistent gender dysphoria" (Singh, 2012).

a knowledge of the ages of initiation of puberty and were therefore not pre-pubertal.[30] Therefore we can see that a high proportion of adolescents do in fact desist.

G. Mastectomy Surgery for Minors

264. Any serious look at long-term effects of surgical treatment would follow subjects out at least ten years. For example, a study was published examining patients who had mild calcium disorders due to a gland called the parathyroid. They compared a group of patients who had surgical removal of the parathyroid to a control group who had not. They examined data ten years after surgery was completed and concluded that parathyroid surgery in this group "did not appear to reduce morbidity or mortality" in that patient group (Pretorius, 2022).

265. To my knowledge there exists no comparable studies of minors with gender dysphoria comparing those who had mastectomy surgery to a control group who had not. There are also no known studies of minors followed for 10 years or more to determine the long-term risks and benefits of mastectomy for gender dysphoria.

266. Good quality studies specifically showing that mastectomy surgery is safe, effective, and optimal for treating minors with gender dysphoria do not exist. For example, there is a study titled "Chest Reconstruction and Chest Dysphoria in Transmasculine Minors and Young Adults Comparisons of Nonsurgical and Postsurgical Cohorts" (Olson-Kennedy, 2018). The study authors conclude that "[c]hest dysphoria was high among presurgical transmasculine youth, and surgical intervention positively affected both minors and young adults." However, there are a number of problems with this study. First, the term "chest dysphoria" is a creation of the study authors and is not found as a diagnosis or even referenced in the DSM-5. Second the "chest dysphoria scale" is a measuring tool created by the authors, but which the authors state "is not yet validated." (*Id*., p. 435) Third, the mastectomies were performed on girls as young as 13 and 14 years old and who thereby lacked the maturity and capacity of good judgment for truly informed consent for this life altering procedure. For this reason, in my professional opinion, the research and surgeries performed were flawed and unethical.

267. There exists another poorly designed study which suffers from similar methodological and ethical problems as the Olson-Kennedy study. A 2021 study published in

[30] To my knowledge the desistance literature does not examine Tanner stages of puberty as part of their studies. However, one can infer based on the ages that many children had at least begun puberty (Tanner stage 2) or were at a more advanced stage of puberty.

Pediatrics examined females aged 13-21 recruited from a gender clinic. Thirty young females had mastectomy procedures and sixteen had not. The average age at surgery was 16.4 years (Mehringer, 2021). The follow up time after surgery was only 19 months and no data is provided or analyzed about key psychiatric information such as comorbid psychological illnesses, self-harming behaviors, psychiatric hospitalizations, psychiatric medication use, or suicide attempts.

268. Information returned from the study surveys were all qualitative and included responses such as "[My chest dysphoria] made me feel like shit, honestly. It made me suicidal. I would have breakdowns". Another respondent stated, "I've been suicidal quite a few times over just looking at myself in the mirror and seeing [my chest]. That's not something that I should have been born with" (Mehringer, 2021). The omission of psychiatric data is a major flaw in the study and also irresponsible given the obviously dangerous psychological states that some of these young people were in.

269. Since such a high proportion of subjects were using testosterone (83%), some of the responses could be attributed to adverse effects of testosterone. For example, as related earlier, high dose testosterone can manifest in irritability and aggressiveness. One study subject responded, "I get tingly and stuff and it kind of makes me want to punch something" (Mehringer, 2022).

270. The testosterone labeling also indicates nausea and depression as adverse reactions which are described by another study subject "There's a feeling of hopelessness, of desperation, of—almost makes me feel physically sick" (Actavis Pharma, Inc., 2018; Mehringer, 2022).

271. The study appears to have been designed, at least in part, to justify insurance companies paying for mastectomy procedure for minors with GD, even though they have provided no long-term statistical evidence of benefit: "These findings...underscore the importance of insurance coverage not being restricted by age" (Mehrniger, 2021). This also appears to be part of the aim of the flawed Olson-Kennedy study, which stated that "changes in clinical practice and in insurance plans' requirements for youth with gender dysphoria who are seeking surgery seem essential" (Olson-Kennedy, 2018). So these two studies, rather than being a thorough examination of the psychological and physical risks and benefits of mastectomy surgery over the long-term appear instead to exist, at least in part, to validate the need for insurance companies to insure the costs of these dubious procedures for minors.

H. Centers for Medicare and Medicaid Services

272. The Centers for Medicare and Medicaid Services ("CMS") has found "inconclusive" clinical evidence regarding gender reassignment surgery. Specifically, the CMS Decision Memo for Gender Dysphoria and Gender Reassignment Surgery (CAG-00446N) (June 19, 2019) states: "The Centers for Medicare & Medicaid Services (CMS) is not issuing a National Coverage Determination (NCD) at this time on gender reassignment surgery for Medicare beneficiaries with gender dysphoria because the clinical evidence is inconclusive for the Medicare population" (emphasis mine) (CMS.gov, 2016).

I. Nations and States Question and Reverse Course on GAT

273. Numerous nations are questioning and reversing course on the WPATH/Endocrine Society's low quality gender affirmative therapy guidelines. For example, in the *Bell v. Tavistock* Judgment in the UK, regarding puberty blockers in GAT, the court concluded that "there is real uncertainty over the short and long-term consequences of the treatment with very limited evidence as to its efficacy, or indeed quite what it is seeking to achieve. This means it is, in our view, properly described as experimental treatment" (*Bell v. Tavistock* Judgment, 2020, emphasis added). The case was appealed and although the medical decision making was returned to clinicians (rather than the courts), it was noted that great pains should be taken to ensure that the child and parents are properly informed before embarking on such treatments.

274. In the bulletin of the Royal College of Psychiatrists in 2021, in a reevaluation of the evidence, Griffin and co-authors write, "As there is evidence that many psychiatric disorders persist despite positive affirmation and medical transition, it is puzzling why transition would come to be seen as a key goal rather than other outcomes, such as improved quality of life and reduced morbidity. When the phenomena related to identity disorders and the evidence base are uncertain, it might be wiser for the profession to admit the uncertainties. Taking a supportive, exploratory approach with gender-questioning patients should not be considered conversion therapy" (Griffin et al., 2021).

275. In 2020, Finland recognized that "[r]esearch data on the treatment of dysphoria due to gender identity conflicts in minors is limited," and recommended prioritizing psychotherapy for gender dysphoria and mental health comorbidities over medical gender affirmation (Council for Choices in Healthcare in Finland, 2020). Additionally, "[s]urgical treatments are not part of the treatment methods for dysphoria caused by gender-related conflicts in minors".

276. In 2021, Sweden's largest adolescent gender clinic announced that it would no longer prescribe puberty blockers or cross-sex hormones to youth under 18 years outside clinical trials (SEGM, 2021). "In December 2019, the SBU (Swedish Agency for Health Technology Assessment and Assessment of Social Services) published an overview of the knowledge base which 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. These treatments are potentially fraught with extensive and irreversible adverse consequences such as cardiovascular disease, osteoporosis, infertility, increased cancer risk, and thrombosis. This makes it challenging to assess the risk / benefit for the individual patient, and even more challenging for the minors or their guardians to be in a position of an informed stance regarding these treatments" (Gauffen and Norgren, 2021).

277. In the nation of Norway, a report from the Norwegian Healthcare Investigation Board (Ukom) was released in March of this year. The report found "there is insufficient evidence for the use of puberty blockers and cross sex hormone treatments in young people, especially for teenagers who are increasingly seeking health services and being referred to specialist healthcare. Ukom defines such treatments as utprøvende behandling, or 'treatments under trial,' said Moen" (Block, "Norway", 2023).

278. Dr Hilary Cass "was appointed by NHS England and NHS Improvement to chair the Independent Review of Gender Identity Services for children and young people in late 2020" (The Cass Review website, 2022). In her interim report dated February 2022, it states that "[e]vidence on the appropriate management of children and young people with gender incongruence and dysphoria is inconclusive both nationally and internationally" (Cass, 2022). This led to the shutting down of their Tavistock child gender identity clinic.

279. In April 2024, the "Independent review of gender identity services for children and young people: Final report", commissioned by NHS England, was published. With respect to comorbid psychological morbidities and distress in gender dysphoria, they recommend that "[s]tandard evidence based psychological and psychopharmacological treatment approaches should be used to support the management of the associated distress and cooccurring conditions" (Cass, 2024, p. 31). With respect to puberty blocking medication they opine that "[t]he rationale for early puberty suppression remains unclear, with weak evidence regarding the impact on gender dysphoria, mental or psychosocial health. The effect on cognitive and psychosexual development remains unknown." (Cass Final Report Web Page, 2024) With regards to opposite sex hormones

for the treatment of youth gender dysphoria they state that "[t]he use of masculinising / feminising hormones in those under the age of 18 also presents many unknowns...The lack of long-term follow-up data on those commencing treatment at an earlier age means we have inadequate information about the range of outcomes for this group." (Id) The final Cass report leaves unchanged the recommendation that surgical treatments for gender dysphoria are reserved for those eighteen years of age or older (Cass, 2024, p. 166).

280. These recent decisions by the medical authorities of other nations demonstrate that a number have reversed course and reduced or eliminated their reliance on the low-quality gender affirmative therapy guidelines put forth by WPATH and the Endocrine Society.

VI. Regarding the Tapering and Cessation of GAT Hormonal Treatments as a Result of HB 668

281. Dr. Ettner makes a number of claims about hormone therapy though she is not an endocrinologist. As a psychologist, she cannot diagnose endocrine disorders nor can she prescribe hormonal treatments. Dr. Ettner states that individuals who abruptly stop gender affirming treatment without appropriate titration will suffer "severe physiologic consequences" (Ettner decl., par 60).

282. It is true that there are certain endocrine conditions in which treatment with hormones is essential, and the withholding of such treatment can result in death due to resulting physiologic derangements. Testosterone and estrogen deficiency conditions are not those.

283. For example adrenal insufficiency is a condition in which the adrenal glands cannot make adequate levels of cortisol. If the patient is not treated with corticosteroid hormones, it can result in adrenal crisis which can manifest with hypotension (low blood pressure), anorexia, vomiting, fever, and confusion. Adrenal crisis is a medical emergency and is treated by fluid resuscitation, administration of corticosteroid therapy and other measures to balance the body's systems. Untreated adrenal crisis can lead to the death of the patient. I have diagnosed, treated and continue to treat a number of people with adrenal insufficiency.

284. Another example is untreated severe hypothyroidism. This is a condition of low to absent thyroid hormone. This can lead to a condition called myxedema coma which is a condition of slowed functioning of multiple organs. Symptoms can include confusion and changes in mental status, hypothermia, hypotension, bradycardia (slow heart rate), and other metabolic disorders.

This is a medical emergency and, left untreated this condition has a high probability of death. I have diagnosed and treated or consulted on a number of patients with myxedema coma.

285. The insulin deficiency of type 1 diabetes (discussed earlier) can lead to the medical emergency of diabetic ketoacidosis and eventual death if not treated by insulin therapy. I treat many people with type 1 diabetes.

286. What I have described are very obvious "severe physiologic consequences" of untreated conditions of very low or absent hormones, specifically cortisol, thyroid hormone, and insulin. By contrast Dr. Ettner does not and cannot describe similar situations caused by conditions of low testosterone or low estrogen (both collectively known as hypogonadism) leading to medical emergencies because of physiologic abnormalities. The reason is simple, because such urgencies, emergencies and near-term fatal consequences from physiologic changes due to hypogonadism do not exist.

287. Furthermore, Dr. Ettner makes the claim that "[a]s cortisol (the body's 'stress hormone') rises with normal aging, the ratio of dehydroepiandrosterone ('DHEA,' a precursor hormone involved in the production of sex hormones—testosterone and estrogen—which decreases with normal aging) to cortisol is affected, which acts to alter brain chemistry and intensify gender dysphoria." (Ettner, par 56) However the psychologist provides no evidence to back up her hormonal hypothesis that alterations in cortisol levels directly affect gender dysphoria.

288. Dr. Ettner also claims that "[i]n addition to the risks outlined above, the potential risks of harm are more severe here than in most other cases because Idaho's law contemplates cutting prisoners off of treatment regardless of medical need", and she goes on to describe natal males who have had an orchiectomy (removal of the testicles) being denied treatment for hypogonadism. (Ettner decl., par 60).

289. However, the law does not prohibit hormone therapy for patients with hypogonadism. For example, natal males who suffer from hypogonadism after discontinuing estrogen can opt to be treated by the standard treatment for natal male hypogonadism which is testosterone. Likewise, premenopausal natal females who suffer from hypogonadism after discontinuing testosterone can be treated by the standard treatment of estrogen replacement, typically with progesterone, if the patient has an intact uterus.[31]

[31] Menopausal natal females may or may not choose to take similar hormone replacement depending on their symptoms and cardiac and breast cancer risk profiles.

290. Dr. Ettner goes on to claim severe risks for "individuals abruptly losing care without appropriate titration causing severe physiological consequences." (Id.) However House Bill 668 does not call for an abrupt cessation of treatment, rather the law allows for patients to be gradually titrated down from high doses of opposite sex hormones.

291. For example, a natal female patient is taking supraphysiologic (high dose) testosterone in the form of an intramuscular injection of 200 mg of testosterone every 2 weeks. This dose may be gradually tapered down by prison physicians by 25 mg every 2 weeks. After about 16 weeks of tapering down, the patient's testosterone levels will very likely be much closer to the normal reference range for natal females. If the patient develops symptoms of hypogonadism and chooses to be treated by hormone replacement with estrogen and progesterone after consultation with a prison physician, this is perfectly acceptable according to the law.

292. Likewise, a natal male patient is taking supraphysiologic doses of estradiol (a type of estrogen) in the form of tablets amounting to 8 mg per day. This dose may be gradually tapered down by prison physicians by 1 mg every 2 weeks. After about 16 weeks of tapering down, the patient's testosterone will very likely be much closer to the normal reference range for natal males. If the patient develops symptoms of hypogonadism and chooses to be treated by hormone replacement with testosterone after consultation with a prison physician, this is perfectly acceptable according to the law.

293. Dr. Ettner describes potential problems with discontinuing spironolactone. Spironolactone is a diuretic medication which has dual effects of lowering blood pressure and also blocking testosterone receptors. As a psychologist, Dr. Ettner cannot prescribe spironolactone. I do prescribe spironolactone and have many patients taking this medication. Dr. Ettner states that "abruptly terminating [spironolactone] treatment can cause a patient's blood pressure to spike, increasing a person's risk of heart attack or stroke." (Ettner, par 62). Again, the law does not prevent patient's spironolactone being tapered over time with monitoring. In truth Dr. Ettner greatly exaggerates the risks of discontinuing spironolactone if a patient is taking it solely for the purpose of its testosterone blocking properties.

294. Puberty blocking medications can be safely discontinued without a taper as it can take 6-18 months for the pituitary to recover normal function after discontinuation Patients will need to be monitored to ensure their pituitary-gonadal signaling system has not been permanently

damaged because of this medication. These patients may also be treated for hypogonadism at the discretion of prison physicians.

295. As to the various psychological changes that Dr. Ettner describes as potential occurrences after discontinuation of high dose opposite sex hormones, these are best addressed by prison psychiatrists, psychologists, and therapists. As stated previously, transgender identifying patients have high rates of comorbid psychiatric conditions and these will require monitoring and adequate care by competent mental health professionals by standard methods.[32]

VII. Conclusion

296. The gender affirmative therapy model espoused by WPATH and the Endocrine Society suffers from serious deficiencies in logic and lacks scientific foundation. The deep error hidden in this model is that one cannot in fact change sex. One cannot acquire the deep characteristics of biological sex in order to gain the complete sexual and reproductive functions of the opposite sex. This is not technologically possible.

297. Children and adolescents are of such immature minds that they are likely to believe that it is possible. In fact they may come to believe that their inherent, biologically necessary puberty is "terrifying" or needs to be stopped. Social transition serves to convince the child or adolescent that they can be the opposite sex. Puberty blockers sustain this state of mind by retaining a childlike state with respect to the genitalia and body habitus. High dose opposite sex hormones then cause medical conditions such as hirsutism and irreversible damage to the vocal cords in females and gynecomastia in males. These conditions serve to convince the young person that they are going through puberty of the opposite sex when in fact they are not developing sexually and are likely infertile.

298. There are known risks from GAT for both adults and minors, some of which I have described above, including cardiovascular disease, cancer, deficiencies in ultimate bone density, harms to sexual function, infertility, and for some permanent sterility. The child or adolescent cannot consent (or assent) to these harms when they are not mature enough to fully comprehend what they mean. Long-term studies regarding the treatment effects specifically for minors with

[32] WPATH's SOC 8 and the ESG are also not standards of care for treatments of comorbid psychological disorders that often accompany gender dysphoria.

hormones and surgeries, using randomized controlled studies or even proper observational studies do not exist.

299. For the reasons set forth above, in my professional opinion as an endocrinologist, no child or adolescent should receive puberty blockers to block normal puberty, nor is it healthy minors or adults to receive supraphysiologic doses of opposite sex hormones to attempt to alter secondary sex characteristics, nor is it healthy for them to have surgeries to remove or alter the breasts, genitalia or reproductive tracts as part of GAT. In fact, all of these interventions harm people's health. There exists insufficient evidence of benefit of GAT, but serious concerns for risk of harm. Persons affected by the law can still be treated by standard medical and psychological interventions. Therefore, I believe that Idaho's House Bill 668 is based on sound medical principles for the protection of human persons.

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References

Actavis Pharma, Inc. Testosterone Cypionate injection. Actavis Pharma, Inc., 2018. Accessed May 17, 2023 via https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d7b57b68-dca6-4df2-b3f2-7017d7b69f17&msclkid=4ed2db18cd5411ecba911bd6e4bded62

Alberts B, Johnson A, Lewis J, et al. "Sperm" in Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002.

Almazan AN, Keuroghlian AS. "Association Between Gender-Affirming Surgeries and Mental Health Outcomes". JAMA Surgery 2021; 156(7): 611–618.

Alzahrani T, Nguyen T, Ryan A, et al. "Cardiovascular disease risk factors and myocardial infarction in the transgender population". Circ Cardiovasc Qual Outcomes. 2019;12(4):e005597

The American Cancer Society medical and editorial team. "Mastectomy". American Cancer Society. https://www.cancer.org/cancer/breastcancer/treatment/surgery-for-breast-cancer/mastectomy.html accessed 06/24/22

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed., text rev.) 2022. https://doi.org/10.1176/appi.books.9780890425787

Amnesty International. (2020). Amnesty International UK and Liberty joint statement on puberty blockers. https://www.amnesty.org.uk/press-releases/amnesty-international-uk-and-liberty-joint-statement-puberty-blockers

Anckarsäter, H., (MD, Ph.D.) and Gillberg, C., (M.D., Ph.D.) "Methodological Shortcomings Undercut Statement in Support of Gender-Affirming Surgery". Am J Psychiatry 2020; 177:764–765; doi: 10.1176/appi.ajp.2020.19111117.

Anderson K, Krakowsky Y, Potter E, Hudson J, Cox AR. Adult transgender care: A review for urologists. Can Urol Assoc J. 2021 Oct;15(10):345-352. doi: 10.5489/cuaj.6949. PMID: 33750518; PMCID: PMC8525536.

Apridonidze T, Essah PA, Iuorno MJ, Nestler JE. "Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome". J Clin Endocrinol Metab. 2005;90(4):1929. Epub 2004 Dec 28.

Arain, et al. Neuropsychiatric Disease and Treatment. "Maturation of the adolescent brain". Neuropsychiatric Disease and Treatment. 2013:9 449–461

Baldassarre M, Giannone FA, Foschini MP, Battaglia C, Busacchi P, Venturoli S, Meriggiola MC. Effects of long-term high dose testosterone administration on vaginal epithelium structure and estrogen receptor-a and -ß expression of young women. Int J Impot Res. 2013 Sep;25(5):172-7. doi: 10.1038/ijir.2013.9. Epub 2013 Apr 4. PMID: 23552580.

Banikarim, C. "Primary Dysmneorrhea in Adolescents". UpToDate. Feb 10, 2021.

Barus R, Bergeron S, Chen Y, Gautier S. Sex differences: From preclinical pharmacology to clinical pharmacology. Therapie. 2023 Mar-Apr;78(2):189-194. doi: 10.1016/j.therap.2022.10.005. Epub 2022 Oct 6. PMID: 36302696.

Bazelon E. "The Battle Over Gender Therapy". The New York Times Magazine. June 15, 2022.

Bentler SE, Liu L, Obrizan M, Cook EA, Wright KB, Geweke JF, Chrischilles EA, Pavlik CE, Wallace RB, Ohsfeldt RL, Jones MP, Rosenthal GE, Wolinsky FD "The aftermath of hip fracture: discharge placement, functional status change, and mortality." Am J Epidemiol. 2009;170(10):1290. Epub 2009 Oct 4.

Bell & Mrs A v The Tavistock And Portman NHS Foundation Trust. Approved Judgment.[2020] EWHC 3274 (Admin) (01 December 2020). https://www.judiciary.uk/wp-content/uploads/2020/12/Bell-v-Tavistock-Judgment.pdf
Bell & Mrs A v The Tavistock And Portman NHS Foundation Trust. Appeal No. C1/2020/2142 (17 September 2021).

Bentler SE, Liu L, Obrizan M, Cook EA, Wright KB, Geweke JF, Chrischilles EA, Pavlik CE, Wallace RB, Ohsfeldt RL, Jones MP, Rosenthal GE, Wolinsky FD "The aftermath of hip fracture: discharge placement, functional status change, and mortality." Am J Epidemiol. 2009;170(10):1290. Epub 2009 Oct 4.

Biggs M. Suicide by Clinic-Referred Transgender Adolescents in the United Kingdom. Arch Sex Behav. 2022 Feb;51(2):685-690. doi: 10.1007/s10508-022-02287-7. Epub 2022 Jan 18. PMID: 35043256; PMCID: PMC8888486.

Block J. Gender dysphoria in young people is rising-and so is professional disagreement. BMJ. 2023 Feb 23;380:p382. doi: 10.1136/bmj.p382.

Block J. Norway's guidance on paediatric gender treatment is unsafe, says review. BMJ. 2023 Mar 23;380:697. doi: 10.1136/bmj.p697.

Bouraïma H, Lireux B, Mittre H, Benhaim A, Herrou M, Mahoudeau J, Guillon-Metz F, Kottler ML, Reznik Y. Major hyperestrogenism in a feminizing adrenocortical adenoma despite a moderate overexpression of the aromatase enzyme. Eur J Endocrinol. 2003 Apr;148(4):457-61. doi: 10.1530/eje.0.1480457. PMID: 12656667.

Bowers M. "A Message from your WPATH President, Dr. Marci Bowers". Letter from WPATH. April 21, 2023. https://listloop.com/wpath/mail.cgi/archive/adhoc/20230421130649/

Bränström R, Pachankis JE. "Reduction in mental health treatment utilization among transgender individuals after gender-affirming surgeries: a total population study". Am J Psychiatry 2020; 177:727–734.

Bränström R, Pachankis JE. "Toward Rigorous Methodologies for Strengthening Causal Inference in the Association Between Gender-Affirming Care and Transgender Individuals'

Mental Health: Response to Letters". Am J Psychiatry 2020; 177:769–772; doi: 10.1176/appi.ajp.2020.20050599.

Brock M. "EXCLUSIVE: Top Trans Pediatric Doctors Admit In Unearthed Video That Puberty Blockers Aren't As 'Reversible' As Advertised". Daily Caller News Foundation. Jan 16, 2024. Accessed on-line Jan 31, 2024. https://dailycaller.com/2024/01/16/child-sex-changes-pediatric-puberty-hormones/

Brown BB & Larson J. Handbook of Adolescent Psychology. 3 Peer Relationships in Adolescence. John Wiley & Sons, Inc. 2009.

Carmichael P, Butler G, Masic U, Cole TJ, De Stavola BL, Davidson S, Skageberg EM, Khadr S, Viner RM. Short-term outcomes of pubertal suppression in a selected cohort of 12 to 15 year old young people with persistent gender dysphoria in the UK. PLoS One. 2021 Feb 2;16(2):e0243894. doi: 10.1371/journal.pone.0243894. PMID: 33529227; PMCID: PMC7853497.

Cass, Hillary. The Cass Review Interim Report. Feb, 2022. https://cass.independent-review.uk/publications/interim-report/

The Cass Review. Website. The Chair. Accessed on-line April 29, 2022. https://cass.independent-review.uk/about-the-review/the-chair/

Cavlan D, Bharwani N, Grossman A. Androgen- and estrogen-secreting adrenal cancers. Semin Oncol. 2010 Dec;37(6):638-48. doi: 10.1053/j.seminoncol.2010.10.016. PMID: 21167382.
CDC. "What is Venous Thromboembolism?" Accessed online 04/27/2022. https://www.cdc.gov/ncbddd/dvt/facts.html?msclkid=7406875bc6a411ecb67829f71b182f45
Chan Y, et al. "Evaluation of the infant with atypical genital appearance (difference of sex development)" UpToDate. Feb 18, 2021.

Chen, D., Abrams, M., Clark, L., Ehrensaft, D., Tishelman, A. C., Chan, Y.-M., Garofalo, R., Olson-Kennedy, J., Rosenthal, S. M., & Hidalgo, M. A. (2021). Psychosocial characteristics of transgender youth seeking gender-affirming medical treatment: Baseline findings from the trans youth care study. Journal of Adolescent Health, 68(6), 1104–1111. https://doi.org/10.1016/j.jadohealth.2020.07.033.

Chen D, Berona J, Chan YM, Ehrensaft D, Garofalo R, Hidalgo MA, Rosenthal SM, Tishelman AC, Olson-Kennedy J. Psychosocial Functioning in Transgender Youth after 2 Years of Hormones. N Engl J Med. 2023 Jan 19;388(3):240-250. doi: 10.1056/NEJMoa2206297. Erratum in: N Engl J Med. 2023 Oct 19;389(16):1540. PMID: 36652355; PMCID: PMC10081536.

Cheng A, Losken A. Essential elements of the preoperative breast reconstruction evaluation. Gland Surg. 2015 Apr;4(2):93-6. doi: 10.3978/j.issn.2227-684X.2015.03.05. PMID: 26005641; PMCID: PMC4409672.

Christel J M de Blok, et al. "Breast cancer risk in transgender people receiving hormone treatment: nationwide cohort study in the Netherlands" BMJ 2019; 365 doi: https://doi.org/10.1136/bmj.l1652 (Published 14 May 2019)

Coleman E, et al. “Standards of Care for the Health of Transgender and Gender Diverse People, Version 8”. International Journal of Transgender Health. 06 Sep 2022. International Journal of Transgender Health.
https://doi.org/10.1080/26895269.2022.2100644
https://www.tandfonline.com/doi/pdf/10.1080/26895269.2022.2100644

Deegan DF, Engel N. Sexual Dimorphism in the Age of Genomics: How, When, Where. Front Cell Dev Biol. 2019 Sep 6;7:186. doi: 10.3389/fcell.2019.00186. PMID: 31552249; PMCID: PMC6743004.

