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

DYLAN BRANDT, et al.,
Plaintiffs,
v.
No. 4:21CV00450 JM
December 1, 2022
Little Rock, Arkansas
9:02 a.m.

LESLIE RUTLEDGE, et al.,
Defendants

TRANSCRIPT OF BENCH TRIAL - VOLUME 8
BEFORE THE HONORABLE JAMES M. MOODY, JR.,
UNITED STATES DISTRICT JUDGE

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APPEARANCES:

On Behalf of the Plaintiffs:

MR. CHASE STRANGIO, Attorney at Law
MS. LESLIE COOPER, Attorney at Law
MR. JAMES D. ESSEKS, Attorney at Law
American Civil Liberties Union
125 Broad Street, Suite 1800
New York, New York 10004-2400

MS. BREEAN WALAS, Attorney at Law
Walas Law Firm, PLLC
Post Office Box 4591
Bozeman, Montana 59772

MR. AVIV S. HALPERN, Attorney at Law
MS. LAURA KABLER OSWELL, Attorney at Law
Sullivan & Cromwell, LLP
1870 Embarcadero Road
Palo Alto, California 94303

MR. GARY L. SULLIVAN, Attorney at Law
ACLU of Arkansas
Legal Division
904 West 2nd Street, Suite One
Little Rock, AR 72201

APPEARANCES CONTINUED:

MR. ARUN BODAPATI, Attorney at Law
MS. LAUREN M. GOLDSMITH, Attorney at Law
Sullivan & Cromwell, LLP
125 Broad Street, Suite 2424
New York, NY 10004-2498

MR. DANIEL J. RICHARDSON, Attorney at Law
Sullivan & Cromwell LLP
1700 New York Avenue
Washington, DC 20006

MS. SHARON ELIZABETH ECHOLS, Attorney at Law
Gill Ragon Owen P.A.
425 West Capitol Avenue, Suite 3800
Little Rock, AR 72201-2413

On Behalf of the Defendants:

MR. DYLAN JACOBS, Attorney at Law
MR. MICHAEL CANTRELL, Attorney at Law
MS. AMANDA LAND, Attorney at Law
MS. HANNAH TEMPLIN, Attorney at Law
Arkansas Attorney General's Office
323 Center Street, Suite 200
Little Rock, Arkansas 72201

Proceedings reported by machine stenography.
Transcript prepared utilizing computer-aided transcription.

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(Proceedings commencing in open court at 9:02 a.m.)

THE COURT: Good morning. Thank you for your patience. We're back on the record. You can call your next witness.

MR. JACOBS: Defendants call Dr. Paul Hruz.

THE COURT: First side of the silver rail, sir. Doctor, would you raise your right hand? Do you swear to tell the truth?

THE WITNESS: I do.

THE COURT: Have a seat please. Make yourself comfortable. Do you need any water or anything?

THE WITNESS: Water would be nice. Thank you.

PAUL HRUZ, DEFENSE WITNESS, DULY SWORN

DIRECT EXAMINATION

BY MR. JACOBS:

Q. Good morning, Dr. Hruz. Could you state your name and spell it for the court reporter?

A. Paul Hruz, H-r-u-z.

Q. Dr. Hruz, what is your profession?

A. I'm a pediatric endocrinologist.

Q. Could you give an overview of your educational background for the Court?

A. I have a degree, both MD and PhD degree. My PhD training was in the field of biochemistry. I received my degree in the 1990s. I began my fellowship training or

pediatric residency training at the University of Washington Seattle, and then went to the Washington University in St. Louis for my pediatric endocrinology fellowship training, and I have been on faculty since that time, since 2000.

Q. So just to confirm, how long in total have you been a pediatric endocrinologist?

A. From the start of my fellowship 25 years.

Q. And, in general, what are some of the conditions that you treat as a pediatric endocrinologist?

A. So pediatric endocrinology is a field of medicine that studies disorders of hormone action, synthesis or secretion. It runs throughout the body in many different organ systems. About half of the practice of endocrinology relates to the treatment of diabetes in its many forms.

THE COURT: Excuse me, Doctor. Treatment of what?

THE WITNESS: Diabetes.

THE COURT: Okay. Thank you.

THE WITNESS: In its many forms. We also treat disorders of growth, puberty, sexual function, thyroid/pituitary disorders, bone and mineral metabolism, anything that relates to something in the body where hormone action is disrupted leading to human disease.

BY MR. JACOBS:
Q. As a pediatric endocrinologist, what are the typical -- what's the typical age range for the patients that you see?
A. I see patients all the way from birth until the early 20s. We follow them often up through their college years.
Q. You mentioned a position on faculty. Could you give an overview of the professional positions that you currently hold?
A. I am currently an associate professor of pediatrics. I have a secondary faculty appointment as associate professor of physiology -- cellular biology and physiology. I have responsibilities in patient care, research, education, and administration.
Q. And are you involved with the fellowship program?
A. For many years, I served as the director of our fellowship program. Currently, I'm serving as the associate director.
Q. What does that entail?
A. It involves the education of our pediatric endocrinology fellows as they prepare to be practicing endocrinologists. One of my main responsibilities is to guide other fellows in the conduct of research.
All fellows in our profession are required during their training to be trained in doing scientific

investigation. I oversee them in choosing their mentors, choosing their research projects, and ensuring that they get a quality education on the rigors of science and how it is done within our profession.