Dhejne, et al., “Long-Term Follow-Up of Transsexual Persons Undergoing Sex Reassignment Surgery: Cohort Study in Sweden,” PLoS One, vol. 6, issue 2 (Feb. 22, 2011)

Diamond M,Transsexuality Among Twins: Identity Concordance, Transition, Rearing, and Orientation, International Journal of Transgenderism. 2013.14:1, 24-38, DOI: 10.1080/15532739.2013.750222

Drugs.com. Microgestin Fe 1/20 Prescribing Information. Accessed 06/09/2024. https://www.drugs.com/pro/microgestin-fe-1-20.html

Drummond KD, Bradley SJ, Peterson-Badali M, Zucker KJ. A follow-up study of girls with gender identity disorder. Dev Psychol. 2008 Jan;44(1):34-45. doi: 10.1037/0012-1649.44.1.34. PMID: 18194003.

Dunaif A, Segal KR, Futterweit W, Dobrjansky A. “Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome”. Diabetes. 1989;38(9):1165.

Elhakeem A, et al. “Association Between Age at Puberty and Bone Accrual From 10 to 25 Years of Age”. JAMA Network Open. 2019;2(8):e198918. doi:10.1001/jamanetworkopen.2019.8918

Emmanuel M & Bokor B. Tanner Stages. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. https://www.ncbi.nlm.nih.gov/books/NBK470280/

Eugster EA. Treatment of Central Precocious Puberty. J Endocr Soc. 2019 Mar 28;3(5):965-972. doi: 10.1210/js.2019-00036.

FDA.gov, regarding celecoxib
https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/020998s026lbl.pdf
accessed 10/01/22.

FDA.gov sumatriptan. “HIGHLIGHTS OF PRESCRIBING INFORMATION...IMITREX (sumatriptan)”. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/020080s054lbl.pdf accessed 10/01/2022.

Florida Department of Health, Board of Medicine. Notice: 26873285, "64B8-9.019 Standards of Practice for the Treatment of Gender Dysphoria in Minors". Chapter: Standards of Practice for Medical Doctors. Effective 03/26/23.
https://www.flrules.org/Gateway/View_notice.asp?id=26873285 accessed 04/04/2023.

Gagnon DR, Zhang T, Brand FN, Kannel WB. "Hematocrit and the risk of cardiovascular disease—The Framingham Study: a 34-year follow-up". Am Heart J. 1994;127(3):674-682.

Gaufen D and Norgren S. "Policy Change Regarding Hormonal Treatment of Minors with Gender Dysphoria at Tema Barn - Astrid Lindgren Children's Hospital". 2021.
https://segm.org/sites/default/files/Karolinska%20Guideline%20K2021-4144%20April%202021%20%28English%2C%20unofficial%20translation%29.pdf

Greenpsan FS & Gardner DG. Basic & Clinical Endocrinology, 7th edition.
Puberty. Lange Medical Books/McGraw-Hill. 2004.

Griffin, L., Clyde, K., Byng, R., & Bewley, S. (2021). "Sex, gender and gender identity: A re-evaluation of the evidence". BJPsych Bulletin, 45(5), 291-299. doi:10.1192/bjb.2020.73

Grynberg M, Fanchin R, Dubost G, Colau J, Brémont-Weil C, Frydman R, Ayoubi J. "Histology of genital tract and breast tissue after long-term testosterone administration in a female-to-male transsexual population". Reprod Biomed Online. 2010 Apr;20(4):553-8.

Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. 2011 Apr;64(4):380-2. doi: 10.1016/j.jclinepi.2010.09.011. Epub 2010 Dec 24. PMID: 21185693.
https://www.jclinepi.com/article/S0895-4356(10)00330-6/fulltext

Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, Norris S, Falck-Ytter Y, Glasziou P, DeBeer H, Jaeschke R, Rind D, Meerpohl J, Dahm P, Schünemann HJ. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011 Apr;64(4):383-94. doi: 10.1016/j.jclinepi.2010.04.026. Epub 2010 Dec 31. PMID: 21195583.

Hall Ryan CW, Hall Richard CW, Chapman MJ. "Psychiatric Complications of Anabolic Steroid Abuse". Psychosomatics 46:4, July-August 2005.

Hardin AP, Hackell JM; COMMITTEE ON PRACTICE AND AMBULATORY MEDICINE. Age Limit of Pediatrics. Pediatrics. 2017 Sep;140(3):e20172151. doi: 10.1542/peds.2017-2151. Epub 2017 Aug 21. PMID: 28827380.

Hembree WC, et al., "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline," The Journal of Clinical Endocrinology & Metabolism, Volume 102, Issue 11 (Nov. 1, 2017).
Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, Gooren LJ, Meyer WJ 3rd, Spack NP, Tangpricha V, Montori VM; Endocrine Society. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2009 Sep;94(9):3132-

54. doi: 10.1210/jc.2009-0345. Epub 2009 Jun 9. Erratum in: J Clin Endocrinol Metab. 2021 Jun 16;106(7):e2852. PMID: 19509099.

IJTH Editorial Board. International Journal of Transgender Health. https://www.tandfonline.com/action/journalInformation?show=editorialBoard&journalCode=wijt21. Accessed Jan. 24, 2024.

IJTH Journal Overview. International Journal of Transgender Health. https://www.tandfonline.com/journals/wijt21. Accessed Jan. 24, 2024.

Institute of Medicine. 2012. Perspectives on Essential Health Benefits: Workshop Report. Washington, DC: The National Academies Press. https://doi.org/10.17226/13182. accessed on-line 02/09/2024 https://nap.nationalacademies.org/read/13182/chapter/7

Irwig MS. “Cardiovascular health in transgender people.” Rev Endocr Metab Disord. 2018;19(3):243–251.

James, A. "Randi Ettner and transgender people".Transgender Map. Accessed on-line 06/30/2024. https://www.transgendermap.com/issues/psychology/randi-ettner/

Joham AE, Ranasinha S, Zoungas S, Moran L, Teede HJ. “Gestational diabetes and type 2 diabetes in reproductive-aged women with polycystic ovary syndrome”. J Clin Endocrinol Metab. 2014 Mar;99(3):E447-52.

Kalin, N.H. “Reassessing Mental Health Treatment Utilization Reduction in Transgender Individuals After Gender-Affirming Surgeries: A Comment by the Editor on the Process by the Editor-in-Chief The American Journal of Psychiatry”. Am J Psychiatry 2020; 177:7 64; doi: 10.1176/appi.ajp.2020.20060803

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

Kralick AE, Zemel BS. Evolutionary Perspectives on the Developing Skeleton and Implications for Lifelong Health. Front Endocrinol (Lausanne). 2020 Mar 4;11:99. doi: 10.3389/fendo.2020.00099. PMID: 32194504; PMCID: PMC7064470. Kuohong W and Hornstein MD. “Causes of female infertility”. UpToDate. Jul 22, 2021.

Labcorp. Estradiol. https://www.labcorp.com/tests/004515/estradiol Accessed 02/04/23.

Laidlaw MK, Cretella M, Donovan K. “The Right to Best Care for Children Does Not Include the Right to Medical Transition”. The American Journal of Bioethics. 19(2), Feb 2019.

Laidlaw MK. “Gender Dysphoria and Children: An Endocrinologist’s Evaluation of ‘I am Jazz’”. Public Discourse, 5 Apr 2018.

Gender Dysphoria and Children: An Endocrinologist's Evaluation of I am Jazz - Public Discourse (thepublicdiscourse.com)

Laidlaw MK. "The Gender Identity Phantom", gdworkinggroup.org, Oct. 24, 2018. http://gdworkinggroup.org/2018/10/24/the-gender-identity-phantom/

Laidlaw MK, Horvath, H. Letter to Office of Inspector General, U.S. Department of Health & Human Services. Nov. 15, 2019. On file with author.

Laidlaw MK, Van Meter Q, Hruz P, Van Mol W, & Malone W, "Letter to the Editor: Endocrine Treatment of Gender-Dsyphoria/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline," J Clin Endocrinol Metab, 104(3) (March 2019).

Laidlaw MK, Van Mol A, Van Meter Q, Hansen JE. Letter to the Editor from M Laidlaw et al.: "Erythrocytosis in a Large Cohort of Trans Men Using Testosterone: A Long-Term Follow-Up Study on Prevalence, Determinants, and Exposure Years." The Journal of Clinical Endocrinology & Metabolism, Volume 106, Issue 12, December 2021, Pages e5275–e5276, https://doi.org/10.1210/clinem/dgab514

Landén, M. "The Effect of Gender-Affirming Treatment on Psychiatric Morbidity Is Still Undecided". Am J Psychiatry 2020; 177:767–768; doi: 10.1176/appi.ajp.2020.19111165.

Larsen PR, et al. Williams Textbook of Endocrinology, 10th edition. Philadelphia, W.B. Saunders Company, 2003.

Levine R. "Remarks by HHS Assistant Secretary for Health ADM Rachel Levine for the 2022 Out For Health Conference" April 30, 2022 Texas Christian University Fort Worth, Texas. Accessed on-line Jan 11, 2024 via HHS https://www.hhs.gov/about/leadership/rachel-levine.html.

Lin LH, Hernandez A, Marcus A, Deng FM, Adler E. Histologic findings in gynecologic tissue from transmasculine individuals undergoing gender-affirming surgery. *Arch Pathol Lab Med*. 2022 Jun 1;146(6):742-748. doi: 10.5858/arpa.2021-0199-OA.

Littman L. "Rapid-onset gender dysphoria in adolescents and young adults: a study of parental reports". PLoS One. 2018;13(8): e0202330

Lu J, Shin Y, Yen MS, Sun SS. Peak Bone Mass and Patterns of Change in Total Bone Mineral Density and Bone Mineral Contents From Childhood Into Young Adulthood. J Clin Densitom. 2016 Apr-Jun;19(2):180-91. doi: 10.1016/j.jocd.2014.08.001. Epub 2014 Oct 18. PMID: 25440183; PMCID: PMC4402109.

Ludvigsson J.F., Adolfsson J., Höistad M., Rydelius P.A., Kriström B., Landén M. (2023). *A systematic review of hormone treatment for children with gender dysphoria and recommendations for research*. ACTA PAEDIATR. doi: 10.1111/apa.16791.

Lupron Depot-Ped. Highlights of Prescribing Information. AbbVie Inc. Accessed May 1, 2022. https://www.rxabbvie.com/pdf/lupronpediatric.pdf

MacKelvie KJ, Khan KM, McKay HA. Is there a critical period for bone response to weight-bearing exercise in children and adolescents? a systematic review. Br J Sports Med. 2002 Aug;36(4):250-7; discussion 257. doi: 10.1136/bjsm.36.4.250. PMID: 12145113; PMCID: PMC1724536.

Madsen MC, van Dijk D, Wiepjes CM, Conemans EB, Thijs A, den Heijer M. "Erythrocytosis in a Large Cohort of Trans Men Using Testosterone: A Long-Term Follow-Up Study on Prevalence, Determinants, and Exposure Years". J Clin Endocrinol Metab. 2021 May 13;106(6):1710-1717. doi: 10.1210/clinem/dgab089.

Malone, W. and Roman, S. "Calling Into Question Whether Gender-Affirming Surgery Relieves Psychological Distress". Am J Psychiatry 2020; 177:766–767; doi: 10.1176/appi.ajp.2020.19111149

Mayo Clinic. "Feminizing Surgery". https://www.mayoclinic.org/tests-procedures/feminizing-surgery/about/pac-20385102 Accessed 07/01/2022.

Mayo Clinic. Hemoglobin Test. Accessed on-line 06/11/2024 https://www.mayoclinic.org/tests-procedures/hemoglobin-test/about/pac-20385075

Mayo Clinic. "Masculinizing Surgery". https://www.mayoclinic.org/testsprocedures/masculinizing-surgery/about/pac-20385105 accessed 06/24/2022.

Mayo Clinic. "Top surgery for transgender men and nonbinary people". https://www.mayoclinic.org/tests-procedures/top-surgery-for-transgendermen/about/pac-20469462 accessed 06/24/2022.

McCartney CR, Corrigan MD, Drake MT, El-Hajj Fuleihan G, Korytkowski MT, Lash RW, Lieb DC, McCall AL, Muniyappa R, Piggott T, Santesso N, Schünemann HJ, Wiercioch W, McDonnell ME, Murad MH. Enhancing the Trustworthiness of the Endocrine Society's Clinical Practice Guidelines. J Clin Endocrinol Metab. 2022 Jul 14;107(8):2129-2138. doi: 10.1210/clinem/dgac290. PMID: 35690966.

McGeary J. A critique of using the Delphi technique for assessing evaluation capability-building need. Evaluation Journal of Australasia, Vol. 9, No. 1, 2009, pp. 31–39.

Medpage Today. "Gender-Affirming Hormones Boost Mental Health for Transgender Youth". January 18, 2023. Accessed on-line 01/28/2024 https://www.medpagetoday.com/endocrinology/generalendocrinology/102687.

Mehringer JE, et al. "Experience of Chest Dysphoria and Masculinizing Chest Surgery in Transmasculine Youth". Pediatrics (2021) 147 (3): e2020013300.

Méndez-Bustos P, Calati R, Rubio-Ramírez F, Olié E, Courtet P, Lopez-Castroman J. Effectiveness of Psychotherapy on Suicidal Risk: A Systematic Review of Observational Studies. Front Psychol. 2019 Feb 19;10:277. doi: 10.3389/fpsyg.2019.00277. PMID: 30837920; PMCID: PMC6389707

Miller M, Stone NJ, Ballantyne C, Bittner V, Criqui MH, Ginsberg HN, Goldberg AC, Howard WJ, Jacobson MS, Kris-Etherton PM, Lennie TA, Levi M, Mazzone T, Pennathur S; American Heart Association Clinical Lipidology, Thrombosis, and Prevention Committee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Nursing; Council on the Kidney in Cardiovascular Disease. Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2011 May 24;123(20):2292-333. doi: 10.1161/CIR.0b013e3182160726. Epub 2011 Apr 18. PMID: 21502576.

Nahata L, Tishelman AC, Caltabellotta NM, Quinn GP. "Low fertility preservation utilization among transgender youth". J Adolesc Health. 2017;61(1):40–44.

National Academy for State Health Policy. "State Definitions of Medical Necessity under the Medicaid EPSDT Benefit". April 23, 2021. Accessed on-line 01/27/24 https://nashp.org/state-tracker/state-definitions-of-medical-necessity-under-the-medicaid-epsdt-benefit/

National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002 Dec 17;106(25):3143-421. PMID: 12485966.

NBC News. "Hormone therapy improves mental health for transgender youths, a new study finds". Accessed on-line 01/28/2024 https://www.nbcnews.com/nbc-out/out-health-and-wellness/hormone-therapy-improves-mental-health-transgender-youths-new-study-fi-rcna66306.

Niederberger M, Spranger J. Delphi Technique in Health Sciences: A Map. Front Public Health. 2020 Sep 22;8:457. doi: 10.3389/fpubh.2020.00457. PMID: 33072683; PMCID: PMC7536299.
Streed CG et al., Assessing and Addressing Cardiovascular Health in People Who Are Transgender and Gender Diverse: A Scientific Statement from the American Heart Association, 144 Circulation e136 (2021).

Olson KR, Durwood L, Horton R, Gallagher NM, Devor A. Gender Identity 5 Years After Social Transition. Pediatrics. 2022 Aug 1;150(2):e2021056082. doi: 10.1542/peds.2021-056082.

Olson-Kennedy J, Okonta V, Belzer M, Clark LF. Chest Reconstruction and Chest Dysphoria in Transmasculine Minors and Young Adults: Comparisons of Nonsurgical and Postsurgical Cohorts. JAMA Pediatr. 2018 May 1;172(5):431-436.

NIH RePORTER. reporter.nih.gov. https://reporter.nih.gov/search/-EEMdHiQ8kyTvxzLPBxGyQ/project-details/10615754 accessed 06/20/23.

Pagadala M. “Comparison of the Concentration of Estrogen and Testosterone Ratio in Male Patients With Cirrhosis and Hypotension”. ClinicalTrials.gov.
https://clinicaltrials.gov/ct2/show/NCT05051293
Accessed 02/05/23.

Palko. Recommendation of the Council for Choices in Health Care in Finland (PALKO / COHERE Finland). 2020.
https://genderreport.ca/wpcontent/uploads/2021/04/Finland_Guidelines_Gender_Variance_In_Minors.pdf

Panchal AR, Bartos JA, Cabañas JG, Donnino MW, Drennan IR, Hirsch KG, Kudenchuk PJ, Kurz MC, Lavonas EJ, Morley PT, O’Neil BJ, Peberdy MA, Rittenberger JC, Rodriguez AJ, Sawyer KN, Berg KM; Adult Basic and Advanced Life Support Writing Group. Part 3: Adult Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020 Oct 20;142(16_suppl_2):S366-S468.

Pretorius M, et al. “Mortality and Morbidity in Mild Primary Hyperparathyroidism: Results From a 10-Year Prospective Randomized Controlled Trial of Parathyroidectomy Versus Observation”. Ann Intern Med. 2022 Apr 19. doi: 10.7326/M21-4416. Online ahead of print.

Quest Diagnostics. Estrogen, Total, Serum. https://testdirectory.questdiagnostics.com/test/test-detail/439/estrogen-totalserum?cc=MASTER
accessed on-line 02/05/23.

Quest Diagnostics. Hematocrit. https://testdirectory.questdiagnostics.com/test/testdetail/509/hematocrit?cc=MASTER
accessed on-line 02/05/23.

Quest Diagnostics. Testosterone, Total, MS. https://testdirectory.questdiagnostics.com/test/test-detail/15983/testosterone-totalms? cc=MASTER
accessed on-line 01/12/23.

RAND Corporation. “Delphi Method”. Accessed on-line 01/27/2024.
https://www.rand.org/topics/delphi-method.html.

Reuters. “Sex-reassignment surgery yields long-term mental health benefits, study finds”. NBC News. Nov 8, 2019. https://www.nbcnews.com/feature/nbc-out/sexreassignment-surgery-yields-long-term-mental-health-benefits-study-n1079911

Ristori J, Steensma TD. Gender dysphoria in childhood. Int Rev Psychiatry. 2016;28(1):13-20. doi: 10.3109/09540261.2015.1115754. Epub 2016 Jan 12. PMID: 26754056.

Santoro N. Update in hyper- and hypogonadotropic amenorrhea. J Clin Endocrinol Metab. 2011 Nov;96(11):3281-8. doi: 10.1210/jc.2011-1419. PMID: 22058375.

Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, McCullough PA, Kasiske BL, Kelepouris E, Klag MJ, Parfrey P, Pfeffer M, Raij L, Spinosa DJ, Wilson PW, American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. “Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical
Cardiology, and Epidemiology and Prevention.” Circulation. 2003;108(17):2154.

Sax L. “How Common is Intersex? A Response to Anne Fausto-Sterling,” Journal of Sex Research 39:3 (August 2002), pp. 174-178.

SBU. Hormone treatment for gender dysphoria - children and young people. Sweden, Feb 22, 2022. https://www-sbu-se.translate.goog/sv/publikationer/SBUutvarderar/hormonbehandling-vidkonsdysfori/?_x_tr_sl=sv&_x_tr_tl=en&_x_tr_hl=en&_x_tr_pto=sc
Accessed on-line 05/17/2023

Shuster E. Fifty years later: the significance of the Nuremberg Code. N Engl J Med. 1997 Nov 13;337(20):1436-40. doi: 10.1056/NEJM199711133372006. PMID: 9358142.

Singal J. "How the Fight Over Transgender Kids Got a Leading Sex Researcher Fired". The Cut. Feb 7, 2016

Singh, D. (2012). A follow-up study of boys with gender identity disorder. Unpublished doctoral dissertation, University of Toronto.

Singh D, Bradley SJ, Zucker KJ. A Follow-Up Study of Boys With Gender Identity Disorder. Front Psychiatry. 2021 Mar 29;12:632784. doi: 10.3389/fpsyt.2021.632784. PMID: 33854450; PMCID: PMC8039393.

Skelton JA and Klish WJ. “Overview of the health consequences of obesity in children and adolescents”. UpToDate. Jan 25, 2023.

Society for Evidence Based Gender Medicine (SEGM). Sweden’s Karolinska Ends All Use of Puberty Blockers and Cross-Sex Hormones for Minors Outside of Clinical Studies (May 5, 2021), https://bit.ly/SEGM_SwedenStops Hormones.

Society for Evidence Based Gender Medicine (SEGM). National Academy of Medicine in France Advises Caution in Pediatric Gender Transition. (Mar 3, 2022), https://segm.org/France-cautions-regarding-puberty-blockers-and-cross-sexhormones-for-youth

Spath MA, Braat DDM. Iatrogenic and non-iatrogenic causes of female fertility loss that may indicate fertility preservation. Acta Obstet Gynecol Scand. 2019 May;98(5):559-562. doi: 10.1111/aogs.13594. Epub 2019 Mar 28. PMID: 30801655.

Statement of Removal, International Journal of Transgender Health, 23:sup1, S259-S259. 2022. DOI: 10.1080/26895269.2022.2125695 https://www.tandfonline.com/doi/pdf/10.1080/26895269.2022.2125695

Steinberg L. "A social neuroscience perspective on adolescent risk-taking". Dev Rev. 2008;28(1):78-106.

Toland MK, Bonasia K, Bentz J, et al. Uterine and ovarian histopathology after testosterone for gender affirmation: A systematic review. *Transgender Health*. 2023 May 18. doi: 10.1089/trgh.2022.0207.

Topjian AA, Raymond TT, Atkins D, Chan M, Duff JP, Joyner BL Jr, Lasa JJ, Lavonas EJ, Levy A, Mahgoub M, Meckler GD, Roberts KE, Sutton RM, Schexnayder SM; Pediatric Basic and Advanced Life Support Collaborators. Part 4: Pediatric Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020 Oct 20;142(16_suppl_2):S469-S523.

TLC UK. Bottom Surgery | I am Jazz. Youtube. Accessed May 1, 2022. https://www.youtube.com/watch?v=lG-U8oFpa8o

Turban JL, King D, Carswell JM, et al. "Pubertal Suppression for Transgender Youth and Risk of Suicidal Ideation". Pediatrics 2020, 145 (2) e20191725.

Van Mol, A., Laidlaw, M. K., Grossman, M., McHugh, P. "Gender-Affirmation Surgery Conclusion Lacks Evidence" Am J Psychiatry 177:8, August 2020 ajp.psychiatryonline.org 765.

Wang AMQ, Tsang V, Mankowski P, Demsey D, Kavanagh A, Genoway K. Outcomes Following Gender Affirming Phalloplasty: A Systematic Review and Meta-Analysis. Sex Med Rev. 2022 Aug 25:S2050-0521(22)00012-9. doi: 10.1016/j.sxmr.2022.03.002. Epub ahead of print. PMID: 36031521.

Warner Chilcott. Estrace Tablets. 2005. Accessed on-line 02/01/24. https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/081295s014,084499s042,084500s044lbl.pdf

Wallien, M.S., & Cohen-Kettenis, P.T. (2008). Psychosexual outcome of gender dysphoric children. Journal of the American Academy of Child and Adolescent Psychiatry, 47, 1413–1423.

Weitzer, D. "Transgender surgery linked with better long-term mental health, study shows". ABC News. Oct 8, 2019. https://abcnews.go.com/Health/transgendersurgery-linked-long-term-mental-health-study/story?id=66125676

Wilson D and Bruno B. Embryology, Mullerian Ducts (Paramesonephric Ducts). StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. https://www.ncbi.nlm.nih.gov/books/NBK557727/

Wold, A. (M.D., Ph.D.) Gender-Corrective Surgery Promoting Mental Health in Persons With Gender Dysphoria Not Supported by Data Presented in Article, Am J Psychiatry 2020; 177:768; doi: 10.1176/appi.ajp.2020.19111170

WPATH. FAQ. "World Professional Association for Transgender Health Standards of Care for Transgender and Gender Diverse People, Version 8 Frequently Asked Questions (FAQs)" Accessed on-line 01/20/2024. https://www.wpath.org/media/cms/Documents/SOC%20v8/SOC-8%20FAQs%20-%20WEBSITE2.pdf.

WPATH member search. https://www.wpath.org/member/search accessed 09/29/2022 and 10/01/2022.

WPATH. Randi Ettner, PhD. Provider. Accessed on-line 06/30/2024. https://www.wpath.org/provider/26

WPATH.org. Schedule for WPATH 27TH SCIENTIFIC SYMPOSIUM. accessed on-line 02/02/2024 https://www.wpath.org/media/cms/Upcoming%20Conferences/2022/Full%20Schedule%20for%20Distribution%20WPATH%202022.pdf?_t=1662650618.

WPATH. Revision Committee. "Establishing the soc8 Revision committee and meet the chairs and lead evidence team" accessed on-line 01/20/24 https://www.wpath.org/soc8/Revision-Committee.

Yelehe M. et al. "Adverse effects of gender-affirming hormonal therapy in transgender persons: Assessing reports in the French pharmacovigilance database." Fundamental and Clinical Pharmacology. June 2, 2022.

Zucker KJ. "Debate: Different strokes for different folks". Child and Adolescent Mental Health, Volume 25, Issue 1 (Feb 2020).

Exhibit 1

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EMPLOYMENT

2006-Present	Michael K Laidlaw, MD Inc. Private Practice – Endocrinology, Diabetes, and Metabolism. Rocklin, CA

EDUCATION

2004-2006	Endocrinology and Metabolism Fellowship - Los Angeles County/University of Southern California Keck School of Medicine
2001-2004	Internal Medicine Residency - Los Angeles County/University of Southern California Keck School of Medicine
1997-2001	University of Southern California Keck School of Medicine Doctor of Medicine Degree May 2001
1990-1997	San Jose State University. Bachelor of Science Degree in Biology with a concentration in Molecular Biology, Cum Laude

LICENSURE

California Medical License – Physician and Surgeon: # A81060: Nov 6, 2002. Exp 5/31/2026.

PROFESSIONAL AFFILIATIONS

Endocrine Society 2006-2024
American Board of Internal Medicine - Endocrinology, Diabetes, and Metabolism – 2006
American Board of Internal Medicine - Internal Medicine - 2005
National Board of Physicians and Surgeons - Endocrinology, Diabetes, & Metabolism 2018-2024
National Board of Physicians and Surgeons - Internal Medicine 2018-2024

HONORS AND RECOGNITION

2010	Endocrine Society Harold Vigersky Practicing Physician Travel Award
2004-2005	Vice President - Joint Council of Interns and Residents
2002-2004	Council Member – Joint Council of Interns and Residents
1996, 1997	Dean's Scholar, San Jose State University
1995	Golden Key National Honor Society

RESEARCH AND PUBLICATIONS

2021 Publication – Michael K Laidlaw, Andre Van Mol, Quentin Van Meter, Jeffrey E Hansen. Letter to the Editor from M Laidlaw et al.: "Erythrocytosis in a Large Cohort of Trans Men Using Testosterone: A Long-Term Follow-Up Study on Prevalence, Determinants, and Exposure Years." The Journal of Clinical Endocrinology & Metabolism, Volume 106, Issue 12, December 2021, Pages e5275–e5276, https://doi.org/10.1210/clinem/dgab514

2020 Publication – Van Mol A, Laidlaw MK, Grossman M, McHugh P. "Correction: Transgender Surgery Provides No Mental Health Benefit." Public Discourse, 13 Sep 2020. https://www.thepublicdiscourse.com/2020/09/71296/

2020 Publication – VanMol A, Laidlaw MK, Grossman M, McHugh P.. "Gender-affirmation surgery conclusion lacks evidence (letter)". Am J Psychiatry 2020; 177:765–766.

2020 Publication – Laidlaw MK. "The Pediatric Endocrine Society's Statement on Puberty Blockers Isn't Just Deceptive. It's Dangerous." Public Discourse. 13 Jan 2020. https://www.thepublicdiscourse.com/2020/01/59422/

2019 Speech to the U.K. House of Lords – Laidlaw MK. "Medical Harms Associated with the Hormonal and Surgical Therapy of Child and Adolescent Gender Dysphoria". Parliament, London, U.K. 15 May 2019.

2019 Publication – Laidlaw MK, Cretella M, Donovan K. "The Right to Best Care for Children Does Not Include the Right to Medical Transition". The American Journal of Bioethics. Volume 19. Published online 20 Feb 2019. 75-77. https://doi.org/10.1080/15265161.2018.1557288

2018 Publication – Laidlaw MK, Van Meter QL, Hruz PW, Van Mol A, Malone WJ. Letter to the Editor: "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline." The Journal of Clinical Endocrinology & Metabolism, Volume 104, Issue 3, 1 March 2019, Pages 686–687, https://doi.org/10.1210/jc.2018-01925 (first published on-line 11/2018)

2018 Publication – Laidlaw MK. "The Gender Identity Phantom". gdworkinggroup.org, 24 Oct 2018.

2018 Publication – Laidlaw MK. "Gender Dysphoria and Children: An Endocrinologist's Evaluation of 'I am Jazz'". Public Discourse, 5 Apr 2018. https://www.thepublicdiscourse.com/2018/04/21220/

2013 Abstract – Poster presentation Jun 2013. Endocrine Society Annual Meeting. A 12 Step Program for the Treatment of Type 2 Diabetes and Obesity.

2011 Abstract – Poster presentation Nov 2011. Journal of Diabetes Science and Technology. A Video Game Teaching Tool for the Prevention of Type 2 Diabetes and Obesity in Children and Young Adults.

2011 Abstract – Journal of Diabetes Science and Technology. A Web-Based Clinical Software Tool to Assist in Meeting Diabetes Guidelines and Documenting Patient Encounters.

2008 Abstract - Accepted to Endocrine Society Annual Meeting 2008. Hypercalcemia with an elevated 1,25 dihydroxy-Vitamin D level and low PTH due to granulomatous disease.

2005-2006 Clinical Research - University of Southern California – Utility of Thyroid Ultrasound in the Detection of Thyroid Cancer. Study involving the use of color flow/power doppler ultrasound and ultrasound guided biopsy to detect the recurrence of thyroid cancer in patients with total thyroidectomies.

2005 Certification - Certification in Diagnostic Thyroid Ultrasound and Biopsy – AACE 2005

2003 Certification - Understanding the Fundamentals: Responsibilities and Requirements for the Protection of Human Subjects in Research. University of Southern California. 29 Sep 2003 - 29 Sep 2006

2002-2005 Clinical Research - University of Southern California - Determining the Role of Magnesium in Osteoporosis. Study involved collecting and analyzing patient data related to patient characteristics, laboratory results, bone mineral density exams, nutrition analysis, and genetic analysis in order to determine a link between magnesium deficiency and osteoporosis.

1995-1996 Research Assistant - San Jose State University. 1) Role of the suprachiasmatic nucleus pacemaker in antelope ground squirrels; 2) Acoustic tolerance test and paste diet study for space shuttle rats.

EXPERT WITNESS WORK AND AMICUS BRIEFS

2024 Expert Witness – Laidlaw MK. KAYLA LOVDAHL, an individual Claimant, v. KAISER FOUNDATION HOSPITALS, INC., a California Corporation, THE PERMANENTE MEDICAL GROUP, INC., a California Corporation, LISA KRISTINE TAYLOR, M.D., an individual, WINNIE MAO YIU TONG, M.D., an individual, SUSANNE E. WATSON, PHD., an individual, MIRNA ESCALANTE, M.D., an individual, and DOES 1 through 50, inclusive, Respondents. Arbitration Case No.: 18496. Assigned for All Purposes to Hon. Donald J. Sullivan (Ret.)

2024 Expert Witness – Laidlaw MK. Victor VOE, et al., Plaintiffs, v. Thomas MANSFIELD et al., Defendants, Phillip E. BERGER, et al., Intervenor-Defendants. Case No 1:23-cv-864. In the United States District Court for the Middle District of North Carolina. Expert declaration.

2024 Expert Witness – Laidlaw MK. A.B., by and through his parents, L.B. and M.B., on his own behalf and on behalf of similarly situated others; L.B.; and M.B., Plaintiffs, vs. Premera Blue Cross, Defendant. Case No. 2:23-cv-00953-TSZ. IN THE UNITED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF WASHINGTON AT SEATTLE. Expert declaration.

2024 Expert Witness – Laidlaw MK. CHLOE E. BROCKMAN a/k/a CHLOE COLE, an individual Plaintiff, v. KAISER FOUNDATION HOSPITALS, INC. et al. SUPERIOR COURT OF THE STATE OF CALIFORNIA IN AND FOR THE COUNTY OF SAN JOAQUIN – STOCKTON BRANCH. Case No.: STK-CV-UMM-2023-0001612. Expert Declaration.

2024 Expert Witness – Laidlaw MK. T.D., by and through his parents, et al. Plaintiffs vs. DREW H. WRIGLEY, in his official capacity as Attorney General for the State of North Dakota, et al. Defendants. Case No.: 08-2023-CV-02189. Testified in Court.

2023 Brief of Amicus Curiae – Laidlaw MK. Laidlaw MK, Van Meter QL, Van Mol A, Hansen JE, Cretella MA, Everitt E. RACHEL G. DAMIANO and KATIE S. MEDART, Plaintiffs-Appellants, v. GRANTS PASS SCHOOL DISTRICT NO. 7, et al. Defendants-Appellees. On Appeal from the United States District Court for the District of Oregon No. 1:21-cv-00859-CL. No. 23-35288. IN THE UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT.

2023 Expert Witness – Laidlaw MK. FOURTH JUDICIAL DISTRICT COURT MISSOULA COUNTY. SCARLET VAN GARDEREN, et al. Plaintiffs, v. STATE OF MONTANA, et al., Defendants. Cause No. DV 2023-0541.

2023 Expert Witness – Laidlaw MK. United States District Court for the Northern District of Georgia Atlanta Division. EMMA KOE et al., Plaintiffs, v. CAYLEE NOGGLE et al., Defendants. Civil Action No. 1:23-cv-02904-SEG.

2023 Expert Witness – Laidlaw MK. United States District Court for the Northern District of Oklahoma. PETER POE, et al., Plaintiffs, v. GENTNER DRUMMOND, et al., Defendants. Case No. 23-cv-00177-JFH-SH.

2023 Expert Witness – Laidlaw MK. United States District Court for the Western District of Kentucky. JANE DOE 1, et al., Plaintiffs, v. WILLIAM C. THORNBURY, JR., MD, in his official capacity as the President of the Kentucky Board of Medical Licensure, et al., Defendants. Case No. 3:23-cv-00230-DJH.

2023 Expert Witness – Laidlaw MK. United States District Court for the Middle District of Tennessee Nashville Division. L.W., by and through her parents and next friends, Samantha Williams and Brian Wil-liams, et al. Plaintiffs, v. JONATHAN SKRMETTI, in his official ca-pacity as the Tennessee Attorney General and Reporter, et al., Defendants. Case No. 3:23-cv-00376.

2022-2023 Expert Witness – Laidlaw MK. United States District Court for the Northern District of Florida Tallahassee Division. AUGUST DEKKER, et al., Plaintiffs, v. SIMONE MARSTILLER, et al., Defendants. Case No. 4:22-cv-00325-RHMAF.

Report October 3, 2022. Testified in court October 12, 2022. Expert Report February 17, 2023. Rebuttal March 10, 2023.

2022 Expert Witness Report – Laidlaw MK. C. P., by and through his parents, Patricia Pritchard and Nolle Pritchard; and PATRICIA PRITCHARD, Plaintiff, vs. BLUE CROSS BLUE SHIELD OF ILLINOIS, Defendants. Case No. 3:20-cv-06145-RJB

2022 Expert Witness Report – Laidlaw MK. DISTRICT COURT OF TRAVIS COUNTY, TEXAS 459th JUDICIAL DISTRICT. PFLAG, INC., ET AL., Plaintiffs, v. GREG ABBOTT, ET AL., Defendants. NO. D-1-GN-22-002569. 3 July 2022.

2022 Expert Witness Report #2 – Laidlaw MK. United States District Court for the District of Arizona. DH and John Doe, Plaintiffs, vs. Jami Snyder, Director of the Arizona Health Care Cost Containment System, in her official capacity, Defendant. Case No. 4:20-cv-00335-SHR. 24 Jun 2022. (Sealed under Protective Order).

2022 Expert Witness Report – Laidlaw MK. United States District Court for the Middle District of Alabama Northern Division. REV. PAUL A. EKNES-TUCKER, et al., Plaintiffs, v. KAY IVEY, in her official capacity as Governor of Alabama, et al., Defendants. Civil Action No. 2:22-cv-184-LCB. 2 May 2022.

2021 Brief of Amicus Curiae – Bursch, John J., McCaleb, Gary S., Van Meter, Quentin L., Laidlaw, Michael K., Van Mol, Andre, Hansen, Jeffrey E. Brief of Amicus Curiae. United States Court of Appeals for the Eight Circuit. DYLAN BRANDT, et al., Plaintiffs-Appellees v. LESLIE RUTLEDGE, in her official capacity as the Arkansas Attorney General, et. al. Defendants-Appellants. 23 Nov 2021.

2021 Expert Witness – JULIANA PAOLI v. JOSEPH HUDSON et al. heard in THE SUPERIOR COURT OF THE STATE OF CALIFORNIA, COUNTY OF TULARE. CASE NO. 279126. 2021.

2021 Brief of Amicus Curiae – Bursch, John J., McCaleb, Gary S., Grossman, Miriam, Van Meter, Quentin L., Laidlaw, Michael K., Van Mol, Andre, Hansen, Jeffrey E. Brief of Amicus Curiae. United States Court of Appeals for the Eleventh Circuit. DREW ADAMS, Plaintiffs-Appellee v. SCHOOL BOARD OF ST. JOHNS COUNTY, FLORIDA, et. al. Defendants-Appellant. 26 Oct 2021.

2020 Expert Witness Affidavit 1 & 2 – Laidlaw MK. Supreme Court of British Columbia. File No. S2011599, Vancouver Registry. Between A.M. Plaintiff and Dr. F and Daniel McKee Defendants. 11/23/20 & 11/25/20.

2020 Brief of Amicus Curiae – Wenger, Randal L., McCaleb, Gary S., Grossman, Miriam, Laidlaw, Michael K., McCaleb, Gary S., Van Meter, Quentin L., Van Mol, Andre. Brief of Amicus Curiae. United States Court of Appeals for the Ninth Circuit. LINDSAY HECOX and JANE DOE, with her next friends Jean Doe and John Doe, Plaintiffs-Appellees v. BRADLEY LITTLE, in his official capacity as Governor of the State of ID, et. al. Defendant-Appellant. 19 Nov 2020

2020 Expert Witness Report – Laidlaw MK. United States District Court for the District of Arizona. DH and John Doe, Plaintiffs, vs. Jami Snyder, Director of the Arizona Health Care Cost Containment System, in her official capacity, Defendant. Case No. 4:20-cv-00335-SHR. 27 Sep 2020.

2019 Expert Witness Affidavit – Laidlaw MK. Court of Appeal File No. CA45940, Vancouver Registry. B.C. Supreme Court File No. E190334, between A.B. Respondent/Claimant, and C.D. Appellant/Respondent, and E.F. Respondent/Respondent. 24 Jun 2019.

2018 Brief of Amicus Curiae – Alliance Defending Freedom, Campbell, James A., Grossman, Miriam, Laidlaw, Michael K., McCaleb, Gary S., Van Meter, Quentin L., Van Mol, Andre. Brief of Amicus Curiae. United States Court of Appeals for the Eleventh Circuit. Drew Adams, Plaintiff-Appellee, v. School Board of St. Johns County, Florida, Defendant-Appellant. 12/27/2018.

2018 Brief of Amici Curiae – DRS. MIRIAM GROSSMAN, PAUL HRUZ, MICHAEL LAIDLAW, QUENTIN VAN METER, ANDRE VAN MOL IN SUPPORT OF PETITIONER. Supreme Court of the United States. JOEL DOE ET AL., Petitioners, v. BOYERTOWN AREA SCHOOL DISTRICT ET AL., Respondents, and PENNSYLVANIA YOUTH CONGRESS FOUNDATION, Respondent-Intervenor. ON PETITION FOR WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT. Parker Douglas, Counsel of Record. No. 18-658. 12/2018.

PERSONAL

Languages: Conversational Spanish, French. Tutor: Biochemistry, computer science, High School mentor. Computers: Ruby, Rails, Javascript, C++, C, Java, and HTML programming

Exhibit 2

4770 Rocklin Rd, Ste #1
Rocklin, CA 95677
(916) 315-9100
(916) 315-0141 Fax

Date: 11/15/2019

Regarding: False Claims Act. Requesting Investigation into Suspected Grant Fraud in NIH Project #1R01HD082554, “The Impact of Early Medical Treatment in Transgender Youth”

Dear Office of Inspector General, U.S. Department of Health & Human Services:

This letter concerns suspected grant fraud in the grant awarded for NIH Project #1R01HD082554, "The Impact of Early Medical Treatment in Transgender Youth". We believe there has been a violation of the False Claims Act.

The issue being that a study was published in JAMA Pediatrics in 2018 entitled "Chest Reconstruction and Chest Dysphoria in Transmasculine Minors and Young Adults Comparisons of Nonsurgical and Postsurgical Cohorts" by Dr. Johanna Olson-Kennedy, et al. (attached) This study references funding via the NIH grant 1R01HD082554-01A1 (p. 436). However the content of the study is entirely different than the aims for which the grant was funded (see appendix of this letter under Specific Aims). Specifically the published study is of mastectomies of the healthy breasts of minor and adult females with gender dysphoria, yet the grant protocol makes no mention of any surgeries of any kind, nor any sort of survey about surgeries. The main intent of the published study appears to be to obtain insurance payments for minors who have undergone mastectomies. There are additional problems and discrepancies between the grant application protocol and the published article which are detailed below.

The study is striking insofar as 33 minor females (under the age of 18) had surgical resection of completely healthy breasts. They did not have breast cancer for example or other physical ailments as indications for breast resection. They had a condition of the mind whereby their internal sense about “gender” varied with their physically female bodies. The authors state that "16 [subjects] were 15 years or younger" with the youngest being 13. Breasts are organs that once resected can never be replaced. As such this is a life altering surgery not to be taken lightly. This is particularly true at such a young age as 13 and 14 years old, whereby these girls cannot fully comprehend the long term consequences of their decision. The plans and considerations for these surgical subject minors are mentioned nowhere in the grant application.

The article also discusses a "Chest Dysphoria Scale" which is nowhere referenced in the grant proposal. This is a scale which the study authors admit was generated "based on the clinical experience of the first author" (p.433) and is "not yet validated" (p. 435). One wonders how a non-validated survey about a condition labeled "chest dysphoria" (which is not a valid medical diagnosis) could ever be used to establish anything scientific? The grant monies were not awarded for such a dubious purpose.

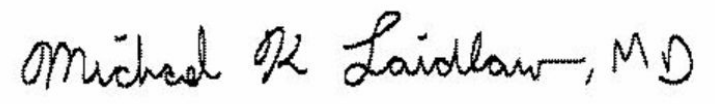
Statutes regarding the special protection of minors involved in human experiments are found under 45 CFR Part 46 - Protection of Human Subjects, Subpart D Additional Protections for Children Involved as Subjects in Research. Again, the grant protocol makes no mention of studying any surgeries of any type, neither in its aims nor study design nor anywhere in the application. A review of any study of the resection of healthy organs of minors or any survey of such surgeries would require special examination for children defined as those "who have not attained the legal age for consent to treatments or procedures involved in the research" (45 CFR p. 145). This would be the case for the majority of minors in the study. Under §46.407 it states "HHS will conduct or fund research that the IRB does not believe meets the requirements of §46.404, §46.405, or §46.406 only if: ...(b) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment" determines it is ethically sound (p. 146). It is clear that this statute for the safeguarding of children was deliberately avoided. Rather there was a deliberate attempt to circumvent such safeguarding. Any attempt to circumvent this statute is both unethical and fraudulent.

The purpose of the mastectomy for minors article becomes clear once one examines the statements about insurance reimbursements. The authors state "many insurance plans continue to impose a mandatory age requirement of 18 years for chest surgery [mastectomy], as well as the use of testosterone for a full year prior to surgery to ensure the best results...We hope to inform future revisions of existing guideline recommendations regarding...minors seeking surgical interventions" (p. 432). So it appears that the plan at the outset was to create a non-validated survey to help circumvent existing protections for minors, and thereby change the guidelines so that girls as young as 13 can have mastectomies of healthy breasts paid for by insurance companies.

In conclusion, it would seem that the authors were anxious to get a study published in the literature in order to insure that surgeons would be reimbursed for the resection of the healthy breasts of minor girls. This is ethically a very dubious purpose. In terms of using these particular grant monies towards the study, the authors of this letter believe it to be a fraudulent use and are recommending an investigation as such.

Thank you for reviewing this letter.

Sincerely,



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Attachments:

1. Appendix
2. Article: Olson-Kennedy J, et al. "Chest Reconstruction and Chest Dysphoria in Transmasculine Minors and Young Adults Comparisons of Nonsurgical and Postsurgical Cohorts" JAMA Pediatrics 2018
3. Specific Aims and Study Design from Grant Application 1R01HD082554
4. 45 CFR Part 46

Appendix

The following is from pages 163-164 of the grant application under “Specific Aims”.

“Aim 1: To evaluate the impact of GnRH agonists administered for puberty suppression, on mental health, psychological well-being, physiologic parameters, and bone health as well as document the safety of GnRH agonists in an early-pubertal cohort (Tanner stages 2-3; n=80) of transgender children and adolescents, comparing baseline and follow-up assessments at 6 months, 1 year, and 2 years after initiating treatment.”

“Aim 2: To evaluate the impact of cross-sex hormones administered for gender transition on mental health, psychological well-being, and metabolic/physiologic parameters as well as document the safety of cross- sex hormones in a late-pubertal cohort (Tanner stages 4-5; n=200) of transgender adolescents, comparing baseline and follow up assessments at 6 months, 1 year, and 2 years after initiating treatment.”

“Aim 3 (Exploratory): Based on evidence of high rates of substance use and HIV infection in some transgender adolescents (specifically, young transgender women), we will determine substance use and sexual risk behavior over time. A priori hypotheses regarding the impact of hormone treatment on sexual and substance use behaviors cannot be specified given that these behaviors increase through adolescence.”

Exhibit 3

A. COVER PAGE

Project Title: The Impact of Early Medical Treatment in Transgender Youth	
Grant Number: 5R01HD082554-02	**Project/Grant Period:** 08/01/2015 - 06/30/2020
Reporting Period: 08/01/2015 - 06/30/2016	**Requested Budget Period:** 07/01/2016 - 06/30/2017
Report Term Frequency: Annual	**Date Submitted:** 05/13/2016
Program Director/Principal Investigator Information: JOHANNA L OLSON , BS MD MS **Phone number:** (818) 679-6757 **Email:** jolson@chla.usc.edu	**Recipient Organization:** CHILDREN'S HOSPITAL OF LOS ANGELES 4650 Sunset Boulevard Mailstop #97 LOS ANGELES, CA 900276062 **DUNS:** 052277936 **EIN:** 1951690977A1 **RECIPIENT ID:** RGF009152
Change of Contact PD/PI: N/A	
Administrative Official: MANNY TRINIDAD SUNGA CHILDREN'S HOSPITAL LOS ANGELES 4650 SUNSET BLVD LOS ANGELES, CA 900276062 **Phone number:** 3233612131 **Email:** msunga@chla.usc.edu	**Signing Official:** JODI OGDEN 4650 Sunset Ave., M.S. #84 Los Angeles, CA 90027 **Phone number:** 323-361-4661 **Email:** jogden@chla.usc.edu
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The objective of the research is to provide evidence-based data to inform clinical care for transgender youth. The study will leverage the partnership between four, university-affiliated, gender clinics across the U.S. to recruit two developmental cohorts and conduct a multi-site, observational study examining the safety of hormonal interventions and the physiological and psychosocial outcomes associated with these treatments.

The Specific Aims are:

Aim 1: To evaluate the impact of GnRH agonists administered for puberty suppression, on mental health, psychological well-being, physiologic parameters, and bone health as well as document the safety of GnRH agonists in an early-pubertal cohort (Tanner stages 2-3; n=80) of transgender children and adolescents, comparing baseline and follow-up assessments at 6 months, 1 year, and 2 years after initiating treatment.

Hypothesis 1a: Patients treated with GnRH agonists will exhibit decreased symptoms of depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

Hypothesis 1b: GnRH agonists will be tolerable and safe for early-pubertal transgender youth, i.e., fasting lipids and glucose, liver enzymes, electrolytes, insulin, and HbA1c will not increase above clinically safe ranges.

Hypothesis 1c: Raw bone density scores will remain stable for early-pubertal transgender youth receiving GnRH agonists; however, age-matched z-scores may decrease.

Aim 2: To evaluate the impact of cross-sex hormones administered for gender transition on mental health, psychological well-being, and metabolic/physiologic parameters as well as document the safety of cross- sex hormones in a late-pubertal cohort (Tanner stages 4-5; n=200) of transgender adolescents, comparing baseline and follow up assessments at 6 months, 1 year, and 2 years after initiating treatment.

Hypothesis 2a: Patients treated with cross-sex hormones will exhibit decreased symptoms of gender dysphoria, depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

Hypothesis 2b: Cross-sex hormones will be tolerable and safe to use for late-pubertal transgender youth initiating phenotypic transition, i.e., will not increase fasting lipids and glucose, liver enzymes, electrolytes, and hemoglobin above clinically safe ranges.

Aim 3 (Exploratory): Based on evidence of high rates of substance use and HIV infection in some transgender adolescents (specifically, young transgender women), we will determine substance use and sexual risk behavior over time. A priori hypotheses regarding the impact of hormone treatment on sexual and substance use behaviors cannot be specified given that these behaviors increase through adolescence.

This multi-center study will be the first in the U.S. to evaluate longitudinal outcomes of medical treatment for transgender youth, and it will provide highly needed evidence-based data on the physiological and psychosocial effects and safety of treatments currently used for transgender youth.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B2 Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

While we hope to obtain IRB approval of the protocol at all sites prior to 6/30/16, if all sites have not received their IRB approval by that date, it will be obtained early in the next reporting period. With NICHD approval, we will begin recruiting participants at the sites, and based on the influx of new patients at the four sites, we expect to recruit at least 75% of the subjects within the next reporting period. As we implement the protocol with subjects, we will monitor challenges that arise through monthly conference calls with the study coordinators and provide technical assistance as needed.

Quality assurance activities will be conducted both at the coordinating site level through the CHLA data manager and at the local site level by the study coordinators. Study coordinators will be expected to conduct quality assurance activities such as data entry accuracy checks on 100% of the data and full visit review for 10% of the visits. The coordinating site data manager will be regularly checking the Access database through programmed customized reports to ensure that data look valid, within expected ranges, and complete. Any data discrepancies will be discussed with the sites to ensure that data are accurate and missing data are minimized. The CHLA data manager will also run regular data checks to ensure the ACASI data files are complete and accurate. She will monitor the recruitment on a weekly basis within and across sites and share data with the PIs as needed. Preliminary data analysis will begin as soon as possible. If any site appears to be having difficulties with implementing the protocol with fidelity, coordinating site center staff will conduct site visits to provide technical assistance.

The PIs and Co-Is will have biweekly phone calls to discuss the progress at each site, review recruitment, and to discuss any events that may arise. Because there are more patients entering care than can be enrolled into the study, the PIs will discuss the recruitment progress to ensure that the participant characteristics are unbiased. Changes to recruitment procedures may be needed to control for bias that may start to appear through the convenience sampling method. Also, as the field of transgender care is rapidly progressing, it may be necessary to further discuss care protocols that may be undergoing change to ensure that the data being collected reflect current care practices.

The PIs will each attend one national conference per year to disseminate findings beginning in Year 2. Data obtained from this study are of great interest and will be presented to participants at gender specific conferences such as the World Professional Association of Transgender Health, Gender Odyssey, Philadelphia TransHealth Conference, and Gender Spectrum, and also at national conferences concerning the health of children and adolescents such as the American Academy of Pediatrics, Society for Adolescent Health and Medicine, Pediatric Academic Societies, and others. In order to disseminate findings, preliminary data will need to be analyzed and related back to the medical care providers of transgender youth.

A revision to the inclusion/exclusion criteria from the original submitted proposal is the exclusion of Spanish-only speaking youth. The protocol was revised so that research participants are required to have the ability to read and understand English. This change was made to the protocol for two reasons. Some of the measures that are being used in this protocol are pilot measures, and are still in the validation process for English speakers. In addition, some of the measures, while validated in English, have not yet been validated for Spanish speakers. The measures that would require validation include the Parent-Report Gender Identity Questionnaire for Children, the Social Transitioning Scale, the Autism Spectrum Quotient, and the Utrecht Gender Dysphoria Scale.

During the first nine months of the grant, the principal investigators and co-investigators, with support from the project staff, have been diligently transitioning the research concept into a written protocol. During the initial phase of this grant, the objective was to finalize the mental health measures and physiologic parameters that would best reflect the changes that the team anticipated would result from early intervention among transgender youth. The operationalization of the research science, made more complex by the inclusion of four sites, has been facilitated through a face-to-face meeting of the PIs, regular conference calls including the PIs and Co-Is, and weekly meetings of the core team at CHLA. An in person meeting of the four PIs in Chicago in September 2015, yielded consensus regarding the physiologic measures necessary to abstract and evaluate, as well as preliminary discussion about ideal mental health measures necessary or missing, in order to capture the impact of early treatment. In conjunction with the Co-Is with expertise in mental health, communication via regular conference calls resulted in solidification of the best available measures to capture mental health diagnoses at baseline and changes in symptomatology over time. Numerous validated and pilot measures were reviewed and carefully considered through healthy discussion regarding the strengths and applicability of each. Particular care with regard to the relevance of each measure to gender was considered. What resulted from these extensive discussions was the identification of the existing, inadequate measures of both gender dysphoria and gender identity. By utilizing pilot measures, we hope to create measures that can be validated through our data collection and be used in future studies.

Weekly meetings of the CHLA team focused on questions related to protocol development, obtaining and finalizing measures as they were agreed upon by the PIs, data management procedures, appropriate data collection and data entry methods, creation of case report forms, and addressing any other related issues. We have worked very hard to pool together existing measures of these constructs and add some of our own questions relevant to these constructs. The protocol was written, revised, and submitted for review by the IRB at Children's Hospital Los Angeles (CHLA), the coordinating center, on 3/9/16. An approval contingent on obtaining the Certificate of Confidentiality was received on 4/18/16. An application for the Certificate of Confidentiality was immediately submitted with approval granted on 4/20/16. The Certificate of Confidentiality has been submitted to the CHLA IRB along with version 2 of the protocol, required due to ongoing discussions regarding bone health of those subjects who are starting cross-sex hormones, but had been on a GnRH agonist when they entered puberty. Once full approval has been obtained at CHLA, the sites will submit the protocol to their site IRBs. In addition, the CHLA IRB approval will be submitted to NICHD for review and approval.

We are currently in the process of finalizing the programming and testing of the Access database and the audio computer-assisted self-interview (ACASI) surveys for the 1) youth in the blocker cohort, 2) parents/caretakers of the youth in the blocker cohort, and 3) the youth in the cross-sex hormone cohort. Study coordinators have been designated to support this study or have been hired at all four sites, and calls have been conducted with staff from the Chicago and Boston sites regarding clinic flow, experience in conducting research, and needs for technical assistance and support from the CHLA team. An initial introductory call was conducted with the new study coordinator at the San Francisco site, and a more in-depth call will be conducted when the newly-hired study coordinator is oriented. Research assistants will be hired as needed as accrual increases. A meeting of all sites will occur in Los Angeles in late June that will focus on training site staff to 1) implement the protocol activities with fidelity; 2) obtain, enter, and transmit data electronically while ensuring accuracy and protecting confidentiality; and 3) meet all human subjects' protection and regulatory requirements. It will also provide the PIs and Co-Is with an opportunity to solidify protocol implementation activities at their site and to discuss the rapidly occurring changes in standard of care for early treatment for transgender youth, especially in response to attending the World Professional Association for Transgender Health International Symposium in June.

Once NICHD approval has been obtained, we will initiate recruitment and enrollment of participants at the CHLA site. Recruitment at the Boston, Chicago, and San Francisco sites will begin as soon as they have received IRB approval. As the sites have a consistent flow of new patients, no challenges to recruitment are expected over the next year.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period?

No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

NOTHING TO REPORT

C.5.b Resource sharing

NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	SS Number	DOB	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
ERA Commons Username	Y	Olson, Johanna L	Personal Information	Personal Information	BS,MS,MD	PD/PI	Months Devoted to Project					NA
	Y	ROSENTHAL, STEPHEN M			BA,MD	PD/PI						NA
	Y	GAROFALO, ROBERT			BS,MPH,MD	PD/PI						NA
	Y	Spack, Norman				PD/PI						NA
	N	McAvoy-Banerjea, Julie			MPH	Clinical Research Manager						NA
	N	Russell, Meredith				Clinical Research Nurse						NA
	N	Lash, Brenna				Project Coordinator						NA
	N	Okonta, Vivian				Non-Student Research Assistant						NA
ERA Commons Username	Y	Hidalgo, Marco			PHD	Co-Investigator						NA
	Y	Clark, Leslie Frances			PHD,MPH	Co-Investigator						NA
	Y	Chen, Diane			BA,MA,PHD	Co-Investigator						NA
	Y	Simons, Lisa			MD	Co-Investigator						NA
	Y	Schrager, Sheree Michelle			BA,MS,MS,PHD	Co-Investigator						NA
	Y	Finlayson, Courtney			MD	Co-Investigator						NA
	Y	Ehrensaft, Diane			PHD	Co-Investigator						NA
ERA Commons Username	Y	BELZER, MARVIN E			BS	Co-Investigator						NA
	Y	Chan, Yee-Ming			PHD,MD,BS	PD/PI						NA
	N	Jensen, Jennifer			ARNP	Research Nurse						NA

ERA Commons Username							Months Devoted to Project		
	Y	Tishelman, Amy C.				Co-Investigator			NA
	N	Bigelow, Lou			BA	Clinical Research Coordinator			NA
	N	Desai, Mona			MPH	Evaluation Manager			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

Yes

Dr. Norman Spack, PI for the Boston Children's Hospital site, retired and transitioned his PI responsibilities to Dr. Yee-Ming Chan. This transition of the Boston PI was submitted to the NICHD Grants Management Specialist and was approved on 3/10/16. Dr. Chan has committed # calendar months to this project this year.

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: Other Support Compiled 2016.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

Yes

File uploaded: D2e Multiple PI Leadership Plan.pdf

- Months Devoted to Project

Program Director/Principal Investigator:
Olson, Johanna

PHS 398/2590 OTHER SUPPORT

BELZER, M.E.

ACTIVE

5 U01 HD 040474-14 (Korelitz) 4/16/2001 – 02/28/2017 # calendar
NIH/NICHD via Westat $450,000
Adolescent Medicine Trials Network for HIV/AIDS Interventions

The major goals of this project are to conduct research, both independently and in collaboration with existing research networks and individual investigators, in HIV-infected and HIV-at-risk pre-adolescents, adolescents, and young adults up to age 25 years.

1 CPIMP141084-01-00 (Martinez) 9/30/2014 – 08/30/2017 # calendar
HHS/Office of Minority Health $375,000
HIV/AIDS Initiative for Minority Men (AIMM)

The goal of the project is to develop a coordinated system of HIV prevention and care for YMSM of color in Los Angeles in partnership with local stakeholders and youth.

1R01MH108442 (Outlaw) 8/1/2015 – 4/30/2020 # calendar
NIH/NIMH $123,864

The goal of this research is test a brief, 2-session, computer-delivered motivational intervention to prevent adherence difficulties among youth newly prescribed ART.

1R01HD082554-01A1 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $952,542

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

1 U01 DA036926-01A1 (Kipke) 8/15/2015 – 7/31/2020 # calendar
NIH/NIDA $497,353

The goal of this project is to recruit and track for cohort of young MSM of color in order to better understand their disproportionately high rates of HIV infection and low rates of linkage to and engagement in HIV-related care and to develop new interventions to reduce HIV/STI risk and transmission and HIV disease progression.

PENDING

Pending Support

Pending Support

Program Director/Principal Investigator:
Olson, Johanna

Pending Support

OVERLAP: None

CLARK, L.F.

ACTIVE

90AP2674 (Desai) 09/30/2010 – 09/29/2016 # calendar
ACYF, PREIS $66,015
Evaluation of AIM 4 Teen Moms

The goal for this proposed project is to reduce rapid repeat pregnancies among teen mothers under age 21. Approximately 1,200 pregnant teens and teen parents (ages 14-18) will be enrolled into the project and randomly assigned to either intervention (an adapted version of Project AIM called AIM 4 Teen Moms) or a control group and followed for 2 years.

1R01HD082554-01A1 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $952,542

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

PENDING: None

OVERLAP: None

GAROFALO, R.

ACTIVE

R01MH094323-01 (Garofalo/Mimiaga) 6/13/2011 – 3/31/2016 # calendar
NIMH $612,000
HIV Prevention Intervention for Young Transgender Women.

The study is a The purpose of this study is to test the efficacy of a uniquely targeted HIV risk reduction intervention for young transgender women (YTW), ages 16 to 24, at risk for HIV acquisition or transmission.

UM1AI069536 (Spector, UCSD) 12/01/2013-11/30/2020 # calendar
NIH/NIAID $360,307
Units for HIV/AIDS Clinical Trials Networks: HIV CURE CTU

This project participates in clinical research proposed by the International Maternal Pediatric Adolescent AIDS Clinical Trial (IMPAACT) network. The CTU is located at the University of California San Diego (UCSD) with Stephen A. Spector serving as the PI. Four Clinical Research Sites (CRSs) are located at Baylor College of Medicine in Houston (William T. Shearer, Leader), Lurie Children's Hospital in Chicago (Northwestern - Ram Yogev, Leader), St. Jude Children's Research Hospital/University of Tennessee in Memphis (Patricia Flynn, Leader), and UCSD (SA Spector, Leader). The HIV Cure CTU recruits subjects into the IMPAACT HIV-infected and at-risk populations that are historically underrepresented in clinical trials, including minorities and people of color with an emphasis on women, pregnant women, youth, children and newborns which will broaden the applicability of clinical trials performed within the DAIDS networks.

R01MH100021 (Fujimoto/Schneider) 7/1/2013-6/30/2018 # calendar
NIMH $780,000

Younger men who have sex with men (YMSM) are at increased risk of HIV and STIs in the United States.

The goal of the proposed longitudinal network study is to investigate the complex interactions between YMSM and both preventive health venues and risk venues to gain a deep understanding of the sometimes conflicting influences and complex interactions that may also provide risk and protection in the same venue. Using two mode "affiliation" social network analysis, the proposed study has potential to advance and expand the utility of social network analysis for understanding and addressing public health issues, which will provide new directions in developing venue-based network interventions and modify individual level interventions targeting those most at risk of HIV/STI infection.

R01HD075655 (Stephenson/Mimiaga/Garofalo) 4/1/2013-3/31/2018 # calendar
NICHD $800,000

From a sample of 3,360 MSM in Atlanta, Boston, and Chicago, 250 HIV-serodiscordant couples will be randomized to either Individual or Couples HIV Counseling and Testing, and then followed prospectively for two years. Couples randomized to couples-based counseling and testing will also receive a dyadic adherence intervention, with the research aimed to determine if couples testing together impacts linkage to HIV care, retention in HIV care, ART adherence and viral suppression.

R01DA041071-01 (Garofalo/Karnik) 9/15/2015-07/31/2020 # calendar
NIDA
Employing eSBI in a Community-based HIV Testing Environment for At-risk Youth

The purpose of this study is to test a structural change to the Seek, Test, Treat and Retain (STTR) model by integrating substance use screening and brief intervention into the traditional community- based HIV testing environment for young MSM and transgender women.

P30 (D'Aquila) 4/9/2015-3/31/2020
NIH
Third Coast Center for AIDS Research

The goal of the Developmental Core is to further the research priorities of the Third Coast CFAR (TC-CFAR) by soliciting and funding developmental core awards, providing strong mentorship for junior faculty and other trainees, and strengthening the capacity for HIV research in community settings.
Role: Co-I

PENDING

Pending Support

Pending Support

Program Director/Principal Investigator:
Olson, Johanna

Pending Support

Pending Support

OVERLAP: None

HIDALGO, M.

ACTIVE

R01HD075655 (Stephenson/Mimiaga/Garofalo) 4/1/13-3/31/18 # calendar
NICHD $800,000

From a sample of 3,360 MSM in Atlanta, Boston, and Chicago, 250 HIV-serodiscordant couples will be randomized to either Individual or Couples HIV Counseling and Testing, and then followed prospectively for two years. Couples randomized to couples-based counseling and testing will also receive a dyadic adherence intervention, with the research aimed to determine if couples testing together impacts linkage to HIV care, retention in HIV care, ART adherence and viral suppression.

P30AI050409-17 (Del Rio) 08/01/15 – 07/31/17 # calendar
NIH/NIAID
PrEP engagement among Latino MSM and Latina TW in Chicago

The CFAR ADELANTE mechanism is intended to decrease HIV-related health disparities in Hispanic/Latino communities, which currently bear a disproportionate burden of the HIV/AIDS epidemic and promote the mentored development of early career investigators who are focusing on HIV/AIDS in these populations.

PENDING: None

OVERLAP: None

OLSON, J.

ACTIVE

1R01HD082554-01A1 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $952,542

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

Program Director/Principal Investigator:
Olson, Johanna

PENDING: None

OVERLAP: None

SCHRAGER, S.M.

ACTIVE

W81XWH-15-1-0700 (Holloway) 09/30/15 – 09/29/17 # calendar
PH/TBI $428,524
Improving Acceptance, Integration, and Health Among LGBT Service Members

The goal of this project is to examine the acceptance, unit integration, and behavioral health outcomes of lesbian, gay, bisexual and transgender (LGBT) service members report feelings of acceptance and integration into the military and their units post-Don't Ask, Don't Tell (DADT), with the ultimate goal of developing a set of actionable recommendations for the Department of Defense aimed at improving the integration of LGBT service members into the military and the current system of health care and support.

1 R21 HD 082813-01A1 (Goldbach/Schrager) 9/25/2014 – 8/31/2016 # calendar
NIH/NICHD $177,288
Measuring Stress Among Diverse Adolescents

We will develop an instrument to measure minority stress among racial and ethnically diverse lesbian, gay and bisexual adolescents. Study results will allow for operationalization of minority stress constructs for adolescents, provide direction for the development of targeted health interventions, and provide an opportunity to measure minority stress through subsequent longitudinal design.

1 R01 DA 034067-01A1 (Lankenau) 7/1/2013 – 6/30/2018 # calendar
NIH/NIDA $301,206
Medical Marijuana, Emerging Adults & Community: Connecting Health and Policy

This five-year study will utilize quantitative and qualitative research methodologies to determine whether: (1) young medical marijuana (MM) patients experience an overall improvement in physical and psychological health; (2) young MM patients experience overall changes in patterns of misuse of alcohol, prescription, and illicit drugs; and (3) MM dispensaries exert positive or negative effects on emerging adults in their communities. Findings will guide members of the public health community towards devising MM policies that maximize health and minimize negative effects on both emerging adults and communities.

2 T73MC00008-19-00 (Vanderbilt) 7/1/2011 – 6/30/2016 # calendar
HRSA $650,973
USC/UAP LEND Project

The California Interdisciplinary Leadership Education in Neurodevelopmental and Related Disabilities (CA-LEND) Training Program prepares professionals for leadership roles in health and related professions that care for infants, children, and adolescents with, or at risk for, neurodevelopmental and related disabilities.

0000 (Schrager) 7/1/2015 – 6/30/2016 # calendar
Division of Hospital Medicine, Children's Hospital Los Angeles $83,966

This is a hard-money position supporting junior faculty development and research efforts within the Division of Hospital Medicine.

PENDING: None

OVERLAP: None

MULTIPLE PI/PD LEADERSHIP PLAN

Revised Plan for 2016 RPPR due to the retirement of Dr. Norman Spack at the Boston site in 2015. Yee-Ming Chan, M.D., added as the Principal Investigator and Jeremi Carswell, M.D., added as a Co-Investigator.

Johanna Olson, M.D., Robert Garofalo M.D., M.P.H., Stephen Rosenthal, M.D., and Dr. Yee-Ming Chan, M.D. will serve as a team of Principal Investigators on this application, each responsible and accountable to the National Institutes of Health (NIH) for the proper conduct of the research. The rationale for the decision to act as a multiple PI team is based on the fact that these four investigators bring unique experiences and knowledge that will integrate and complement one another in the implementation of this project. Additionally, the involvement of these four sites provides larger numbers than a single site could of potential participants for a research endeavor seeking to understand an uncommon experience. The PIs serve as the Medical Directors of four university-affiliated programs in the United States currently providing care for transgender youth.

Dr. Johanna Olson, M.D. (Pediatrics and Adolescent Medicine), is the Medical Director of the Center for Transyouth Health and Development at Children's Hospital Los Angeles (University of Southern California). She and her team based at CHLA, including Co-Is Marvin Belzer, M.D., Leslie Clark, Ph.D., M.P.H., and Sheree Schrager, Ph.D., M.S., lead the largest transgender youth program in the United States. The combined expertise of this team provides both comprehensive clinical knowledge and extensive research expertise in the area of transgender adolescents. Patients seek care at this center from as far away as Shanghai. While we acknowledge that Dr. Olson, the lead PI, is still early in her career, she is surrounded by an experienced team of mentors at her own site and at the three other sites participating in the proposed project. Dr. Belzer has extensive experience managing clinical trials, including his participation as a site PI in the NICHD supported REACH and ATN Networks for the past 20 years as well as the PACTG/IMPAACT Network for 15 years. Dr. Belzer will serve as the primary mentor for Dr. Olson, a role he has had for the past four years. Drs. Clark and Schrager bring an extensive portfolio of skills including the design and implementation of behavioral interventions, expertise in research methodology and statistical analysis, and prior experience managing multi-site studies.

Dr. Yee-Ming Chan, M.D. (Pediatric Endocrinology), and his team, including Co-Is Psychologist Amy Tishelman, Ph.D., and Jeremi Carswell, M.D., are principals in Boston Children's Hospital's Gender Management Service (GeMS) which opened in2007. GeMS was the first pediatric academic program in the western hemisphere to treat pubescent teens. Dr. Chan is Director of the Reproductive Endocrinology Program; provides clinical care to patients with disorders of puberty, patients with disorders of sex development, and transgender youth; and conducts clinical and translational research in these areas. 75% of GeMS' patients come from a 150 mile radius of Boston; the rest come from throughout the US. Dr. Carswell is the clinical director of the GeMS Program, and Dr. Tishelman is a clinical psychologist with significant expertise in scholarship and clinical realms; before joining the GeMS team she was the Director of Child Protection Clinical Services at Boston Children's Hospital and subsequently Director of Training and Research for that program. She has decades of experience evaluating children and families and is a recognized expert in the area of trauma and interpersonal violence with an interest in helping vulnerable children and adolescents.

Dr. Robert Garofalo, M.D., M.P.H. (Pediatrics and Adolescent Medicine), is Co-Director of the Gender and Sex Development Program, Division Head of Adolescent Medicine at Lurie Children's Hospital of Chicago, and Associate Professor of Pediatrics at Northwestern University's Feinberg School of Medicine. He will serve as the PI for the Chicago site. He and his team, including Co-Is Marco Hidalgo, Ph.D., Lisa Simons, M.D., Courtney Finlayson, M.D., and Scott Leibowitz, M.D., Diane Chen Ph.D., and Ethicist Joel Frader, M.D., bring a wealth of expertise caring for and conducting research in adolescent populations, with particular focus on transgender and other sexual minority youth. The Chicago team has been providing clinical services to gender non- conforming youth for more than a decade. Their multidisciplinary program for gender non-conforming youth and transgender youth undergoing medical suppression of puberty or initiating cross-sex hormone therapy brings together experts in pediatrics/adolescent care, endocrinology, psychology and child development, psychiatry, surgical subspecialties, and medical ethics. The team has extensive experience conducting NIH- funded multisite clinical and behavioral research with marginalized populations of youth.

Dr. Stephen M. Rosenthal, M.D. (Pediatric Endocrinology), Professor of Pediatrics, Program Director for Pediatric Endocrinology, Co-Director of the Disorders of Sex Development Clinic, and Medical Director of the Child and Adolescent Gender Center (CAGC) at the University of California San Francisco (UCSF) Benioff Children's Hospital, is an established clinical investigator with greater than 30 years of experience in child and adolescent endocrinology. He will serve as PI for the UCSF site. His Co-Investigator, Diane Ehrensaft, Ph.D., and Mental Health Director of the UCSF CAGC, is an internationally recognized child psychologist/gender specialist. His Co-Investigator, David Glidden, Ph.D., Professor of Epidemiology and Biostatistics at UCSF, brings extensive expertise in research design and statistical analysis. The UCSF CAGC has been providing multi-disciplinary care for gender non-conforming/transgender youth and adolescents for the past six years. The UCSF CAGC is the only such multi-disciplinary gender program in Northern California and attracts patients not only from California, but from as far away as Florida and Egypt.

Primary Roles and Areas of Responsibility for Each PI

- Administrative
  - Upon successful funding, the award will be made to Children's Hospital Los Angeles (CHLA). All participants will be enrolled at one of the four study sites – The Center for Transyouth Health and Development (CHLA), The Child and Adolescent Gender Center (University of California San Francisco), The Gender, Sexuality and HIV Prevention Center (Lurie Children's Hospital of Chicago), or the Gender Management Service (Boston Children's Hospital). Drs. Olson, Garofalo, Rosenthal, and Chan will work collaboratively to prepare reports and other requirements for submission to the NIH. Each will oversee the administrative responsibilities at each of their respective institutions.
- Technical
  - Dr. Olson, given her experience conducting the pilot studies that serve as the principal preliminary data for the current application, will work with Drs. Rosenthal, Chan, and Garofalo to finalize study implementation protocols at each site, so that each site carries out the project in the same manner. Data will be collected systematically, with identical operating procedures including CRFs, ACASI programming, and data flow sheets to facilitate the creation of a data repository that is suitable for analysis and available for all four sites to explore. The data will be owned equally by each of the four participating sites.
  - Dr. Olson will oversee the protocols for data collection, including physiologic and psychosocial at each site.
  - All four PIs will finalize protocols for each cohort in the study and standardize these to ensure that there is consistency in delivery across the four study sites.
  - All four PIs, with the project directors/Co-Is at each site, will direct recruitment, retention, data collection, and intervention delivery, with support from the project team at each of their respective sites. Data will be stored at all sites and safely transferred via secure protocols to CHLA for cleaning and merging.
  - Drs. Clark and Schrager will direct data management, including integration and verification at CHLA.
  - Drs. Clark, Schrager, and Glidden will direct data analysis at CHLA and UCSF.
  - Dr. Garofalo will be involved in scientific direction and support data interpretation and dissemination.

Governance/Structure

- Communication plan
  - These four sites are positioned across the U.S., necessitating ongoing communication via teleconference. The investigators have budgeted for a training at the beginning of the study, in which all of the teams will meet at one of the principal sites. The investigators have also budgeted travel for mid-study team meetings that will allow the research team to review study progress and ensure successful completion. In the final year, the investigators have budgeted travel for the purpose of meeting around data analysis, interpretation, and manuscript writing.
  - During the accelerated startup phase of the study, the PIs and Co-Is will meet twice weekly via Skype/phone with the project managers at each site to discuss scientific issues, intervention sessions, recruitment, implementation, etc. Additional meetings will be scheduled with members of the study team as needed.

  - Decisions on scientific direction will be made during the weekly meetings. Dr. Olson will make final decisions on the delivery of the intervention protocol, whereas Drs. Clark and Schrager will make final decisions regarding instruments, data collection tools, and the statistical analyses for manuscript preparation.
- Procedures for resolving conflicts – The four sites have determined that the following domains may require third party arbitration in the event of conflict that is not resolved through discussion amongst the sites:
  - Authorship dispute – issues of conflict will be heard by an objective observer from the WPATHexecutive board.
  - Scientific dispute – scientific conflict will be arbitrated by a pediatric endocrinologist faculty member at Children's Hospital of Pennsylvania.
  - Safety – a data safety monitoring board will be established by the end of month three to provide periodic assessment of the protocol and preliminary results, and assist with conflict arising from potential safety issues.
- Distribution of resources to four sites – CHLA will be the primary institution for the receipt of the award and the three other sites will be supported through subcontracts from CHLA. Primary responsibility for administration at the CHLA site is Dr. Marvin Belzer, along with financial administrator Priscilla Brown. This team has extensive experience with financial administration of multiple site projects.

Dissemination

- In order to share process and outcome data from this project with the broader scientific community, abstracts will be submitted for presentation to at least one scientific conference per year. Conferences where data may be presented include annual meetings of the Society for Adolescent Health and Medicine, The American Academy of Pediatrics, The World Professional Association of Transgender Health, Pediatric Academic Societies, The Endocrine Society, The American Public Health Association, The American Psychological Association, The American Psychiatric Association, and others. Manuscripts are planned on the following topics:
  - Description of the sample and preliminary results
  - Description of the intervention
  - Primary outcomes

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES? Not Applicable
E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE? NOTHING TO REPORT
E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER? Not Applicable
E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)? NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

Due to the paucity of validated measures that could be utilized in evaluating the medical and psychosocial impact of using GnRH agonists and cross-sex hormones with transgender and gender non-conforming youth, the time required for the PIs and Co-Is to find and select the best measures took longer than originally planned in the timeline. This was slightly further confounded by the fact that just over a month was lost at the beginning of the reporting period due to receipt of the NOA being delayed until mid-August. This in turn, led to a delay in the submission of the finalized protocol to the CHLA IRB; however, we expect to have full IRB approval before the end of May, and recruitment should begin in June at the CHLA site. Due to the large volume of new patients accessing the four sites, we believe that we will meet the enrollment goals with at least 75% of the participants on study prior to the close of the next reporting period.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: The Impact of Early Medical Treatment in Transgender Youth

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional	Address

		District	
Primary: Children's Hospital Los Angeles	052277936	CA-028	4650 Sunset Blvd., MS #97 Los Angeles CA 900276062
Boston Children's Hospital	076593722	MA-007	300 Longwood Avenue Boston MA 021155724
Lurie Children's Hospital of Chicago	074438755	IL-005	225 East Chicago Avenue Chicago IL 606143393
University of California at San Francisco	094878337	CA-012	400 Parnassus Ave, Second Floor San Francisco CA 941430296
CHILDREN'S HOSPITAL LOS ANGELES	052277936		4650 Sunset Boulevard Mailstop #97 LOS ANGELES CA 900276062
Children's Hospital Los Angeles	052277936	CA-028	4650 Sunset Blvd., MS #97 Los Angeles CA 900276062
Boston Children's Hospital	076593722	MA-007	300 Longwood Avenue Boston MA 021155724
Lurie Children's Hospital of Chicago	074438755	IL-005	225 East Chicago Avenue Chicago IL 606143393
University of California at San Francisco	094878337	CA-012	400 Parnassus Ave, Second Floor San Francisco CA 941430296

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 1037621

Using an Existing Dataset or Resource: No

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial: No

Study Title: The Impact of Early Medical Treatment in Transgender Youth

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	1	1		0	0					**2**
Asian	19	16		0	0					**35**
Native Hawaiian or Other Pacific Islander	1	1		0	0					**2**
Black or African American	41	40		0	0					**81**
White	109	67		12	10					**198**
More than One Race	34	14		28	22					**98**
Unknown or Not Reported										
Total	**205**	**139**		**40**	**32**					**416**

Cumulative Enrollment

Comments: Enrollment has not yet initiated.

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0	0	0	0	0	0	0	0	**0**
Asian	0	0	0	0	0	0	0	0	0	**0**
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	**0**
Black or African American	0	0	0	0	0	0	0	0	0	**0**
White	0	0	0	0	0	0	0	0	0	**0**
More than One Race	0	0	0	0	0	0	0	0	0	**0**
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	**0**
Total	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**

A. COVER PAGE

Project Title: The Impact of Early Medical Treatment in Transgender Youth	
Grant Number: 5R01HD082554-03	**Project/Grant Period:** 08/01/2015 - 06/30/2020
Reporting Period: 07/01/2016 - 06/30/2017	**Requested Budget Period:** 07/01/2017 - 06/30/2018
Report Term Frequency: Annual	**Date Submitted:** 05/10/2017
Program Director/Principal Investigator Information: JOHANNA L OLSON , BS MS MD **Phone number:** (818) 679-6757 **Email:** jolson@chla.usc.edu	**Recipient Organization:** CHILDREN'S HOSPITAL OF LOS ANGELES 4650 Sunset Boulevard Mailstop #97 LOS ANGELES, CA 900276062 **DUNS:** 052277936 **EIN:** 1951690977A1 **RECIPIENT ID:** 8011-RGF009152-00
Change of Contact PD/PI: N/A	
Administrative Official: NAGHMA AHMAD 4650 Sunset Blvd, MS# 97 Los Angeles, CA 900276062 **Phone number:** 323-361-8560 **Email:** nahmad@chla.usc.edu	**Signing Official:** KAREN SUE NIEMEIER 4650 Sunset Blvd. #84 Los Angeles, CA 90027 **Phone number:** 3233616309 **Email:** kniemeier@chla.usc.edu
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The objective of the research is to provide evidence-based data to inform clinical care for transgender youth. The study will leverage the partnership between four, university-affiliated, gender clinics across the U.S. to recruit two developmental cohorts and conduct a multi-site, observational study examining the safety of hormonal interventions and the physiological and psychosocial outcomes associated with these treatments.

The Specific Aims are:

Aim 1: To evaluate the impact of GnRH agonists administered for puberty suppression, on mental health, psychological well-being, physiologic parameters, and bone health as well as document the safety of GnRH agonists in an early-pubertal cohort (Tanner stages 2-3; n=80) of transgender children and adolescents, comparing baseline and follow-up assessments at 6 months, 1 year, and 2 years after initiating treatment.

Hypothesis 1a: Patients treated with GnRH agonists will exhibit decreased symptoms of depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

Hypothesis 1b: GnRH agonists will be tolerable and safe for early-pubertal transgender youth, i.e., fasting lipids and glucose, liver enzymes, electrolytes, insulin, and HbA1c will not increase above clinically safe ranges.

Hypothesis 1c: Raw bone density scores will remain stable for early-pubertal transgender youth receiving GnRH agonists; however, age-matched z-scores may decrease.

Aim 2: To evaluate the impact of cross-sex hormones administered for gender transition on mental health, psychological well-being, and metabolic/physiologic parameters as well as document the safety of cross- sex hormones in a late-pubertal cohort (Tanner stages 4-5; n=200) of transgender adolescents, comparing baseline and follow up assessments at 6 months, 1 year, and 2 years after initiating treatment.

Hypothesis 2a: Patients treated with cross-sex hormones will exhibit decreased symptoms of gender dysphoria, depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

Hypothesis 2b: Cross-sex hormones will be tolerable and safe to use for late-pubertal transgender youth initiating phenotypic transition, i.e., will not increase fasting lipids and glucose, liver enzymes, electrolytes, and hemoglobin above clinically safe ranges.

Aim 3 (Exploratory): Based on evidence of high rates of substance use and HIV infection in some transgender adolescents (specifically, young transgender women), we will determine substance use and sexual risk behavior over time. A priori hypotheses regarding the impact of hormone treatment on sexual and substance use behaviors cannot be specified given that these behaviors increase through adolescence.

This multi-center study will be the first in the U.S. to evaluate longitudinal outcomes of medical treatment for transgender youth, and it will provide highly needed evidence-based data on the physiological and psychosocial effects and safety of treatments currently used for transgender youth.

B.1.a Have the major goals changed since the initial competing award or previous report?

Yes

Revised goals:

The objective of the research is to provide evidence-based data to inform clinical care for transgender youth. The study leverages the partnership between four, university-affiliated, gender clinics across the U.S. to recruit two developmental cohorts and conduct a multi-site, observational study examining the safety of hormonal interventions and the physiological and psychosocial outcomes associated with these treatments.

The major objective of the study (above) has not changed since the previous report; however, minor revisions were made to the specific aims. Revisions include increasing the Cross-Sex cohort to an n of 300 (240 for analysis with a 20% attrition) in order to include up to 60 cross-sex hormone youth who had a GnRH agonist to prevent puberty; expanding the Tanner Stage inclusion criteria for the Blocker Cohort; and adding an 18-month assessment for both cohorts.

The revised Specific Aims are:

Aim 1: To evaluate the impact of GnRH agonists administered for puberty suppression, on mental health, psychological well-being, physiologic parameters, and bone health as well as document the safety of GnRH agonists in early and late pubertal cohorts (Tanner stages 2-4; n=80) of transgender children and adolescents, comparing baseline and follow-up assessments at 6 months, 1 year, 18 months, and 2 years after initiating treatment.

Hypothesis 1a: Patients treated with GnRH agonists will exhibit decreased symptoms of depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

Hypothesis 1b: GnRH agonists will be tolerable and safe for early-pubertal transgender youth, i.e., fasting lipids and glucose, liver enzymes, electrolytes, insulin, and HbA1c will not increase above clinically safe ranges.

Hypothesis 1c: Raw bone density scores will remain stable for early-pubertal transgender youth receiving GnRH agonists; however, age-matched z-scores may decrease.

Aim 2: To evaluate the impact of cross-sex hormones administered for gender transition on mental health, psychological well-being, and metabolic/physiologic parameters as well as document the safety of cross- sex hormones in a late-pubertal cohort (Tanner stages 4-5; n=240) of transgender adolescents, comparing baseline and follow up assessments at 6 months, 1 year, 18 months, and 2 years after initiating treatment.

Hypothesis 2a: Patients treated with cross-sex hormones will exhibit decreased symptoms of gender dysphoria, depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

Hypothesis 2b: Cross-sex hormones will be tolerable and safe to use for late-pubertal transgender youth initiating phenotypic transition, i.e., will not increase fasting lipids and glucose, liver enzymes, electrolytes, and hemoglobin above clinically safe ranges.

Aim 3 (Exploratory): Based on evidence of high rates of substance use and HIV infection in some transgender adolescents (specifically, young transgender women), we will determine substance use and sexual risk behavior over time. A priori hypotheses regarding the impact of hormone treatment on sexual and substance use behaviors cannot be specified given that these behaviors increase through adolescence.

This multi-center study will be the first in the U.S. to evaluate longitudinal outcomes of medical treatment for transgender youth, and it will provide highly needed evidence-based data on the physiological and psychosocial effects and safety of treatments currently used for transgender youth.

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: 2017 RPPR Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

During the third grant year, the study sites will continue to recruit subjects to both cohorts and conduct the month 6 study visits. In addition, the 1-year study visits will be starting in July 2017. The CHLA Coordinating Center research team will continue ongoing data management and cleaning activities. We will continue basic analyses of the initial data to ensure that the data are accurately representing the study population, to examine initial data on study population, and to begin work on manuscripts. Preliminary data analysis activities include reviewing screening tool data for those enrolled vs. those not enrolled and examining initial differences in demographics, risk behaviors, and mental health for the two cohorts.

The team also plans to continue working on preparing manuscripts for publication. Manuscript plans include:
•A manuscript outlining the process of multisite collaboration and the challenges of choosing measures that capture the impact of gender dysphoria and subsequent medical intervention in a culturally relevant manner.
•A descriptive paper(s) on the baseline data based on cohort – including differences between sites, gender, race, etc.

The study coordinators will continue to participate in monthly conference calls to share best practices, discuss challenges that arise, receive ongoing training and technical assistance, and ensure protocol fidelity. All sites will continue ongoing risk-based and random quality assurance activities, including verifying the accuracy and completeness of chart abstraction, confirming data entry, reviewing consent/assent/permission documents to ensure they are complete and valid, and ensuring protocol fidelity during study visits.

The principal investigators will continue with semimonthly calls throughout the third year. In addition, a project meeting is scheduled for September 25 and 26, 2017, in Los Angeles, and all principal investigators, co-investigators, study coordinators, and coordinating site research team members are invited. The agenda will focus on wrapping up recruitment, any ongoing challenges with protocol implementation, quality assurance activities, preliminary results, data request needs and protocols, dissemination of results via conference presentations, and manuscript outlines and plans.

Modifications to the original plans, as discussed in F Changes and B Accomplishments, are: 1) increasing the N for the Cross-Sex Youth Cohort to 300 in order to include up to 60 youth who have previous GnRH agonist experience to prevent puberty; 2) the expansion of the Blocker Youth Cohort inclusion criteria from Tanner Stage 2 – 3 to 2 – 4; 3) the inclusion of an 18-month assessment; and 4) the change in the neuropsychiatric assessment tool from the DISC to the Mini International Neuropsychiatric Interview (M.I.N.I.) or Mini International Neuropsychiatric Interview for Children and Adolescents (M.I.N.I. Kid).

B.2. ACCOMPLISHMENTS

This second year of research implementation commenced with the enrollment of the first study participant in July 2016. Since then, the four sites have enrolled a total of 174 participants (24 blocker cohort; 24 parent/guardian of blocker cohort; 126 cross-sex hormone cohort). To date, our follow-up retention rate is 100%. It is expected that the study will meet its recruitment goals.

Initial data from youth enrolled in the Blocker Youth Cohort across all study sites (n=24) show that participants range in age from 8 to 14 years old, with a mean age of 11 +/- 1.7 years. Half (50%) of all Blocker Youth Cohort participants were assigned female at birth, and half (50%) were assigned male at birth. Ninety percent of Blocker Youth self-identify as white, and 15% self-identify as Hispanic or Latino. All Blocker Youth report being currently enrolled in school, with grade levels ranging from 3rd grade to 9th grade. A quarter of participants are enrolled in the 5th grade, 35% report that they are currently enrolled in the 6th grade, and 20% are enrolled in the 8th grade.

Within the Cross-Sex Hormone (CSH) Cohort, 126 participants have been enrolled across all study sites. Participants range in age from 12 to 20 years old, with a mean age of 16 +/- 1.9 years. About two thirds of CSH participants (67%) were assigned female at birth and 33% assigned male at birth. Over half (60%) of CSH participants self-identify as white, and 25% self-identify as Hispanic or Latino. The vast majority (82%) of CSH participants report that they are students, with 67% having completed at least the eighth grade. Approximately 14% report their current educational status as 8th grade or less, and less than 10% have completed their high school education.

In October 2016, the principal and co-investigators, study coordinators, and coordinating center research team met for two days in Los Angeles to discuss progress, implementation activities, and future undertakings, including data analysis and dissemination. During this meeting, one of the most significant, in-depth discussions was regarding the youth and parent informant versions of the Diagnostic Interview Schedule for Children (DISC and DISC-Y) that were being utilized. The study coordinators conveyed that participants were reporting that the DISC was too lengthy and mentally and emotionally onerous and that body language of participants during the DISC endorsed the participant feedback. As it required such thorough examination of numerous potential diagnoses, participants were finding it overwhelming to complete, especially for those participants who were easily triggered by the extensive detailed questioning involved in the interview process. There were concerns that for some participants, conducting the DISC interview may further pathologize participants as related to their gender dysphoria. After much discussion and recognizing that it was a significant change to the measures, it was decided that the DISC and DISC-Y would be replaced with the Mini International Neuropsychiatric Interview (M.I.N.I.) and the M.I.N.I.

Kid for Children and Adolescents. After IRB approval, the M.I.N.I. (age 17 and older at baseline) and the M.I.N.I. Kid (age 16 and younger at baseline) have been utilized to interview the participants, and for some participants their parents/legally authorized representative, with a much more positive response from participants.

As protocol implementation became more solidly grounded at the sites, the regularity of the principal investigator calls has decreased from weekly to semimonthly. During these calls the focus has been on recruitment and enrollment, quality assurance, advances in healthcare for transgender youth (including additional examination of the Lupron AERS article produced by the Kaiser Health News), plans for analyses and publication of initial data, and the addition of needed measures (breast hemi-circumference measures, Ferriman-Gallwey scale, and positive/negative side effects of using cross-sex hormones added to the follow-up visit survey for the cross-sex hormone cohort). Amendments reflecting changes made to the protocol were submitted to and approved by the coordinating and local IRBs prior to implementation.

The study coordinators participated in monthly conference calls throughout the grant year. These calls provided an opportunity to discuss recruitment efforts, share best practices in conducting research visits and abstracting data, support protocol fidelity, and provide technical assistance in response to challenges encountered. Site visits were conducted at UCSF and Boston Children's Hospital by the coordinating center to perform quality assurance activities and provide technical assistance. These visits were helpful in ensuring that the protocol was being implemented with fidelity and that the data being collected were uniform across sites and accurately represented the clinical care provided and impact of the utilization of GnRH agonists or cross-sex hormones.

While members of the principal and co-investigator, study coordinator, and coordinating center research teams have attended transgender healthcare conferences, including USPATH, Gender Spectrum, and Gender Odyssey, there have not yet been any formal presentations to communities of interest. The principal and co-investigators have presented on transgender healthcare; however, they did not share data from this protocol as of yet.

C. PRODUCTS

C.1 PUBLICATIONS
Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?
No
C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)
Nothing to report
C.3 TECHNOLOGIES OR TECHNIQUES
NOTHING TO REPORT
C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES
Have inventions, patent applications and/or licenses resulted from the award during the reporting period?
No
C.5 OTHER PRODUCTS AND RESOURCE SHARING
NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
ERA Commons Username	Y	Olson, Johanna L	BS,MS,MD	PD/PI	Months Devoted to Project					NA
	Y	ROSENTHAL, STEPHEN M	BA,MD	PD/PI						NA
	Y	Chan, Yee-Ming	BS,PHD,MD	PD/PI						NA
	Y	GAROFALO, ROBERT	BS,MPH,MD	PD/PI						NA
	N	McAvoy-Banerjea, Julie	MPH	Clinical Research Manager						NA
	N	Abrams, Mere		Study Coordinator						NA
	N	Bigelow, Lou	BA	Clinical Research Coordinator						NA
	N	Brache, Shelly		Secretarial/Clerical/Research Assistant						NA
	N	Desai, Mona	MPH	Evaluation Manager						NA
	N	Jensen, Jennifer	ARNP	Research Nurse						NA
	N	Lash, Brenna		Project Coordinator						NA
	N	Pilcher, Sarah		Research Nurse						NA
ERA Commons Username	N	Tishelman, Amy C.		Co-Investigator						NA
	N	Okonta, Vivian		Non-Student Research Assistant						NA
	N	Kim, Peter		Non-Student Research Assistant						NA
	N	Ehrensaft, Diane	PHD	Co-Investigator						NA
ERA Commons Username	N	Clark, Leslie Frances	PHD,MPH	Co-Investigator						NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other

Sum - Person Months (Summer)	NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

Yes

Dr. Scott Leibowitz, Psychiatry Co-Investigator, was budgeted at # calendar months at the Lurie Children's Hospital of Chicago site across all 5 years. He left the institution and is not supporting research activities for this project. He was removed from the budget prior to project implementation, and no project funding has been utilized to support him.

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: 2017 RPPR Other Support.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

No

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PHS 2590/RPPR OTHER SUPPORT

BELZER, M.E.

ACTIVE

(NEW)

Adolescent Trials Network (Naar/Parsons) 9/1/2016 – 5/31/2020 # calendar
NIH/NICHD $77,786

The goal of this project is to conduct studies focused on the process of improving self-management in youth living with HIV. Strategies include the identification of interventions that are efficacious and effective for improving self-management in at risk and YLH, and how the assessment of the five components of self-management and how these vary over time, are directly improved by interventions and mediate intervention effects.

1 U01 DA036926 (Kipke) 8/15/2015 – 7/31/2020 # calendar
NIH/NIDA $497,353

The goal of this project is to recruit and track for cohort of young MSM of color in order to better understand their disproportionately high rates of HIV infection and low rates of linkage to and engagement in HIV-related care and to develop new interventions to reduce HIV/STI risk and transmission and HIV disease progression.

1R01HD082554 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

1R01MH108442 (Outlaw) 8/1/2015 – 4/30/2020 # calendar
NIH/NIMH $123,864

The goal of this research is test a brief, 2-session, computer-delivered motivational intervention to prevent adherence difficulties among youth newly prescribed ART.

1 CPIMP141084-01-00 (Martinez) 9/30/2014 – 8/30/2017 # calendar
HHS/Office of Minority Health $375,000
HIV/AIDS Initiative for Minority Men (AIMM)

The goal of the project is to develop a coordinated system of HIV prevention and care for YMSM of color in Los Angeles in partnership with local stakeholders and youth.

INACTIVE:

5 U01 HD 040474-14 (Korelitz) 4/16/2001 – 02/28/2017 Months Devoted to Project calendar
NIH/NICHD via Westat $450,000
Adolescent Medicine Trials Network for HIV/AIDS Interventions

The major goals of this project are to conduct research, both independently and in collaboration with existing research networks and individual investigators, in HIV-infected and HIV-at-risk pre-adolescents, adolescents, and young adults up to age 25 years.

OVERLAP: None

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CARSWELL, J.
ACTIVE

1 R01 HD082554-01A1 (Olson) 8/01/2015 – 6/30/2020 Months Devoted to Project calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The major goal of this research project is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in early pubertal and late pubertal transgender youth.

OVERLAP: None

CHAN, Y.
ACTIVE

(NEW)
R01 HD090071 (Chan) 4/11/2017-3/31/2022 calendar
NIH/NICHD $207,500
Delayed Puberty: Causes and Consequences, Genotypes and Phenotypes

The goal of this project is to chart the clinical heterogeneity, adult outcomes, and genetic causes of delayed puberty.

(NEW)
R01 HD089521 (Hirschhorn, Holm) 7/1/2016-6/30/2021 # calendar
NIH/NICHD $75,000
Exome Sequencing in Disorders of Sex Development: Impact on Patients and Families

The goals of this project are to identify genetic causes of disorders of sex development and related conditions through whole-exome sequencing, and to assess the impact of returning genetic results on families.

(NEW)
R21 HD089526 (Crerand, Tishelman) 7/1/2016-6/30/2018 # calendar
NIH/NICHD $66,880
Quality of Life and Psychosocial Functioning in Adolescents and Young Adults with Disorders of Sex Development

The goals of this project are to assess quality of life, resilience, and psychosocial well-being in adolescents and young adults with disorders of sex development, to measure the effects of genital appearance, fertility issues, and how patients learned about their diagnosis on these outcomes, and to identify mediators and moderators of these effects.

R01 HD082554 (Olson) 8/1/2015-6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of this multi-site observational study is to examine the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in early-pubertal and late-pubertal transgender youth.

R01 HD074579 (Wisniewski) 5/1/2015-4/30/2018 # calendar
NIH/NICHD $5,000
Short-Term Outcomes of Interventions for Reproductive Dysfunction

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The goals of this project are to assess physician and parent perceptions of outcomes of genital surgery in children with ambiguous genitalia, and to examine the impact on parental stress.

OVERLAP: None

CHEN, D.
ACTIVE

(NEW)
R21 HD087839 (Chen) 1/23/2017 – 12/31/2018 # calendar
NICHD $125,000
Structured Pubertal Suppression Readiness Assessment for Gender Dysphoric Youth

The goal of this study is to develop an assessment tool that can aid mental health clinicians in systematically assessing readiness for pubertal suppression treatment from a medical decisional capacity framework.

(NEW)
Targeted Research Grant (Chen) 1/1/2017 – 12/31/2017 # calendar
Private Support $20,000
Development of a Fertility-Related Decision Aid for Transgender Youth and Their Parents

The objective of this study is to expand the scope of the REACH grant funding to recruit a younger cohort of peri-pubertal transgender youth and conduct a decisional needs assessment of youth and their parents in an effort to develop a patient-centered Decision Aid About Fertility for Transgender Youth (DAAF-TY).

(NEW)
R01 NR017098 (Mimiaga/Garofalo) 10/1/16 – 9/30/21 # calendar
NINR $496,006
Adaptive Intervention Strategies Trial for Strengthening Adherence to Antiretroviral HIV Treatment among Youth

The purpose of this study is to determine the efficacy of the Positive STEPS, stepped-care intervention in comparison to standard-of-care comparison condition on the primary outcomes: Improvements in HIV viral load and ART adherence among HIV infected adolescents, ages 16-24, who are prescribed ART.

1R01HD082554 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

OVERLAP: None

CLARK, L.
ACTIVE

(NEW)
90AP2683-01-00 (Clark) 9/30/2016 – 9/29/2021 # calendar
Project Legacy for Homeless Youth $960,000

The goal for this project is test the effectiveness of an intervention to reduce pregnancies and sexually transmitted disease among homeless adolescents or those at risk for homelessness. Using a randomized

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group design, approximately 600 youth (15-19) receiving youth services half of youth will be assigned to receive either a six week, 11 session behavioral intervention (Project Legacy) or to a usual services control condition and followed for 1 year.

1R01HD082554 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

90AP2674 (Desai) 9/30/2010 – 9/29/2017 # calendar
ACYF, PREIS $421,903
Evaluation of AIM 4 Teen Moms

The goal for this proposed project is to reduce rapid repeat pregnancies among teen mothers under age 21. Approximately 1,200 pregnant teens and teen parents (ages 14-18) will be enrolled into the project and randomly assigned to either intervention (an adapted version of Project AIM called AIM 4 Teen Moms) or a control group and followed for 2 years.

OVERLAP: None

EHRENSAFT, D.
ACTIVE
1R01HD082554 (Olson) 8/1/2015 – 6/30/2020 calendar
NIH/NICHD $991,416

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

OVERLAP: None

FINLAYSON, C.
ACTIVE
(NEW)
R21 HD087839 (Chen) 1/23/2017 – 12/31/2018
NICHD $125,000
Structured Pubertal Suppression Readiness Assessment for Gender Dysphoric Youth

The goal of this study is to develop an assessment tool that can aid mental health clinicians in systematically assessing readiness for pubertal suppression treatment from a medical decisional capacity framework.

(NEW)
Targeted Research Grant (Chen) 1/1/2017 – 12/31/2017
Private Support $20,000
Development of a Fertility-Related Decision Aid for Transgender Youth and Their Parents

The objective of this study is to expand the scope of the REACH grant funding to recruit a younger cohort of peri-pubertal transgender youth and conduct a decisional needs assessment of youth and their parents in an effort to develop a patient-centered Decision Aid About Fertility for Transgender Youth (DAAF-TY).

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1R01HD082554 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

INACTIVE
0000 (Finlayson) 4/1/2015 – 3/31/2016 # calendar
Private Support $9,000
Germ Cells in Gonads of Patients with Disorders of Sex Development

The study is to determine the presence and quality of germ cells in gonads of patients with disorders of sex development who have undergone gonadectomy.

OVERLAP: None

FRADER, J.
ACTIVE
1R01HD082554 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

INACTIVE
0000 (Michelson) 1/1/2015-12/31/15 # calendar
Private Support $7,332
Improving Communication in the Pediatric Intensive Care Unit

The purpose of this study is to improve processes impacting communication in the Pediatric Intensive Care Unit at Lurie Children's Hospital.

0000 (Michelson) 1/1/2015-12/31/15 # calendar
Private Support $1,283
Cancer Care in the PICU

The purpose of this support is to assess the oncological care provided in Lurie's Children's Pediatric Intensive Care Unit.

OVERLAP: None

GAROFALO, R.
ACTIVE
(NEW)
R21 HD087839 (Chen) 1/23/2017 – 12/31/2018 # calendar
NICHD $125,000
Structured Pubertal Suppression Readiness Assessment for Gender Dysphoric Youth

OMB No. 0925-0002 (Rev. 11/16 Approved Through 10/31/2018)

The goal of this study is to develop an assessment tool that can aid mental health clinicians in systematically assessing readiness for pubertal suppression treatment from a medical decisional capacity framework.

(NEW)
3U24HD089880-01S1 (Carpenter) 9/30/2016-5/31/2021 # calendar
NIH/NICHD
(Prime) Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) Coordinating Center. SubProject: Work to Prevent: Employment as HIV Prevention for Young Men who have Sex with Men and Transgender Women

The objective of the proposed study is to target economic stability (i.e., employment) as a structural-level intervention for preventing adolescent HIV risk. In particular, the proposed study will adapt and pilot-test an effective theoretically-driven, employment training program for HIV-positive adults (iFOUR) to the needs of at-risk YMSM/YTW, ages 16-24. This study is responsive to the NIH HIV/AIDS high priority topic by specifically addressing health disparities in the incidence of new HIV infections. Further, the proposed project includes populations at elevated risk for HIV infection and addresses health and social issues that are clearly linked with HIV

(NEW)
1U01PS005140-01 (Kuhns/Perloff/Garofalo) 9/30/2016-9/29/2020 # calendar
CDC $54,700
Evaluation of TransLife Center: A Locally-Developed Combination Prevention Intervention for Transgender Women at High Risk of HIV Infection

The study will address the current gap in transgender-specific combination HIV prevention interventions by testing a promising and potentially effective, culturally specific, and highly accessible intervention to reduce disparities in TW by directly targeting the social determinants of HIV infection in this extremely high risk group.

(NEW)
1R01NR017098-01 (Garofalo/Mimiaga) 9/26/2016-6/30/2021 # calendar
NINR $300,000
Adaptive intervention strategies trial for strengthening adherence to antiretroviral HIV treatment among youth

The goal of this project is to test the efficacy of a stepped-care “adaptive” ART adherence intervention (“Positive STEPS”) for HIV infected adolescents, ages 16 to 24. Stepped-care is an efficiency healthcare delivery model in which the least resource intensive part of an intervention is delivered first, and only those who do not improve then receive the high intensity, more resource intensive part of an intervention.

(NEW)
1U01MD011279-01 (Schnall/Garofalo/Kuhns) 9/1/2016-4/30/2021 # calendar
NIH $120,000
A Pragmatic Clinical Trial of MyPEEPS Mobile to Improve HIV prevention behaviors in Diverse Adolescent MSM

Using a participatory approach, our study will incorporate user-centered design in the translation of the MyPEEPS intervention onto a mobile platform. MyPEEPS was tested with older adolescents (16-18 year olds) and prior to the availability of non-occupational post-exposure prophylaxis (nPEP) and pre-exposure prophylaxis (PrEP); therefore, in addition to the mobile adaptation, we will update the intervention content.

(NEW)
1R21NR017097-01 (Dworkin/Garofalo) 9/01/2016-8/31/2018 # calendar
NIH $6,929

OMB No. 0925-0002 (Rev. 11/16 Approved Through 10/31/2018)

Strategically Measuring Adherence in Real-time in Young African American MSM

This award will develop and pilot a mobile phone application that improves the proportion of young African American men who have sex with men (MSM) engaged in the HIV Care Continuum. The preliminary impact of this project will inform the design of a large scale randomized controlled trial.

R21 NR16420-01 (Dworkin/Garofalo) 9/28/2015-8/31/2017 # calendar
NIH (R21) $4,619
May I Help You? An Avatar Health Concierge for HIV-infected African American MSM

This exploratory/developmental application proposes to systematically develop and then evaluate the feasibility, acceptability, utilization, and preliminary impact of a theory-based innovative Avatar mobile phone application to engage young HIV-infected African American men who have sex with men in multiple stages of the HIV Care Continuum.

R01DA041071-01 (Garofalo/Karnik) 9/15/2015-7/31/2020 # calendar
NIDA
Employing eSBI in a Community-based HIV Testing Environment for At-risk Youth

The purpose of this study is to test a structural change to the Seek, Test, Treat and Retain (STTR) model by integrating substance use screening and brief intervention into the traditional community-based HIV testing environment for young MSM and transgender women.

1R01HD082554 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

R01MH100021 (Fujimoto/Schneider) 7/1/2013-6/30/2018 # calendar
NIMH $780,000
Younger men who have sex with men (YMSM) are at increased risk of HIV and STIs in the United States.

The goal of the proposed longitudinal network study is to investigate the complex interactions between YMSM and both preventive health venues and risk venues to gain a deep understanding of the sometimes conflicting influences and complex interactions that may also provide risk and protection in the same venue. Using two mode "affiliation" social network analysis, the proposed study has potential to advance and expand the utility of social network analysis for understanding and addressing public health issues, which will provide new directions in developing venue-based network interventions and modify individual level interventions targeting those most at risk of HIV/STI infection.

INACTIVE

P30 (D'Aquila) 4/9/2015-3/31/2020
NIH
Third Coast Center for AIDS Research

The goal of the Developmental Core is to further the research priorities of the Third Coast CFAR (TC-CFAR) by soliciting and funding developmental core awards, providing strong mentorship for junior faculty and other trainees, and strengthening the capacity for HIV research in community settings.

UM1AI069536 (Spector, UCSD) 12/01/2013-11/30/2020 # calendar
NIH/NIAID $360,307

OMB No. 0925-0002 (Rev. 11/16 Approved Through 10/31/2018)

Units for HIV/AIDS Clinical Trials Networks: HIV CURE CTU

This project participates in clinical research proposed by the International Maternal Pediatric Adolescent AIDS Clinical Trial (IMPAACT) network. The CTU is located at the University of California San Diego (UCSD) with Stephen A. Spector serving as the PI. Four Clinical Research Sites (CRSs) are located at Baylor College of Medicine in Houston (William T. Shearer, Leader), Lurie Children's Hospital in Chicago (Northwestern - Ram Yogev, Leader), St. Jude Children's Research Hospital/University of Tennessee in Memphis (Patricia Flynn, Leader), and UCSD (SA Spector, Leader). The HIV Cure CTU recruits subjects into the IMPAACT HIV-infected and at-risk populations that are historically underrepresented in clinical trials, including minorities and people of color with an emphasis on women, pregnant women, youth, children and newborns which will broaden the applicability of clinical trials performed within the DAIDS networks.

R01HD075655 (Stephenson/Mimiaga/Garofalo) 4/1/2013-3/31/2018 # calendar
NICHD $800,000
CVCTPlus: A Couples-Based Approach to Linkage to Care and ARV Adherence

From a sample of 3,360 MSM in Atlanta, Boston, and Chicago, 250 HIV-serodiscordant couples will be randomized to either Individual or Couples HIV Counseling and Testing, and then followed prospectively for two years. Couples randomized to couples-based counseling and testing will also receive a dyadic adherence intervention, with the research aimed to determine if couples testing together impacts linkage to HIV care, retention in HIV care, ART adherence and viral suppression.

R01MH094323-01 (Garofalo/Mimiaga) 6/13/2011 – 3/31/2016 # calendar
NIMH $612,000
HIV Prevention Intervention for Young Transgender Women

The study is a The purpose of this study is to test the efficacy of a uniquely targeted HIV risk reduction intervention for young transgender women (YTW), ages 16 to 24, at risk for HIV acquisition or transmission.

OVERLAP: None

GLIDDEN, D.

ACTIVE

1R01HD082554 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

INACTIVE

U01 AI069911 (Martin) 8/5/2006 - 7/31/2016 # calendar
NIH $12,264
East Africa IEDEA Regional Consortium

The major goal of this research is to contribute and analyze data for the International Epidemiologic Databases to Evaluate AIDS (IEDEA) from the Mbarara, Uganda-based ISS and UARTO cohorts.

OVERLAP: None

OMB No. 0925-0002 (Rev. 11/16 Approved Through 10/31/2018)

HIDALGO, M.
ACTIVE

(NEW)
1U01MD011279-01 (Schnall/Garofalo/Kuhns) 9/1/2016-4/30/2021 # calendar
NIH (U01)
A Pragmatic Clinical Trial of MyPEEPS Mobile to Improve HIV prevention behaviors in Diverse Adolescent MSM

Using a participatory approach, our study will incorporate user-centered design in the translation of the MyPEEPS intervention onto a mobile platform. MyPEEPS was tested with older adolescents (16-18 year olds) and prior to the availability of non-occupational post-exposure prophylaxis (nPEP) and pre-exposure prophylaxis (PrEP); therefore, in addition to the mobile adaptation, we will update the intervention content.

P30AI050409-17 (Del Rio) 8/1/2015 – 7/31/2017 # calendar
NIH/NIAID
PrEP Engagement among Latino MSM and Latina TW in Chicago

The CFAR ADELANTE mechanism is intended to decrease HIV-related health disparities in Hispanic/Latino communities, which currently bear a disproportionate burden of the HIV/AIDS epidemic and promote the mentored development of early career investigators who are focusing on HIV/AIDS in these populations.

1R01HD082554 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

R01HD075655 (Stephenson/Mimiaga/Garofalo) 4/1/2013-3/31/2018 # calendar
NIH/NICHD $800,000

From a sample of 3,360 MSM in Atlanta, Boston, and Chicago, 250 HIV-serodiscordant couples will be randomized to either Individual or Couples HIV Counseling and Testing, and then followed prospectively for two years. Couples randomized to couples-based counseling and testing will also receive a dyadic adherence intervention, with the research aimed to determine if couples testing together impacts linkage to HIV care, retention in HIV care, ART adherence and viral suppression.

OVERLAP: None

OLSON-KENNEDY, J.
ACTIVE

1R01HD082554-01A1 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

OVERLAP: None

OMB No. 0925-0002 (Rev. 11/16 Approved Through 10/31/2018)

ROSENTHAL, S.

ACTIVE

1R01HD082554-01A1 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

Private Support (Rosenthal) 02/28/2014 – 02/07/2024 # calendar
Private Support $22,988
An Open-Label, Long-Term Extension Study of the Safety and Efficacy of A Long-acting Human Growth Hormone (VRS-317) in Children with Growth Hormone Deficiency

The major goals of this project are to evaluate the safety, tolerability, and efficacy of a long-acting human growth hormone in children with growth hormone deficiency.

INACTIVE

R01 HD 068138 (Vilain) 9/26/2011 – 6/30/2016 # Calendar
NIH/NICHD $32,276
Disorders of Sex Development: Platform for Basic and Translational Research

The major goals of this project are to establish a research infrastructure and multi-site consortium to examine the genetic determinants and psychological consequences of Disorders of Sexual Development (DSD) and to provide improved evidence-based and standardized diagnostic and treatment protocols for patients and families affected by DSD.

OVERLAP: None

SCHRAGER, S.

ACTIVE

W81XWH-15-1-0700 (Holloway) 9/30/2015 – 9/29/2017 # calendar
PH/TBI $428,524
Improving Acceptance, Integration, and Health Among LGBT Service Members

The goal of this project is to examine the acceptance, unit integration, and behavioral health outcomes of lesbian, gay, bisexual and transgender (LGBT) service members report feelings of acceptance and integration into the military and their units post-Don't Ask, Don't Tell (DADT), with the ultimate goal of developing a set of actionable recommendations for the Department of Defense aimed at improving the integration of LGBT service members into the military and the current system of health care and support.

1R01HD082554-01A1 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

1 R21 HD 082813-01A1 (Goldbach/Schrager) 9/25/2014 – 8/31/2017 # calendar
NIH/NICHD $177,288
Measuring Stress Among Diverse Adolescents

OMB No. 0925-0002 (Rev. 11/16 Approved Through 10/31/2018)

We will develop an instrument to measure minority stress among racial and ethnically diverse lesbian, gay and bisexual adolescents. Study results will allow for operationalization of minority stress constructs for adolescents, provide direction for the development of targeted health interventions, and provide an opportunity to measure minority stress through subsequent longitudinal design.

1 R01 DA 034067-01A1 (Lankenau) 7/1/2013 – 6/30/2018 # calendar
NIH/NIDA $301,206
Medical Marijuana, Emerging Adults & Community: Connecting Health and Policy

This five-year study will utilize quantitative and qualitative research methodologies to determine whether: (1) young medical marijuana (MM) patients experience an overall improvement in physical and psychological health; (2) young MM patients experience overall changes in patterns of misuse of alcohol, prescription, and illicit drugs; and (3) MM dispensaries exert positive or negative effects on emerging adults in their communities. Findings will guide members of the public health community towards devising MM policies that maximize health and minimize negative effects on both emerging adults and communities.

INACTIVE
2 T73MC00008-19-00 (Vanderbilt) 7/1/2011 – 6/30/2016 # calendar
HRSA $650,973
USC/UAP LEND Project

The California Interdisciplinary Leadership Education in Neurodevelopmental and Related Disabilities (CA-LEND) Training Program prepares professionals for leadership roles in health and related professions that care for infants, children, and adolescents with, or at risk for, neurodevelopmental and related disabilities.

0000 (Schrager) 7/1/2015 – 6/30/2016 # calendar
Division of Hospital Medicine, Children's Hospital Los Angeles $83,966

This is a hard-money position supporting junior faculty development and research efforts within the Division of Hospital Medicine.

OVERLAP: None

SIMONS, L.
ACTIVE
1R01HD082554-01A1 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

(NEW)
UM1AI069536 (Spector, UCSD) 12/01/13-11/30/20 # calendar
NIH/NIAID $274,842
Units for HIV/AIDS Clinical Trials Networks: HIV CURE CTU

This project participates in clinical research proposed by the International Maternal Pediatric Adolescent AIDS Clinical Trial (IMPAACT) network. The CTU is located at the University of California San Diego (UCSD) with Stephen A. Spector serving as the PI. Four Clinical Research Sites (CRSs) are located at Baylor College of Medicine in Houston (William T. Shearer, Leader), Lurie Children's Hospital in Chicago (Northwestern - Ram Yogev, Leader), St. Jude Children's Research Hospital/University of Tennessee in Memphis (Patricia Flynn, Leader), and UCSD (SA Spector, Leader). The HIV Cure CTU recruits subjects

into the IMPAACT HIV-infected and at-risk populations that are historically underrepresented in clinical trials, including minorities and people of color with an emphasis on women, pregnant women, youth, children and newborns which will broaden the applicability of clinical trials performed within the DAIDS networks.

OVERLAP: None

TISHELMAN, A.
ACTIVE
(NEW)
R21 HD089526-01 (Crerand, Tishelman) 9/12/2016 – 8/31/2018 # calendar
NIH
Factors Influencing Psychosocial Outcomes in Disorders of Sex Development

The goal of this research is to conduct a cross-sectional study using a mixed-methods qualitative and quantitative approach to examine diagnosis-related and general developmental factors associated with resilience, quality of life and psychosocial adjustment in adolescents and young adults with DSD conditions.

1R01HD082554-01A1 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

OVERLAP: None

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES? Not Applicable
E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE? NOTHING TO REPORT
E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER? Not Applicable
E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)? NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

In order to completely capture the impact on all youth undergoing treatment with GnRH agonists, recruitment will be expanded to include those youth in Tanner 4 of development. In addition, the minimum age for the cross-sex hormone cohort inclusion criteria was decreased from 13 to 8 to ensure that a potential participant who could be eligible for cross-sex hormones based on Tanner Staging would not be excluded due to age alone. The Principal Investigators assert that this will not impact the data analysis and results of the research study.

Due to the substantial burden on participants for completing the DISC, the Principal Investigators and Co-Investigators decided to stop utilizing the DISC and implement the Mini International Neuropsychiatric Interview (M.I.N.I.) and the M.I.N.I. for Children and Adolescents (M.I.N.I. Kid), version 7.0.2 for DSM-5, as a replacement. This transition means that there is a portion of participants for whom we are missing the baseline diagnostic data due the time it takes for coordinating center and local IRBs to approve the transition in instruments.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

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F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

F.3.a. HUMAN SUBJECTS

In order to completely capture the impact on all youth undergoing treatment with GnRH agonists, recruitment will be expanded to include those youth in Tanner 4 of development. Due to the increased use of GnRH agonists to prevent puberty, the cross-sex hormone cohort was increased from 240 to 300 to allow for up to 60 blocker-experienced youth in the cross-sex hormone cohort. An 18-month assessment was added in order to better capture change that may be occurring mid-year. A neuropsychiatric diagnostic interview was added to obtain data regarding the presences of diagnoses and not just symptoms of diagnoses. Additional data being captured include: concomitant medications, breast hemi-circumference measurements, Modified Ferriman-Gallwey Scale, medical procedures, and symptoms of using cross-sex hormones.

PROTECTION OF HUMAN SUBJECTS

Risks to Human Subjects

a. Human Subjects Involvement, Characteristics, and Design

Transgender children and adolescents, those who experience incongruence between assigned birth sex and internal gender identity, are a poorly understood and distinctly understudied population in the United States. The limited available data suggest that transgender youth who are gender dysphoric (persistently distressed about their gender incongruence) are at increased risk for numerous health disparities in comparison to their peers, including higher rates of anxiety, depression, suicide, and substance use. The development of undesired secondary sex characteristics during puberty intensifies the distress associated with gender incongruence and increases the risk for these conditions. Current clinical practice guidelines include strategies for treating transgender youth with the use of: 1) gonadotropin releasing hormone (GnRH) agonists to suppress endogenous puberty in early pubertal adolescents in order to avoid the development of undesired secondary sex characteristics and 2) cross sex hormones to induce masculine or feminine features in late pubertal adolescents. The goal of these interventions is to decrease gender dysphoria and ameliorate other potential negative health outcomes. These guidelines are used at academic and community-based centers across the U.S.; however, they are only partially empirically derived and based on very limited data, largely from non-U.S. sources. Further, there are no data available examining the physiologic and metabolic consequences of these treatments in adolescents. This represents an obvious gap in the literature that has significant implications for clinical practice across the U.S. The general lack of U.S. data leaves healthcare providers uncertain about optimal care for these highly vulnerable youth. This proposed research will fill gaps in knowledge, provide empirical evidence to inform

clinical care, and would be the first study of its kind evaluating longitudinal outcomes of medical treatment for multi-ethnic, transgender youth in the U.S.

The proposed research study will collect data from 388 transgender youth (88 early pubertal [Tanner stages 2, 3, and 4] and 300 late pubertal youth [Tanner stages 4 and 5]) and 88 parents of the early pubertal group in order to evaluate the impact of hormone therapy. The number of participants with previous blocker experience to prevent puberty is limited to 60 of the 300 late pubertal youth cohort.

Potential participants will be receiving services at one of the four sites (Boston, Chicago, Los Angeles, and San Francisco) and seeking hormonal intervention to either delay the progression of puberty through the use of GnRH agonists or begin phenotypic gender transition by adding cross-sex hormones. Recruitment will be conducted by one of the care providers at the site, and ongoing retention will be supported through the participants receiving transgender care services.

Inclusion criteria for early pubertal cohort includes the presence of gender dysphoria, expressed anxiety about endogenous puberty and/or the development of undesired secondary sexual characteristics, Tanner stage 2, 3, or 4 of sexual development, and a desire to undergo puberty suppression. Patients and parents/legal guardians must be able to read and understand English. To be eligible for enrollment, the participants cannot have utilized GnRH agonists or hormones prior to the initial visit.

Inclusion criteria for the late pubertal cohort includes transgender youth between 8 and 21 years of age with gender dysphoria, Tanner stage 4 or 5 of sexual development, and an interest in pursuing a phenotypic gender change with cross-sex hormones. Patients must be able to read and understand English. To be eligible for enrollment, the participants cannot have utilized cross-sex hormones prior to the initial visit.

The involvement of children is required as this study focuses on transgender youth who are either early pubertal or late pubertal. The hormonal interventions are ideally utilized in Tanner stages 2, 3, and 4 for puberty delay or Tanner stages 4 and 5 for phenotypic gender change. No other special vulnerable populations will be enrolled.

Physiologic, psychosocial, behavioral, and medical data will be collected at the baseline visit (T0), 6 months (T1), 12 months (T2), 18 months (T3) and 24 months (T4). The timeline for data collection is correlated with expected standard of care clinical visits so as to not overly burden the participants or their parents/legal guardians with additional study visits. Physiologic data will be abstracted from medical records or directly from participants; demographic, psychosocial, and behavioral data will be collected via Audio Computer-Assisted Self-Interviewing (ACASI) technology; diagnostic data will be collected via interview using validated instruments.

The research is being conducted at Children's Hospital Los Angeles, University of California San Francisco Benioff Children's Hospital, Lurie Children's Hospital of Chicago, and Boston Children's Hospital in order to investigate the impact of the treatment on multi-ethnic transgender youth in the United States. These four academic hospitals situated strategically across the country have dedicated transgender youth clinics and are considered the national leaders in the care of transgender children and adolescents. All four sites employ a similar model for care that includes medical and mental health professionals and represent some of the most experienced providers in the country doing this work.

ACASI data collected at the collaborating sites will be encrypted and transferred to CHLA. Upon transfer of the encrypted data to CHLA, the data will be stored on CHLA's secured network (with firewall protection), which cannot be accessed by anyone outside of CHLA. All case report forms (CRFs) will be entered into password protected databases at the site and be transmitted securely with an ID core to CHLA. A password will be used to access survey data and chart abstraction files and will be made accessible only to the Principal Investigators and study staff. These data will be archived in a password-protected database on the local network on a daily basis. The data coordination staff, housed at CHLA, will support all PIs with the generation of a cross-site protocol for data collection and templates for the Institutional Review Boards at each site. Study-wide data management procedures, including integration and verification of multi-site data, will take place at CHLA.

b. Sources of Materials

Case report forms (CRFs) will be used for abstracting physiological and anthropomorphic parameters (height, weight, BMI, Tanner stage, breast hemi-circumference, Modified Ferriman-Gallwey Scale), hormone levels and other relevant lab results, medications, diagnoses, insurance status, and bone health data.

Data will be collected directly from participants and the parents/legal guardians of the early pubertal group, via ACASI to minimize concerns about confidentiality. Demographic data for the early pubertal group collected will include age, ethnicity, educational level and birth city/country, as well as data specific to the transgender population, such as age of realization of transgender status, age of first living in the desired gender role, and domains where they are living in their desired gender role, if any. Demographic, mental health, and behavioral data will also be collected from the parents of the youth in the early pubertal group.

Demographic data for the late pubertal group collected will include age, ethnicity, educational level, and birth city/country, as well as data specific to the transgender population, such as age of realization of transgender status, age of first transitioning or

"real life experience" in the desired gender role, prior sexual activity, sexual orientation, previous hormone use, and length of treatment. Psychosocial indicators from the late pubertal group include gender dysphoria, quality of life, body esteem, depression, suicidal ideation, drug use, sex work, and high-risk sexual behavior. Data will be collected from the late pubertal group regarding the symptoms they experience from the use of cross-sex hormones.

Diagnostic data will be collected annually through verbal interview via the Mini International Neuropsychiatric Interview (M.I.N.I.) version 7.0.2 for DSM-5 or the Mini International Neuropsychiatric Interview for Children and Adolescents (M.I.N.I. Kid) version 7.0.2 for DSM-5.

Only site-specific research staff and local institution IRB personnel conducting quality assurance activities will have access to individually identifiable private information about the participants.

No personal identifying information (e.g., name, tracking information, etc.) will be placed on any of the CRFs or collected within the ACASI survey. All study-specific records will be identified by a coded number only, to maintain confidentiality. Only the research staff will have access to the database linking the participant's unique ID code and name in a secure network, password-protected file or in a secure location under double-lock when not in use and with restricted access during work hours and/or when unattended.

Data will be collected or abstracted by trained research staff and recorded on CRFs. All CRFs will be entered into password protected databases at the site and transmitted securely with an ID to CHLA.

For the ACASI baseline and follow-up surveys each participant will be assigned a code and their pre- and post-surveys will be linked via this code. A master list of the codes assigned to participants will be kept in a secure, password protected file at each site or in a secured location under double-lock when not in use and with restricted access during work hours and/or when unattended.

c. Potential Risks

The risks of participation in this study are minimal and are not greater than those that would be accepted by other persons not participating in the study. Participants are expected to be exposed only to minimal risk based on questions asked and the confidential system of data collection. While all safeguards will be in place to protect their identity, there is also potential risk that identifying information collected could be accessed by someone other than the research team. A number of precautions and safeguards have been developed in order to protect the confidentiality of individuals who participate in the study. No personal identifying information will be used on the

CRFs or ACASIs. Consent forms will be filed and stored separate from the raw data in a secured location under double-lock when not in use and with restricted access during work hours and/or when unattended.

As this is an observational study, there are no alternative treatments or procedures.

Adequacy of Protection Against Risks

a. Recruitment and Informed Consent

Site care members will recruit participants for the study by speaking with patients and their parents/legal guardians face-to-face or by telephone. Information regarding the study will be provided and interest in participation will be assessed.

If the potential participants are interested in enrolling in the study, staff members from Children's Hospital Los Angeles, Boston Children's Hospital, Lurie Children's Hospital of Chicago, and University of California at San Francisco who have received IRB certification will consent participants. The Institutional Review Boards at all sites requires that all research participants review and sign an informed consent/permission/assent form or be given an information sheet (if a waiver of written consent is obtained). The informed consent/permission/assent form covers information about the overall purpose of the study, what the study entails, potential risks, potential benefits to participating individuals and society, the confidentiality of data, and contact information for the Principal Investigator and the IRB. Once informed consent/permission/assent has been obtained, the research staff will have the form reviewed by a fellow research team member, who will confirm that it is fully completed before it is filed in a secure location under double-lock when not in use and with restricted access during work hours and/or when unattended.

For participants aged 7 to 13 years old, the participant will sign an age-appropriate assent form, and the parent/legal guardian will sign a consent/permission/assent form.

For participants aged 14 to 17 years old, the participant and the parent/legal guardian will sign a consent/permission/assent form.

For participants aged 18 years or older, the participant will sign a consent/permission/assent form.

Project Staff will inform participants that they have the right to skip any survey questions that make them feel uncomfortable. Participants will be informed that participation is completely voluntary and that they are free to stop their involvement in the study at any time without any negative consequences. They will be informed of their rights to privacy and confidentiality and will be told that their answers to the survey will be kept confidential and not shared with others outside of the research staff. They will be

informed that no information about them or provided by them during the research will be disclosed to others without their written permission, except if necessary to protect their rights or welfare (for example, if they are injured and need emergency care) or if required by law (i.e., child or elder abuse, harm to self or others, or reports of certain infectious diseases).

Participation in all phases of the data collection process is voluntary. There will be no mandatory participation through any venue (e.g., court-ordered, condition of probation, compliance with agreement to work, or to maintain housing). The consent/permission/assent form clearly states that participation is voluntary and that a decision to not participate is entirely up to each individual.

b. Protections Against Risk

A number of precautions and safeguards have been developed in order to protect the confidentiality of individuals who participate in the study.

No personal identifying information (e.g., names) of the participants will appear in any computer files associated with this research project in any location. Participants will be assigned a unique identification number code. A key file that matches the ID number to the participant and organization will be maintained in a secure data repository within the project offices at each of the four sites. Data will be kept strictly confidential, except as required by law, and stored on a secure network, with password protection such that only authorized users will have access to the file server. All computers will be located in locked facilities, and consent forms will be filed and stored separate from the raw data in a secured location under double-lock when not in use and with restricted access during work hours and/or when unattended. Any temporary data files kept on removable storage devices, as well as printouts derived from data analysis, will be stored in a locked compartment when not in use.

After a subject completes the ACASI survey at a site, the ACASI data will be secured by being saved in a password-protected compressed file. As each section of the survey is completed, the section will be saved and encrypted so that no one is able to look at previous screens to view the data. If the subject completing the interview requires a short break, it is possible to stop the interview and return later to complete it. Only authorized users with a login name and password will be able to open the survey on the laptop.

Data will remain on the CHLA server during data collection, verification, cleaning, and analysis. At the closure of the study, electronic and hardcopy data will be maintained for a minimum of six years per CHLA IRB policy. The local site data will be retained at the local site for the length of time as defined the local site's IRB policy. Project binders at

CHLA containing archival information will be stored a minimum of six years and will then be eligible to be destroyed.

The research staff and protocol will be certified through the local IRB at each of the four sites to conduct research on human subjects, especially as related to children. This observational study is 46.404, research not involving greater than minimal risk, and 46.408 requirements for permission by parents or guardians and for assent by children will be followed. Within the first two months of funding, the project staff will submit an application to the IRB for protocol approval. Throughout the project, staff will continue to work with IRB at their respective sites to protect the rights and confidentiality of all individuals who participate in data collection.

As this is an observational study, adverse events are not anticipated. However, there is some risk that answering questions about some of the topics may be uncomfortable or upsetting. In the event of discomfort or upset, there are medical and psychological professionals on the research team who can provide ongoing support as needed. Participants do not have to answer any question in the computerized interview that they do not want to answer. Furthermore, participants will be informed that at any point, they may stop if they do not wish to continue the questionnaire. In the event of an adverse event, it will be reported to the IRB as per protocol to ensure the safety of participants.

Potential Benefits of the Proposed Research to Human Subjects and Others

While there are no potential direct benefits to the research participants, the risks involved in this study are minimal and the anticipated societal benefits outweigh them.

Importance of the Knowledge to be Gained

As described above the risks involved in this study are minimal and the anticipated societal benefits outweigh them. The proposed research provides the opportunity to obtain a better understanding of transgender youth, improve their care, and share information on a local and national level about how to provide care and hormone therapy for gender dysphoric children and adolescents. The information that is learned from this project will support innovative approaches to identifying, understanding, and providing optimal care for early pubertal and late pubertal, multi-ethnic transgender youth.

Data and Safety Monitoring Plan

Not applicable as the proposed research does not include a clinical trial.

ClinicalTrials.gov Requirements

Not applicable as the proposed research does not include a clinical trial.

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: The Impact of Early Medical Treatment in Transgender Youth

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

Yes

Peter Kim, research associate, completed the Collaborative Institutional Training Initiative (CITI) Human Subjects Research course. The course provides an introduction to research with a focus on the protection of human subjects, and it offers historic and current information on regulatory and ethical issues important to the conduct of research involving human subjects.

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: Children's Hospital Los Angeles	052277936	CA-028	4650 Sunset Blvd., MS #97 Los Angeles CA 900276062
Boston Children's Hospital	076593722	MA-007	300 Longwood Avenue Boston MA 021155724
Lurie Children's Hospital of Chicago	074438755	IL-005	225 East Chicago Avenue Chicago IL 606143393
University of California at San Francisco	094878337	CA-012	400 Parnassus Ave, Second Floor San Francisco CA 941430296
CHILDREN'S HOSPITAL LOS ANGELES	052277936		4650 Sunset Boulevard Mailstop #97 LOS ANGELES CA 900276062
Children's Hospital Los Angeles	052277936	CA-028	4650 Sunset Blvd., MS #97 Los Angeles CA 900276062
Boston Children's Hospital	076593722	MA-007	300 Longwood Avenue Boston MA 021155724
Lurie Children's Hospital of Chicago	074438755	IL-005	225 East Chicago Avenue Chicago IL 606143393
University of California at San Francisco	094878337	CA-012	400 Parnassus Ave, Second Floor San Francisco CA 941430296
CHILDREN'S HOSPITAL LOS ANGELES	052277936		4650 Sunset Boulevard Mailstop #97 LOS ANGELES CA 900276062
Children's Hospital Los Angeles	052277936	CA-028	4650 Sunset Blvd., MS #97 Los Angeles CA 900276062
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CHILDREN'S HOSPITAL LOS ANGELES	052277936		4650 Sunset Boulevard Mailstop #97 LOS ANGELES CA 900276062
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Boston Children's Hospital	076593722	MA-007	300 Longwood Avenue Boston MA 021155724
Lurie Children's Hospital of Chicago	074438755	IL-005	225 East Chicago Avenue Chicago IL 606143393
University of California at San Francisco	094878337	CA-012	400 Parnassus Ave, Second Floor San Francisco CA 941430296

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 1037621

Using an Existing Dataset or Resource: No

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial: No

Study Title: The Impact of Early Medical Treatment in Transgender Youth

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	1	1		0	0					**2**
Asian	19	16		0	0					**35**
Native Hawaiian or Other Pacific Islander	1	1		0	0					**2**
Black or African American	41	40		0	0					**81**
White	109	67		12	10					**198**
More than One Race	34	14		28	22					**98**
Unknown or Not Reported										
Total	**205**	**139**		**40**	**32**					**416**

Cumulative Enrollment

Comments: Enrollment data as of 4/30/17.

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	2	0	0	0	0	0	0	0	0	**2**
Asian	4	1	0	0	0	0	0	0	0	**5**
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	**0**
Black or African American	6	3	0	0	0	0	0	0	0	**9**
White	70	38	0	0	0	0	0	0	0	**108**
More than One Race	8	2	0	2	4	0	0	0	0	**16**
Unknown or Not Reported	23	11	0	0	0	0	0	0	0	**34**
Total	**113**	**55**	**0**	**2**	**4**	**0**	**0**	**0**	**0**	**174**

A. COVER PAGE

Project Title: The Impact of Early Medical Treatment in Transgender Youth	
Grant Number: 5R01HD082554-04	**Project/Grant Period:** 08/01/2015 - 06/30/2020
Reporting Period: 07/01/2017 - 06/30/2018	**Requested Budget Period:** 07/01/2018 - 06/30/2019
Report Term Frequency: Annual	**Date Submitted:** 05/15/2018
Program Director/Principal Investigator Information: JOHANNA L OLSONKENNEDY , BS MS MD MS **Phone number:** 323-361-3128 **Email:** jolson@chla.usc.edu	**Recipient Organization:** CHILDREN'S HOSPITAL OF LOS ANGELES 4650 Sunset Boulevard Mailstop #97 LOS ANGELES, CA 900276062 **DUNS:** 052277936 **EIN:** 1951690977A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: NAGHMA AHMAD 4650 Sunset Blvd, MS# 97 Los Angeles, CA 900276062 **Phone number:** 323-361-8560 **Email:** nahmad@chla.usc.edu	**Signing Official:** MANNY TRINIDAD SUNGA CHILDREN'S HOSPITAL LOS ANGELES 4650 SUNSET BLVD LOS ANGELES, CA 900276062 **Phone number:** 3233612131 **Email:** msunga@chla.usc.edu
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The objective of the research is to provide evidence-based data to inform clinical care for transgender youth. The study leverages the partnership between four, university-affiliated, gender clinics across the U.S. to recruit two developmental cohorts and conduct a multi-site, observational study examining the safety of hormonal interventions and the physiological and psychosocial outcomes associated with these treatments.

The major objective of the study (above) has not changed since the previous report; however, minor revisions were made to the specific aims. Revisions include increasing the Cross-Sex cohort to an n of 300 (240 for analysis with a 20% attrition) in order to include up to 60 cross-sex hormone youth who had a GnRH agonist to prevent puberty; expanding the Tanner Stage inclusion criteria for the Blocker Cohort; and adding an 18-month assessment for both cohorts.

The revised Specific Aims are:

Aim 1: To evaluate the impact of GnRH agonists administered for puberty suppression, on mental health, psychological well-being, physiologic parameters, and bone health as well as document the safety of GnRH agonists in early and late pubertal cohorts (Tanner stages 2-4; n=80) of transgender children and adolescents, comparing baseline and follow-up assessments at 6 months, 1 year, 18 months, and 2 years after initiating treatment.

Hypothesis 1a: Patients treated with GnRH agonists will exhibit decreased symptoms of depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

Hypothesis 1b: GnRH agonists will be tolerable and safe for early-pubertal transgender youth, i.e., fasting lipids and glucose, liver enzymes, electrolytes, insulin, and HbA1c will not increase above clinically safe ranges.

Hypothesis 1c: Raw bone density scores will remain stable for early-pubertal transgender youth receiving GnRH agonists; however, age-matched z-scores may decrease.

Aim 2: To evaluate the impact of cross-sex hormones administered for gender transition on mental health, psychological well-being, and metabolic/physiologic parameters as well as document the safety of cross- sex hormones in a late-pubertal cohort (Tanner stages 4-5; n=240) of transgender adolescents, comparing baseline and follow up assessments at 6 months, 1 year, 18 months, and 2 years after initiating treatment.

Hypothesis 2a: Patients treated with cross-sex hormones will exhibit decreased symptoms of gender dysphoria, depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

Hypothesis 2b: Cross-sex hormones will be tolerable and safe to use for late-pubertal transgender youth initiating phenotypic transition, i.e., will not increase fasting lipids and glucose, liver enzymes, electrolytes, and hemoglobin above clinically safe ranges.

Aim 3 (Exploratory): Based on evidence of high rates of substance use and HIV infection in some transgender adolescents (specifically, young transgender women), we will determine substance use and sexual risk behavior over time. A priori hypotheses regarding the impact of hormone treatment on sexual and substance use behaviors cannot be specified given that these behaviors increase through adolescence.

This multi-center study will be the first in the U.S. to evaluate longitudinal outcomes of medical treatment for transgender youth, and it will provide highly needed evidence-based data on the physiological and psychosocial effects and safety of treatments currently used for transgender youth.

B.1.a Have the major goals changed since the initial competing award or previous report?

Yes

Revised goals:

The objective of the research is to provide evidence-based data to inform clinical care for transgender youth. The study leverages the partnership between four, university-affiliated, gender clinics across the U.S. to recruit two developmental cohorts and conduct a multi-site, observational study examining the safety of hormonal interventions and the physiological and psychosocial outcomes associated with these treatments.

The major objective of the study (above) has not changed since the previous report; however, minor revisions were made to the specific aims. Revisions include expanding the Tanner Stage inclusion criteria for the Blocker Cohort and adding an 18-month assessment for both cohorts.

The revised Specific Aims are:

Aim 1: To evaluate the impact of GnRH agonists administered for puberty suppression, on mental health, psychological well-being,

physiologic parameters, and bone health as well as document the safety of GnRH agonists in early and late pubertal cohorts (Tanner stages 2-4; n=80) of transgender children and adolescents, comparing baseline and follow-up assessments at 6 months, 1 year, 18 months, and 2 years after initiating treatment.

Hypothesis 1a: Patients treated with GnRH agonists will exhibit decreased symptoms of depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

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Hypothesis 1c: Raw bone density scores will remain stable for early-pubertal transgender youth receiving GnRH agonists; however, age-matched z-scores may decrease.

Aim 2: To evaluate the impact of cross-sex hormones administered for gender transition on mental health, psychological well-being, and metabolic/physiologic parameters as well as document the safety of cross- sex hormones in a late-pubertal cohort (Tanner stages 4-5; n=240) of transgender adolescents, comparing baseline and follow up assessments at 6 months, 1 year, 18 months, and 2 years after initiating treatment.

Hypothesis 2a: Patients treated with cross-sex hormones will exhibit decreased symptoms of gender dysphoria, depression, anxiety, trauma symptoms, self-injury, and suicidality and increased body esteem and quality of life over time.

Hypothesis 2b: Cross-sex hormones will be tolerable and safe to use for late-pubertal transgender youth initiating phenotypic transition, i.e., will not increase fasting lipids and glucose, liver enzymes, electrolytes, and hemoglobin above clinically safe ranges.

Aim 3 (Exploratory): Based on evidence of high rates of substance use and HIV infection in some transgender adolescents (specifically, young transgender women), we will determine substance use and sexual risk behavior over time. A priori hypotheses regarding the impact of hormone treatment on sexual and substance use behaviors cannot be specified given that these behaviors increase through adolescence.

This multi-center study will be the first in the U.S. to evaluate longitudinal outcomes of medical treatment for transgender youth, and it will provide highly needed evidence-based data on the physiological and psychosocial effects and safety of treatments currently used for transgender youth.

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: 2018 TransYouthCare Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Throughout the grant year, numerous presentations, lectures, and symposiums have been conducted by project personnel both domestically and internationally. The audiences attending these educational opportunities were not limited to healthcare or research professionals, but also included transgender and gender nonconforming youth, their families, allies, advocates, other unlicensed care providers, and other types of professionals such as educators and lawyers. Of note, presenters were not only PIs and Co-Is; the study coordinators also presented on the research study process with transgender and gender nonconforming youth and their families.

Mere Abrams and Brenna Lash (study coordinators at UCSF and Boston Children's Hospital) presented at the Gender Spectrum Conference in Moraga, CA, on 7/21/17. The title of their presentation was “Conducting Research with Trans Youth Using a Participant Informed Gender-Affirmative Model.”

Drs. Diane Chen and Amy Tishelman (Co-Is at Lurie Children's Hospital of Chicago and Boston Children's Hospital) conducted a workshop titled “Ethical Dilemmas in Pediatric Transgender Health Care” at the annual convention of the American Psychological Association in Washington, D.C., in August 2017.

Dr. Courtney Finlayson (Co-I at Lurie Children's Hospital of Chicago) conducted a lecture titled “Medical Care of Transgender Youth” at the Great Plains Pediatric Endocrine Society Annual Conference in Kansas City, MO, in 2017. She was also the “Transgender Children and Adults” Moderator and Speaker at the Endocrine Society Annual Conference in Chicago, IL, in 2018.

Also at the Endocrine Society Annual Conference, Dr. Diane Tishelman (Co-I at Boston Children's Hospital) conducted an invited talk titled "Psychosocial Aspects of Transgender Medicine". Dr. Tishelman also conducted a workshop presentation titled, "Serving Transgender Youth" in April 2018, at Dartmouth Hitchcock Hospital. She was also an invited panelist for a session titled, "State of the Science Related to Gender Non-Conforming Children and Transgender Youth: The Trans Youth Research "Network"" at the Pediatric Endocrine Society, in Toronto, Canada in May 2018.

Drs. Diane Chen and Courtney Finlayson (Co-Is at Lurie Children's Hospital) conducted an oral abstract presentation titled "Knowledge of Fertility and Reproductive Health Options among Transgender Adolescents and Young Adults" at the Society of Pediatric Psychology in Orlando, FL, in April 2018. They also conducted a poster presentation on the same topic at the Oncofertility Consortium in Chicago, IL, in 2017.

Throughout this grant year, Dr. Johanna Olson-Kennedy (PI at CHLA) conducted 16 invited lectures, 2 symposiums, and 25 continuing medical education/educational lectures throughout the United States and in Mexico and Norway. Presentation venues included medical settings such as hospital and medical schools, health care professional meetings and symposiums, transgender health conferences, transgender youth conferences, and family conferences. A sample of titles include, "Caring for Gender Non-Conforming and Transgender Youth"; "Gender Dysphoria, Beyond the Diagnosis"; "Just a Boy, Just a Girl"; "Rethinking Gender"; "Transyouth Care - Self-reflection on Personal Biases and their Impact on Care"; "Providing 360 Degree Transgender Hormone Therapy: Beyond the Protocols"; "Puberty Blockers: What, When, and How"; and "Gender Non-Conforming and Transgender Children and Adolescents: A Multidisciplinary Approach."

Dr. Marco Hidalgo (Co-I at CHLA since January 2018; former Co-I at Lurie Children's Hospital until December 2017) was an invited panelist at Public Responsibility In Medicine and Research (PRIM&R) annual conference "Advancing Ethical Research" held in San Antonio, TX, on 11/7/17. Dr. Hidalgo also conducted two trainings to audiences of mental health professionals and trainees titled "Gender Health-related Assessments with Trans* and Gender-expansive Youth" (at Community Network Training Day in Naperville, IL, 12/1/17) and "Gender Diversity in Children and Adolescents" (at Ascend Healthcare in Encino, CA), an audience of mental health clinicians specializing in pediatric residential treatment (4/11/ 18).

Dr. Diane Ehrensaft (Co-I at UCSF) presented the following in 2018: "From Small ts to Elder Ts, Transgender Care across the Lifespan" at The Psychotherapy Institute in Berkeley, CA; "What's Your Gender? Understanding and Supporting Gender Expansive and Transgender Youth" at the GEMS Conference in Salt Lake City, UT; an invited lecture titled, "The small t in LGBT" at the University of California School of Law, Davis, CA; "Working with Gender Expansive Children and Youth" to the University of California San Francisco Medical School; and two scientific conferences titled "Adolescence as a Co-Occurring Condition" and "Working with Transgender Youth across the Developmental Span" at the USPATH Scientific Conference. In 2017, she presented "The Gender Affirmative Model of Care for Youth" at The Transgender Health Summit sponsored by UCSF; was keynote speaker ("The small t in LGBT") at the ANZPATH Annual Conference, Sydney, Australia; presented "The Gender Affirmative Model: An Interdisciplinary Approach to Child and Adolescent Care" at the Colegio Asociación Colombiana de Endocrinología Pediátrica and the Gender Infinity Professionals Conference; presented "Navigating Gender Creativity in a Gender Binary World: A Child's Challenging Journey" at Marquette University; presented "What's Your Gender? Understanding the Gender Creative Child" at the Sexual Orientation and Gender Identity Conference: Advances in Evidence-Based Psychotherapy for Gender and Sexual Minorities; "Re-learning Gender: Teaching Gender Identity Development in the Age of Gender Diversity" at the Society for Research on Child Development; and presented "Two Cultures, Same Goal: Comparison of Services for Gender Diverse Children and Adolescents" at the Gender Spectrum Professionals Symposium Workshop at UCSF and the University of Cape Town, South Africa.

Dr. Stephen Rosenthal (PI at UCSF) presented numerous invited lectures and symposia regarding our transgender youth research network during the present grant year: Internationally, Dr. Rosenthal was the National University of Singapore Wong Hock Boon Professor in Paediatrics, lecturing on "Transgender Youth: Current Concepts, Management, & Priorities for Research", and gave plenary lectures on transgender youth research at the Saudi Diabetes and Endocrine Association, 2nd Highlights of Endocrinology Conference, Al Khobar, Saudi Arabia; at the 1st Bangkok International Pediatrics Update, Thailand; at the 10th International Meeting of Pediatric Endocrinology in Washington, DC.; at the Hospital for Sick Children at the University of Toronto Faculty of Medicine, Canada; and at the 5th Annual Endocrinology Debate and Global Exchange (EDGE) Conference in Rio de Janeiro, Brazil. Nationally, Dr. Rosenthal was invited as named lecturer on transgender youth research, including the Ian M. Burr Lectureship at Vanderbilt University, and as the Del Fisher Visiting Professor at UCLA. Dr. Rosenthal was an invited lecturer on transgender youth research at the "Critical Issues Facing Children and Adolescents" conference in Salt Lake City; at the 2018 annual meetings of the Pediatric Academic Societies/Pediatric Endocrine Society ("State of the Science Related to Gender Non-Conforming Children and Transgender Youth: The Trans Youth Research Network"); and the Endocrine Society.

Finally, the team presented together at the most recent Pediatric Academic Societies meeting in Toronto in an invited science presentation entitled: State of the Science Related to Gender Non-Conforming Children and Transgender Youth: The Trans Youth Research "Network". Speakers included Rob Garofalo (PI), Johanna Olson-Kennedy (PI), Stephen Rosenthal (PI) and Amy Tishelman (Co-I).

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

During the fourth year of the grant, the study sites will continue to recruit participants in both cohorts through September 30, 2018. During this period, we hope over-recruit the cross-sex hormone cohort in order to increase the number of transfeminine youth and trans youth of color enrolled in the study. We will continue to conduct visits at baseline, and months 6, 12, and 18. In July, we will begin to conduct the final 24-month study visit. The CHLA Coordinating Center will continue to do ongoing data management and cleaning activities, which have coincided with data collection. Basic analyses of the data will continue to be conducted to ensure that the data are accurately representing the study population. In addition, the coordinating center has been conducting directed data analysis at the request of the

PIs and Co-Is to support dissemination activities, especially as it relates to lectures and symposium or conference presentations. With the closure of enrollment, the data team will begin conducting descriptive analyses of the baseline data under the guidance of the PIs and Co-Is for interpretation and manuscript development. Building on this year's manuscripts, presentations, and lectures, the PIs and Co-Is will continue to disseminate information obtained through the study activities.

The study coordinators will continue to participate in monthly conference calls to share best practices, discuss challenges that arise, receive ongoing training and technical assistance, support human subjects protection, and ensure protocol fidelity. All sites will continue ongoing risk-based and randomized quality assurance activities, including verifying the accuracy and completeness of chart abstraction, confirming data entry, reviewing consent/assent/permission documents to ensure they are complete and valid, and ensuring protocol fidelity during study visits.

The principal investigators will continue with monthly calls throughout the fourth year. In addition, a protocol team meeting will be scheduled for September or October in Los Angeles, and all principal investigators, co-investigators, study coordinators, and coordinating site research team members will be invited. The agenda will focus on any ongoing challenges with protocol implementation, preliminary data analyses, dissemination of results via conference presentations, and manuscript outlines and plans.

Under the guidance of the principal investigators and co-investigators, three study coordinators (Boston Children's Hospital, CHLA, and UCSF) are creating a sub-study to investigate participants' perceptions of their involvement in this research study. Utilizing an analysis of which questions are most often refused to be answered by participants in addition to validated research involvement measures, they are creating additional questions that will be incorporated into the 24-month survey to obtain feedback from participants. Once the questions have been finalized, the revised survey will be submitted to all IRBs for review and approval. With this additional data, the study coordinators will be able to disseminate information to researchers about the experience of youth who identify as transgender and gender nonconforming of participating in a research study focused on their gender identity.

B.2 What was accomplished under these goals?

As of April 30, 2018, we have enrolled 279 participants in the cross-sex hormone (CSH) cohort and 71 participants and their parent/legally authorized representative (LAR) in the puberty blocker (GnRHa) cohort, for a total of 421 participants. We have fully met and exceeded our enrollment goal of 240 participants for the CSH cohort. We are at 81% of our recruitment goal for the GnRHa participants and their parent/LAR, and we expect to meet our enrollment goal of 88 youth participants and 88 parent/LAR participants for the blocker cohort by September 30, 2018.

In the previous RPPR we proposed to recruit up to 60 additional participants into the CSH cohort in order to include cases in which GnRHa and CSH were prescribed to youth in the early stages of puberty. Over the past year, it has become evident that few clinical cases with this profile are observed across sites. To date, we have only recruited 19 of the 60 participants, and they make up only 6.8% of the CSH cohort. Due to low number of these types of clinical patients, we are dropping the additional objective to recruit these extra 60 participants. This does not impact the aims of the initial funded research strategy.

During this past year, we conducted baseline and 6, 12, and 18-month visits with study participants. To date, our follow-up retention rate for each study visit is as follows: 94% for the 6-month visit, 84% for the 12-month visit, and 76% for the 18-month visit. The n for the 18-month visit is only 33 visits, which began in February 2018, and we anticipate that the retention percentage will increase as we conduct more 18 month visits.

Initial data from youth enrolled in the GnRHa cohort across all study sites (n=71) show that participants range in age from 8 to 14 years old, with a mean age of 11 +/- 1.4 years. Slightly more than half (52%) of all GnRHa cohort participants are assigned female at birth, and 48% are assigned male at birth. Eighty-two percent of GnRHa cohort self-identify as white, and 18% self-identify as Hispanic or Latino. All participants of the GnRHa cohort report being currently enrolled in school, with grade levels ranging from 3rd grade to 9th grade. Slightly less than a quarter (24%) of the sample is enrolled in the 5th grade, 35% report that they are currently enrolled in the 6th grade, and 20% is enrolled in the 8th grade.

Within the CSH cohort, 279 participants have been enrolled across all study sites. Participants range in age from 11 to 20 years old, with a mean age of 16 +/- 1.9 years. About two-thirds of CSH participants (68%) are assigned female at birth and 32% assigned male at birth. Over half (63%) of CSH participants self-identify as white, and 22% self-identify as Hispanic or Latino. The vast majority (89%) of CSH participants report that they are students, with approximately 15% reporting their current educational status as 8th grade or less and 66% currently enrolled in high school. As the first

enrolled participants will not complete their ear 2 visit until July 2018, no impact data are available to report for the study objectives, aims, and hypotheses.

In September 2017, the principal investigators (PI) and co-investigators (Co-I), study coordinators, and coordinating center research team met for two days in Los Angeles for a protocol team meeting to discuss study progress, implementation activities, and future undertakings, including data analysis and dissemination. During the 2016 protocol team meeting, we decided to discontinue use of the Diagnostic Interview Schedule for Children (DISC and DISC-Y) and transition to the Mini International Neuropsychiatric Interview (M.I.N.I.) and the M.I.N.I. Kid for Children. During the 2017 protocol team meeting, the study coordinators reported that the M.I.N.I. and M.I.N.I. Kid appeared to be much more acceptable to participants than the time-intensive DISC and DISC-Y, and yields similar data. The M.I.N.I. and M.I.N.I. Kid are being conducted with participants at the Baseline, Year 1, and Year 2 study visits.

Also related to instruments, it was noted that the survey was missing an instrument to collect life events that may occur and may impact the responses to the other measures within the instrument. After researching potential life event scales, the protocol team decided to add the Adolescent Life-Change Event Scale published by Mental Health America to the Year 1 and 2 surveys.

Progress in enrolling the study population was discussed, and it was agreed that the study would not be fully enrolled by 12/31/17. It was decided that we would extend enrollment through 9/30/18 with a goal of over-recruiting transfeminine participants and participants of color for the cross-sex hormone cohort, and to reach 100% of our blocker cohort for a total of 88 participants and their parent/LAR.

PI calls have continued on a monthly basis with a focus on recruitment and enrollment, quality assurance, advances in healthcare for transgender youth, and plans for analyses and publication of initial data. Amendments reflecting changes made to the protocol were submitted to and approved by the coordinating and local IRBs prior to implementation. The study coordinators participated in monthly conference calls throughout the grant year. These calls provide an opportunity to discuss recruitment efforts, share best practices in conducting research visits and abstracting data, support protocol fidelity, and provide technical assistance in response to challenges encountered. These calls are helpful in ensuring that the protocol is being implemented with fidelity and that data are being collected uniformly across sites and accurately represent the clinical care provided and impact of the utilization of GnRHa or CSH.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	Chen D, Hidalgo MA, Leibowitz S, Leininger J, Simons L, Finlayson C, Garofalo R. Multidisciplinary Care for Gender-Diverse Youth: A Narrative Review and Unique Model of Gender-Affirming Care. Transgender health. 2016;1(1):117-123. PubMed PMID: 28861529; PubMed Central PMCID: PMC5549539.
Complete	Hidalgo MA, Chen D, Garofalo R, Forbes C. Perceived Parental Attitudes of Gender Expansiveness: Development and Preliminary Factor Structure of a Self-Report Youth Questionnaire. Transgender health. 2017;2(1):180-187. PubMed PMID: 29159312; PubMed Central PMCID: PMC5685204.
Complete	Chen D, Simons L, Johnson EK, Lockart BA, Finlayson C. Fertility Preservation for Transgender Adolescents. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2017 July;61(1):120-123. PubMed PMID: 28363716; PubMed Central PMCID: PMC5604229.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
ERA Commons Username	Y	Olson-Kennedy, Johanna L	BS,MS,MS,MD	PD/PI	Months Devoted to Project					NA
	Y	ROSENTHAL, STEPHEN M	BA,MD	PD/PI						NA
	Y	Chan, Yee-Ming	BS,PHD,MD	PD/PI						NA
	Y	GAROFALO, ROBERT	BS,MPH,MD	PD/PI						NA
	N	McAvoy-Banerjea, Julie	MPH	Clinical Research Manager						NA
	N	Bambardella, Kristian		Study Coordinator						NA
	N	Bigelow, Lou	BA	Clinical Research Coordinator						NA
	N	Buttar, Aliya	MPH	Data Manager						NA
	N	Desai, Mona	MPH	Evaluation Manager						NA
	N	Jensen, Jennifer	ARNP	Research Nurse						NA
	N	Lash, Brenna		Project Coordinator						NA
	N	Pilcher, Sarah		Research Nurse						NA
	N	Rojas, Lucas		Study Coordinator						NA
ERA Commons Username	N	Clark, Leslie Frances	PHD,MPH	Co-Investigator						NA
	N	Tishelman, Amy C.		Co-Investigator						NA
	N	Kim, Peter		Non-Student Research Assistant						NA
	N	Ehrensaft, Diane	PHD	Co-Investigator						NA
	N	Abrams, Mere		Study Coordinator						NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement

Cal - Person Months (Calendar)	DI - Diversity Supplement
Aca - Person Months (Academic)	OT - Other
Sum - Person Months (Summer)	NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: TransYouthCare 2018 RPPR Other Support.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

No

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PHS 2590/RPPR OTHER SUPPORT

NEW SENIOR/KEY PERSONNEL (D.2.b)

None

CHANGES IN OTHER SUPPORT (D.2.c)

BELZER, M.E.
ACTIVE

(NEW)
5U19HD089881 (Reback/Horvath) 9/1/2017 – 5/31/21 # calendar
NIH/NICHD $112,315

ATN: Comparing Technology-based Approaches to Increase Advancement along the HIV Prevention Continuum and Motivational PrEP Cascade among Transgender Youth
The goal of the project is to determine differential immediate and sustained effects of a Text message intervention versus a mobile App intervention versus a combined Text message + mobile App intervention among high-risk, HIV-negative trans* youth (12-24 years old) for advancement along the HIV Prevention Continuum and the Motivational PrEP Cascade.

(NEW)
1R01MD011773-01 (Cunningham) 8/8/17 – 3/31/22 # calendar
NIH/NIMHD $97,274
Youth Service Navigation Intervention for HIV+ Adolescents and Young Adults Being Released from Incarceration

The goal of this project is to adapt an existing peer navigation intervention for adults to create a Youth Service Navigation intervention sensitive to sexual and gender minority culture that guides youth to needed services along the continuum of HIV care. Using a two- group randomized control trial design, we will test the effectiveness of the new youth service navigation, youth sexual and gender minority-sensitive intervention among criminal justice-involved youth living with HIV aged 16-25, compared to controls offered standard referrals to services.

U19HD089875 (Naar/Parsons) 9/1/2016 – 5/31/2021 # calendar
NIH/NICHD $75,594
ATN: Scale It Up: Effectiveness-implementation Research to Enhance HIV-related Self-management among Youth

The goal of this project is to conduct studies focused on the process of improving self-management in youth living with HIV. Strategies include the identification of interventions that are efficacious and effective for improving self-management in at risk and YLH, and how the assessment of the five components of self-management and how these vary over time, are directly improved by interventions and mediate intervention effects.

U01DA036926 (Kipke) 8/15/2015 – 7/31/2020 # calendar
NIH/NIDA $9,963
Young Men of Color who have Sex with Men Cohort Study

The goal of this project is to recruit and track for cohort of young MSM of color in order to better understand their disproportionately high rates of HIV infection and low rates of linkage to and engagement in HIV-related care and to develop new interventions to reduce HIV/STI risk and transmission and HIV disease progression.

(THIS AWARD)
1R01HD082554 (Olson-Kennedy) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $368,000

The Impact of Early Medical Treatment in Transgender Youth
The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

OVERLAP No Overlap

INACTIVE
1 CPIMP141084-01-00 (Martinez) 9/30/2014 – 8/30/2017 # calendar
HHS/Office of Minority Health $375,000
HIV/AIDS Initiative for Minority Men (AIMM)

The goal of the project is to develop a coordinated system of HIV prevention and care for YMSM of color in Los Angeles in partnership with local stakeholders and youth.

1R01MH108442 (Outlaw) 8/1/2015 – 4/30/2018 # calendar
NIH/NIMH $123,864

The goal of this research is test a brief, 2-session, computer-delivered motivational intervention to prevent adherence difficulties among youth newly prescribed ART.

CHEN, D.
ACTIVE
(THIS AWARD)
1R01HD082554 (Garofalo) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

1R01NR017098-01 (R. Garofalo/ M. Mimiaga) 9/26/16-6/30/21 # calendar
NINR $300,000
Adaptive intervention strategies trial for strengthening adherence to antiretroviral HIV treatment among youth

The goal of this project is to test the efficacy of a stepped-care “adaptive” ART adherence intervention (“Positive STEPS”) for HIV infected adolescents, ages 16 to 24. Stepped-care is an efficiency healthcare delivery model in which the least resource intensive part of an intervention is delivered first, and only those who do not improve then receive the high intensity, more resource intensive part of an intervention.

R21 HD087839 (Chen) 1/23/2017 – 12/31/2018 # calendar
NICHD $125,000
Structured Pubertal Suppression Readiness Assessment for Gender Dysphoric Youth

The goal of this study is to develop an assessment tool that can aid mental health clinicians in systematically assessing readiness for pubertal suppression treatment from a medical decisional capacity framework.

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R01 NR017098 (Mimiaga/Garofalo) 10/1/2016 – 9/30/21 # calendar
NINR $496,006
Adaptive Intervention Strategies Trial for Strengthening Adherence to Antiretroviral HIV Treatment among Youth

The purpose of this study is to determine the efficacy of the Positive STEPS, stepped-care intervention in comparison to standard-of-care comparison condition on the primary outcomes: Improvements in HIV viral load and ART adherence among HIV infected adolescents, ages 16-24, who are prescribed ART.

OVERLAP No Overlap

GAROFALO, R.

ACTIVE
(THIS AWARD)
1R01HD082554 (Garofalo) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

R01MH100021 (K.Fujimoto/J.Schneider) 7/1/13-2/28/19 (No Cost Extension) # CM
NIMH $155,580
YMAP: Young Men's Affiliation Project of HIV Risk & Prevention Venue

The goal of the proposed longitudinal network study is to investigate the complex interactions between YMSM and both preventive health venues and risk venues to gain a deep understanding of the sometimes conflicting influences and complex interactions that may also provide risk and protection in the same venue. Using two mode "affiliation" social network analysis, the proposed study has potential to advance and expand the utility of social network analysis for understanding and addressing public health issues, which will provide new directions in developing venue-based network interventions and modify individual level interventions targeting those most at risk of HIV/STI infection.

(NEW)
R01HD075655 (Stephenson/Mimiaga/Garofalo) 4/1/13-12/31/18 (No Cost Extension) # CM
NICHD $173,500
CVCTPlus: A Couples-Based Approach to Linkage to Care and ARV Adherence

From a sample of 3,360 MSM in Atlanta, Boston, and Chicago, 250 HIV-serodiscordant couples will be randomized to either Individual or Couples HIV Counseling and Testing, and then followed prospectively for two years. Couples randomized to couples-based counseling and testing will also receive a dyadic adherence intervention, with the research aimed to determine if couples testing together impacts linkage to HIV care, retention in HIV care, ART adherence and viral suppression.

1R01NR017098-01 (R. Garofalo/ M. Mimiaga) 9/26/16-6/30/21 # CM
NINR $300,000
Adaptive intervention strategies trial for strengthening adherence to antiretroviral
HIV treatment among youth

The goal of this project is to test the efficacy of a stepped-care "adaptive" ART adherence intervention ("Positive STEPS") for HIV infected adolescents, ages 16 to 24. Stepped-care is an efficiency healthcare

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delivery model in which the least resource intensive part of an intervention is delivered first, and only those who do not improve then receive the high intensity, more resource intensive part of an intervention.

R01DA041071-01 (R. Garofalo/N.Karnik) 09/15/15-07/31/20 CM
NIDA $600,000
Employing eSBI in a Community-based HIV Testing Environment for At-risk Youth

The purpose of this study is to test a structural change to the Seek, Test, Treat and Retain (STTR) model by integrating substance use screening and brief intervention into the traditional community- based HIV testing environment for young MSM and transgender women.

1U01MD011279-01 (R. Schnall/R. Garofalo) 09/01/16-04/30/21 CM
NIH (U01) $120,000
A Pragmatic Clinical Trial of of MyPEEPS Mobile to Improve HIV prevention behaviors in Diverse Adolescent MSM

Using a participatory approach, our study will incorporate user-centered design in the translation of the MyPEEPS intervention onto a mobile platform. MyPEEPS was tested with older adolescents (16-18 year olds) and prior to the availability of non-occupational post-exposure prophylaxis (nPEP) and pre-exposure prophylaxis (PrEP); therefore, in addition to the mobile adaptation, we will update the intervention content.

1R21NR017097-01 (M. Dworkin) 09/01/16-08/31/2018 CM
NIH
Strategically Measuring Adherence in Real-time in Young African American MSM

This award will develop and pilot a mobile phone application that improves the proportion of young African American men who have sex with men (MSM) engaged in the HIV Care Continuum. The preliminary impact of this project will inform the design of a large scale randomized controlled trial.

1U01PS005140-01 (L. Kuhns/J. Perloff) 09/30/16-09/29/20 CM
CDC $54,700
Evaluation of TransLife Center: A Locally-Developed Combination Prevention Intervention for Transgender Women at High Risk of HIV Infection

The study will address the current gap in transgender-specific combination HIV prevention interventions by testing a promising and potentially effective, culturally specific, and highly accessible intervention to reduce disparities in TW by directly targeting the social determinants of HIV infection in this extremely high risk group.

3U24HD089880-01S1 (Carpenter, M.) 09/30/16-05/31/21 CM
NIH $14,767
(Prime)*Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) Coordinating Center.*
SubProject: *Work to Prevent: Employment as HIV Prevention for Young Men who have sex with men and Transgender Women*

The objective of the proposed study is to target economic stability (i.e., employment) as a structural-level intervention for preventing adolescent HIV risk. In particular, the proposed study will adapt and pilot-test an effective theoretically-driven, employment training program for HIV-positive adults (iFOUR) to the needs of at-risk YMSM/YTW, ages 16-24. This study is responsive to the NIH HIV/AIDS high priority topic by specifically addressing health disparities in the incidence of new HIV infections. Further, the proposed project includes populations at elevated risk for HIV infection and addresses health and social issues that are clearly linked with HIV

R21 HD087839 (D. Chen) 1/1/2017-12/31/19 CM
NIH $275,000

OMB No. 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

Structured Pubertal Suppression Readiness Assessment for Gender Dysphoric Youth

The goal of the proposed study is to develop an assessment tool that can aid mental health clinicians in systematically assessing readiness for pubertal suppression from a decisional capacity framework.

OVERLAP No Overlap

INACTIVE

R21 NR16420-01 (Dworkin/Garofalo) 9/28/2015-8/31/2017 # calendar
NIH (R21) $4,619
May I Help You? An Avatar Health Concierge for HIV-infected African American MSM

This exploratory/developmental application proposes to systematically develop and then evaluate the feasibility, acceptability, utilization, and preliminary impact of a theory-based innovative Avatar mobile phone application to engage young HIV-infected African American men who have sex with men in multiple stages of the HIV Care Continuum.

GLIDDEN, D.V.

ACTIVE

(2U01AI69911-11 (Wools-Kaloustian/Yiannoutsos) 08/01/16-07/31/21 # calendar
NIH-NIAID $400,832
East Africa IeDEA Regional Consortium

The goal of Consortium is to link database across the East African Region in order to address questions related to HIV care.

P01NS082330 (Ferriero) 01/01/14 – 12/31/18
NIH/ NINDS $834,635
Repair after Neonatal Brain Injury

This grant proposes to study both structural and functional correlates of brain developmental maturation and network organization using advanced imaging techniques in our human populations and similar correlates in newborn rodents with a focus on defining basic mechanisms of repair. We will translate these findings to the development of appropriate hardware and software for imaging the fragile newborn to enhance our capabilities in understanding how and when reparative processes originate and are executed.

Core A $132,971 # calendar
Administrative Core

The goal is to provide administrative support to the program project.

(THIS AWARD)
R01HD082554 (Rosenthal) 07/01/16 06/30/20 # calendar
NIH $205,510
The Impact of Early Medical Treatment in Transgender Youth

This multi-center study will be the first in the U.S. to evaluate longitudinal outcomes of medical treatment for transgender youth and will provide essential evidence-based data on the physiological and psychosocial effects and safety of treatments currently used for transgender youth.

U54 CA190153 (Martin) 09/1/14 – 08/30/19 # calendar
NIH-NCI $631,202
Uganda-UCSF Consortium on Prevention and Early Detection of HIV-Associated Cancer

The goal of this project is to build research capacity in Uganda in the field of HIV-associated malignancies by training and mentoring East African researchers in the areas of prevention and early detection of infection-related HIV-associated cancers

R01AI114310 (Wei) 09/17/14 - 08/31/19 # calendar
Univ of North Carolina at Chapel Hill (NIH) $80,085
Spurring Innovation in HIV Testing and Linkage: A Crowdsourcing Approach
The goal of this project is too increase knowledge and innovative strategies to reduce HIV incidence – Pre-Exposure
Prophylaxis.

R03AI120819 (Glidden) 06/19/15 – 05/31/18 # calendar
NIH $50,000 (NCE)
Chemoprophylaxis for HIV Prevention: Analysis of Bone and Metabolic Effects
This project will clarify the extent to which bone toxicity of Truvada® is resolves after it is stopped. Secondly, it will estimate the expected bone loss associated with perfect adherence to Truvada®. Finally, it will examine if there are a subgroups of potential PrEP users that are more vulnerable to bone loss from Truvada®

OVERLAP No Overlap

INACTIVE

P30 CA82103 (McCormick) 08/05/99 - 05/31/17 # calendar
NIH-NCI $4,924,570
Cancer Center Support Grant

The University of California San Francisco Comprehensive Cancer aims to: (1) support cancer research of the highest possible quality, in the areas of laboratory, clinical and population sciences; (2) develop patient outreach and education programs to increase the value of the Center to the local community; (3) promote and develop first-class care for cancer patients in our affiliated hospitals; and (4) create an integrated community of investigators dedicated to the shared goal of translating innovative science into improved clinical care.

U01AI099959 (Havlir) 06/01/12 – 06/30/17 # calendar
NIH/NIAID $8,770,142 (NCE)
Reducing Failure-to-Initiate ART: Streamlined ART Start Strategy (START)

The major goal of this project is to test our Streamlined ART Start Strategy (START) in a randomized, controlled trial in 24 clinics in Uganda.

U01 AI069911 (Yiannoutsos; Martin PI UCSF subcontract) 08/05/06 – 07/31/17 # calendar
NIH/University of Indiana $159,999 UCSF
East Africa IEDEA Regional Consortium

To contribute and analyze data for the International Epidemiologic Databases to Evaluate AIDS (IEDEA) from the Mbarara, Uganda-based ISS and UARTO cohorts.

R03AI122908 (Glidden) 01/10/16 – 12/31/17 # calendar
NIAID/NIH $50,000
Comparison of Pharmacologic Markers of Exposure to HIV Pre-Exposure Prophylaxis

This project examines the amount of Truvada® needed to protect against HIV infection and amounts which cause stress on the kidneys and bone. This work will help to select the best strategies for objective assessment of Truvada use for HIV prevention in the community and in future clinical studies.

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ROSENTHAL, S.

ACTIVE

1R01HD082554-01A1 (Olson) 8/1/2015 – 6/30/2020 # calendar
NIH/NICHD $991,416
The Impact of Early Medical Treatment in Transgender Youth

The goal of the research is to conduct a multi-site observational study examining the physiological and psychosocial outcomes of existing medical treatment protocols for gender dysphoria in two cohorts: early pubertal and late pubertal transgender youth.

INACTIVE

R01 HD 068138 (Vilain) 9/26/2011 – 6/30/2016 # Calendar
NIH/NICHD $32,276
Disorders of Sex Development: Platform for Basic and Translational Research

The major goals of this project are to establish a research infrastructure and multi-site consortium to examine the genetic determinants and psychological consequences of Disorders of Sexual Development (DSD) and to provide improved evidence-based and standardized diagnostic and treatment protocols for patients and families affected by DSD.

OVERLAP No Overlap

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES? Not Applicable
E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE? NOTHING TO REPORT
E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER? Not Applicable
E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)? NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

The four sites have worked diligently to recruit participants. We have met our proposed goal for the cross-sex hormone cohort, and we are close to meeting 100% of our blocker cohort (GnRHa) recruitment goal despite a somewhat late enrollment start (launched in July 2016). Also, because the participant population has been more homogenous than we expected in terms of race and sex assigned at birth, we will continue to recruit participants through 9/30/18. Our effort during this period is to over-recruit participants of color and transfeminine participants. To assist in recruiting participants of color, we have created a UCSF satellite site at UCSF Benioff Children's Hospital-Oakland and have initiated enrollment from that location. Even with the delay in the recruitment initiation and with the population being more homogenous than expected, the investigative team has been academically productive, disseminating initial study results to the community of providers, transyouth, and their families who have a vested interest in the study findings.

In the previous RPPR we proposed to recruit up to 60 additional participants into the CSH cohort in order to include cases in which GnRHa and CSH were prescribed to youth in the early stages of puberty. Over the past year, it has become evident that few clinical cases with this profile are observed across sites. To date, we have only recruited 19 of the 60 participants, and they make up only 6.8% of the CSH cohort. Due to low number of these types of clinical patients, we are dropping the additional objective to recruit these extra 60 participants. This does not impact the aims of the initial funded research strategy.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: The Impact of Early Medical Treatment in Transgender Youth

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

Yes

Kristian Gamabrdella started in November 2017 as a study coordinator at UCSF. He completed the CITI GCP and HSP courses with a social/behavioral focus that are required by the UCSF Human Subjects Protection Program.

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: Children's Hospital Los Angeles	052277936	CA-028	4650 Sunset Blvd., MS #97 Los Angeles CA 900276062
Boston Children's Hospital	076593722	MA-007	300 Longwood Avenue Boston MA 021155724
Lurie Children's Hospital of Chicago	074438755	IL-005	225 East Chicago Avenue Chicago IL 606143393
University of California at San Francisco	094878337	CA-012	400 Parnassus Ave, Second Floor San Francisco CA 941430296
CHILDREN'S HOSPITAL LOS ANGELES	052277936		4650 Sunset Boulevard Mailstop #97 LOS ANGELES CA 900276062
Children's Hospital Los Angeles	052277936	CA-028	4650 Sunset Blvd., MS #97 Los Angeles CA 900276062
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G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 1037621

Using an Existing Dataset or Resource: No

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial: No

Study Title: The Impact of Early Medical Treatment in Transgender Youth

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	1	1		0	0					**2**
Asian	19	16		0	0					**35**
Native Hawaiian or Other Pacific Islander	1	1		0	0					**2**
Black or African American	41	40		0	0					**81**
White	109	67		12	10					**198**
More than One Race	34	14		28	22					**98**
Unknown or Not Reported										
Total	**205**	**139**		**40**	**32**					**416**

Cumulative Enrollment

Comments: Enrollment data as of 4/30/18.

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	2	0	0	0	0	0	0	0	0	**2**
Asian	11	3	0	0	1	0	0	0	0	**15**
Native Hawaiian or Other Pacific Islander	1	0	0	0	0	0	0	0	0	**1**
Black or African American	11	2	0	0	3	0	0	0	0	**16**
White	174	74	0	0	0	0	0	0	0	**248**
More than One Race	8	7	0	1	1	0	3	5	0	**25**
Unknown or Not Reported	0	1	0	50	21	1	29	9	3	**114**
Total	**207**	**87**	**0**	**51**	**26**	**1**	**32**	**14**	**3**	**421**

Exhibit 4

The Kelsey Coalition
Working to change the systems that failed our kids

April 5, 2019

Jerry Menikoff, M.D., J.D.
Director
Office for Human Research Protections
1001 Wootton Parkway, Suite 200
Rockville, MD 20852

Re: "The Impact of Early Medical Treatment in Transgender Youth"
NIH Project #1R01HD082554-01A1
Application # 8965408

Dear Dr. Menikoff:

We request that the Office for Human Research Protections (OHRP) place an immediate moratorium on the above-referenced study, *The Impact of Early Medical Treatment in Transgender Youth,* while investigating whether informed consent laws have been violated. We make this request on behalf of the Kelsey Coaliton, a new and rapidly growing national group of hundreds of parents whose children suddenly began identifying as transgender.

In 2015, the National Institutes of Health awarded a five-year, $5.7 million dollar grant to a consortium of four pediatric gender clinics for an observational study that purportedly will "evaluate longitudinal outcomes of medical treatment for transgender youth and will provide essential evidence-based data on the physiological and psychosocial effects and safety of treatments.[1] Given the numerous deleterious side effects of these medications that we will describe, and the lack of FDA approval for cross-sex hormones even in adult populations, the likelihood of serious harms accruing in these young patients is very great.

The medical protocol for this study involves treating transgender-identifying children who are otherwise perfectly healthy with powerful drugs that radically modify their endocrine systems, and indeed, their entire young bodies. Children in early puberty are given "puberty blockers"; older children are given cross-sex hormones. These treatments negatively impact fertility, sexual function, cardiovascular health, bone health, and brain development.[2] [3] This study has no control group and is not randomized. It is simply an observational experiment on otherwise unremarkable, healthy children with confusion about their sexed bodies. Fertility and sexual functioning will certainly be impacted, as hypogonadotropic hypogonadism is being

[1] NIH Grant: The Impact of Early Medical Treatment in Transgender Youth., Project No. 1R01HD082554-01A1. SF 424 (R&R) 05/2015.

iatrogenically induced by GnRH agonists such as Lupron. This puberty blockade is being used on children as early as Tanner Stage 2, before fertility is established. When these children go on to cross-sex hormones and then gonadectomy, they will be permanently sterilized.[23]

Due to our concerns regarding possible ethical violations, the lack of ability of children or their parents to consent to the serious side effects of this therapy, and potential violations of laws protecting human subjects, we submitted a FOIA request to the NIH to examine the research protocol and progress reports.

After multiple attempts, we were unable to obtain the blank templates used for the informed consent forms used in this study (which was clearly listed as being in Appendix B of the protocol).[4]

But what we recently discovered from the 2017 progress report was alarming: the minimum age for cross-sex hormone inclusion was decreased from age 13 to age 8.

> "the minimum age for the cross-sex hormone cohort inclusion criteria was decreased from 13 to 8 to ensure that a potential participant who could be eligible for cross-sex hormones based on Tanner Staging [meaning stage of puberty] would not be excluded due to age alone."[5]

Furthermore, the 2018 progress report shows that 19 children were recruited in the new 8-12 year-old group to receive harmful cross sex hormones.

> "To date we have recruited...19 of the 60 participants and they make up 6.8% of the CSH [cross sex hormone] cohort."[6]

This means potentially that girls as young as eight years old are being given testosterone to simulate a false puberty of the opposite sex. Boys as young as nine are being given estrogen to attempt to crudely mimic female puberty. The doses given are far in excess of the normal range for their respective sexes. Cross-sex hormones have already been shown to lead to an

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[2] Laidlaw MK, Van Meter QL, Hruz PW, Van Mol A, Malone WJ. Letter to the Editor: "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline". The Journal of Clinical Endocrinology & Metabolism, Volume 104, Issue 3, 1 March 2019, 686–687, https://doi.org/10.1210/jc.2018-01925

[3] Laidlaw MK, Cretella M, Donovan K. "The Right to Best Care for Children Does Not Include the Right to Medical Transition". The American Journal of Bioethics. Volume 19. Published online 20 Feb 2019. 75-77. https://doi.org/10.1080/15265161.2018.1557288.

[4] NIH Grant: The Impact of Early Medical Treatment in Transgender Youth., Project No. 1R01HD082554-01A1. SF 424 (R&R) 05/2015, p.1.

[5] 2017 Progress Report. "The Impact of Early Medical Treatment in Transgender Youth". NIH Project #1R01HD082554-01A1. p.23 F.2.

[6] 2018 Progress Report. "The Impact of Early Medical Treatment in Transgender Youth". NIH Project #1R01HD082554-01A1. P.19 F.2.

increased risk of myocardial infarction and death due to cardiovascular disease in adult males and females.[7]

The basis for inclusion in the study is little more than a child's self-identification as transgender. There are no blood tests, genetic tests or imaging to prove this "identity." Indeed, increasing evidence shows that many underlying factors[8] influence transgender identities: mental health issues, autism, ADHD, trauma, sexual confusion, as well as peer and media influences.[9]

It is impossible to predict whether these children in the study will change their minds, or if these hormonal interventions will be regretted after they have already caused serious irreversible harms, including infertility.

We contend that neither children, nor their parents, can meaningfully consent to permanent infertility, or other potentially serious medical harms, to treat a non-medical condition. We question whether these parents were fully informed of the health risks, or the possibility of tragic regret, before allowing their children to be treated with dangerous hormones for five years, and quite likely, much longer.

Thus, we believe that this trial violates Department of Health and Human Services (HHS) regulations protecting human subjects, specifically the general requirements and documentation required for informed consent, 45 CFR § §46.116-17.

Because this study poses irreversible medical harms (including infertility) to children, we request an immediate moratorium and investigation. Thank you for your prompt attention to this important and urgent matter.

Sincerely,

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[7] Irwig MS.Cardiovascular health in transgender people .Rev Endocr Metab Disord. 2018;19(3):243–251.

[8] Holt V, Skagerberg E & Dunsford M. (2014). Young people with features of gender dysphoria: Demographics and associated difficulties. Clinical child psychology and psychiatry. 21. 10.1177/1359104514558431.

[9] Littman L (2019) Parent reports of adolescents and young adults perceived to show signs of a rapid onset of gender dysphoria. PLOS ONE 14(3): e0214157.

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Attachments:

(1) Grant-Protocol-r_R01HD082554-01A1.pdf
(2) Olson-NIH-Progress-Report-2018.pdf
(3) Olson-NIH-Progress-Report-2017.pdf
(4) ajob-affirmative-care-Laidlaw-Cretella-Donovan-final.pdf
(5) JCEM-letter to ed-laidlaw-et-al.pdf

Exhibit 5

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health
Eunice Kennedy Shriver National Institute of Child Health and Human Development
Bethesda, Maryland 20892

May 23, 2019

Michael K. Laidlaw, M.D.
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Dear Dr. Laidlaw:

Thank you for providing Alex M. Azar II, Secretary of Health and Human Services (HHS), and Dr. Francis Collins, Director of the National Institutes of Health (NIH), with a copy of your letter to Dr. Jerry Menikoff, Director of the Office of Human Research Protections (OHRP) at HHS. Your letter outlined your concerns regarding an NIH-funded study (R01 HD082554-01A1: *The Impact of Early Medical Treatment in Transgender Youth*). The study, which is in the fifth and final year, is funded by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). As the Director of NICHD, I have been asked to respond to your letter. An important part of NICHD's scientific mission is to ensure that every person is born healthy and that all children have the chance to fulfill their potential to live healthy and productive lives.

Upon learning of the concerns of the Kelsey Coalition, NIH shared all pertinent grant materials, including the protocols, consent forms, and assent forms, with OHRP. OHRP is currently reviewing these materials for an assessment of the risk to human subjects and the adequacy of the consent process.

The application was originally submitted in response to a Funding Opportunity Announcement (PA12-111) entitled: "Research on the Health of LGBTI Populations." Prior to award, the application went through a rigorous peer review process, receiving a highly meritorious score in the study section, indicating that the scientific community considered that the proposed work would have a high impact on the medical community. The application was also reviewed by NICHD's Advisory Council. My predecessor at NICHD, Dr. Alan Guttmacher, made the final funding decision. To ensure that appropriate progress is being made and appropriate patient protections are in place, NICHD scientific staff have rigorously reviewed the grant each year.

The main purpose of this observational study is to gather evidence on the hormonal treatment of transgender youth to inform the medical community of potential yet unknown benefits or risks that may lead to changes in current treatment guidelines for such individuals. This multicenter study is the first in the United States to evaluate longitudinal outcomes of medical treatment for transgender youth. Children with gender dysphoria are brought to endocrine clinics by their

parents and often referred by their local primary care physician. Physicians at the funded academic centers follow current guidelines for the therapy of transgender youth.[1] Independent of the administration of hormonal therapy, each transgender child and their parent/guardian, who are willing to enter the study, sign an assent or consent for further evaluation by the study investigators. The transgender youth and their parent/guardian sign the protocol consent only if they wish to participate in the NIH-sponsored observational study to allow study personnel to follow their progress. Therefore, study personnel collect data on both treated and untreated children who seek advice and therapy for gender dysphoria.

Notably, these research participants and their parents sought and obtained the hormonal therapies independent of the protocol. Therefore, termination of the protocol would not end the treatments; rather, it would only end the compilation of data needed to advance scientific understanding of the risks and likely outcomes of those treatments. The parents and transgender youth sign consent/assent for the study investigators to monitor outcomes to help them assess the effects of hormonal therapy, including medical risks, and physical and psychological outcomes. As there are few studies to inform physicians about care for this patient population, these data are critical to assure improved outcomes. *Nature Reviews Endocrinology* has published an excellent review[2] of this topic.

Thank you again for writing and for your continued interest in the research activities supported by NIH and NICHD.

Sincerely,

Diana W. Bianchi MD

Diana W. Bianchi, M.D.
Director, NICHD

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[1] Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline J Clin Endocrinol Metab 2017 Nov 1;102(11):3869-3903. doi: 10.1210/jc.2017-01658.

[2] Kreukels BP, Cohen-Kettenis PT. Puberty suppression in gender identity disorder: the Amsterdam experience. Nature Rev Endocrinol. 2011 May 17;7(8):466-72. doi: 10.1038/nrendo.2011.78. Review.