Q. As a professor, what sort of courses have you taught in your career?

A. We give lectures on a variety of topics related to our field throughout my career, including journal clubs where we critically evaluate research papers, where we present the basic physiology for various disorders. And I have been called upon throughout my career to teach in virtually all of those areas of pediatric endocrinology practice.

Q. Are you involved in research in the field of medicine?

A. Yes, I have. In my appointment as a physician scientist, I am appointed to the investigator track. That is how my career is gauged as far as my contribution to the mission of our university. For 20 years, I had an active basic science research laboratory that -- where I had a number of research studies. For the first ten years of that time, I was investigating adverse drug effects related to the treatment of HIV infection, being able to understand how the administration of medications can lead to adverse effects that are not intended and to search for

ways that we could avoid those adverse effects.

I've also been involved in translational research projects, and more recently that has been a major focus of my research efforts in the area of drug development, being able to develop drugs that are both efficacious in treating diseases but also are safe for administration to human beings, again, taking it from the investigational stages in experimental in vitro, test tube type of experiments, to animal experiments and now in the process of moving it into treatment of human beings.

I've also been involved in the evaluation of clinical trials with my colleagues more often as a consultant or a collaborator on those project where my colleagues would have the primary effort in those areas.

Q. You mentioned the term "translation research." Could you just explain what you mean by that term?

A. Translational science runs a spectrum from the very first stages where you take any early discovery in the laboratory and begin to apply that to human beings, all the way up to population-based studies to look at delivering of health care in their many different stages.

Our institution at Washington University has an institute of clinical and translational sciences, one of the few centers in the country that has this special program. And the goal is to be able to take that

information that we learn in the laboratory and to be able to make it useful in clinical practice, again, to improve the quality of the care that we deliver.

Q. Has any of the research you've done been published?

A. Throughout my career, I have been publishing in the -- in a number of journals. I've had over 60 publications. Most of them have been published in peer reviewed, top tiered journals within my field. And I've also published several review articles in other analyses of research done by others.

Q. Have you ever served as a reviewer for any journals?

A. I continue to serve as reviewer. I've done that throughout my career and have been involved in assessing the quality of evidence that is being put forward for publication. It is a service that myself and most of my colleagues that are involved on the investigator track are called to do on a regular basis. I have done that throughout my career, so I can say that I've reviewed probably over a hundred papers in my career.

Q. Are you familiar with the condition of gender dysphoria?

A. Yes.

Q. Could you just explain what your understanding of that condition is?

A. Gender dysphoria is a condition where an individual

will have an experience of their gender identity that is discordant with their biological sex and this dysphoric which leads to discomfort from that discordance.

Q. Is gender dysphoria related or topics been a subject of your research?

A. I have been involved in investigating the treatment of gender dysphoria for the past decade, yes.

MR. JACOBS: I'll pause here in case there is voir dire of the witness before proceeding on.

THE COURT: Anybody want to --

MR. STRANGIO: No voir dire.

MR. JACOBS: Thank you. Thank you.

BY MR. JACOBS:

Q. And you mentioned a moment ago that you started investigating gender dysphoria and gender dysphoria treatments a decade ago.

Could you just briefly explain how that came about to happen?

A. I became involved in the investigation of the treatment of gender dysphoria a decade ago. It was when I was serving as chief of our division of pediatric endocrinology at Washington University. One of my colleagues approached me, asking to be able to start a gender center. At that point in time, this was just beginning to come to the attention of the medical

community.

In my job as chief of the division, it was necessary for me to understand in -- what the condition was, what the treatment approach that was being proposed was to offer, and the merits of that program. And that was how I began investigating the question as to whether the engagement of my profession, pediatric endocrinology, in the alleviation of the suffering that is experienced by people who have gender dysphoria, is an appropriate course of action.

Because I found in that process that there were many questions that remained unanswered, it led me to dig deeper and deeper into the literature, into the hypotheses that were being put forward, the scientific premises that were being used to direct the care that was being offered, side effects, outcomes, and benefits.

Q. I want to switch gears just a little bit and talk about some specific endocrine treatments. Are you familiar with what a GnRH agonist is?

A. I'm very familiar with GnRH agonist. They're also referred to as puberty blockers.

Q. Do you ever prescribe puberty blockers in your clinical practice?

A. Yes, I do.

Q. What conditions would you prescribe them for?

A. Again, the field of endocrinology is directed toward the care of endocrine diseases where there's disruption in the normal function of the endocrine system. In pediatric endocrinology, the area that involves the use of GnRH agonist is that of central precocious puberty.

Q. What is central precocious puberty?

A. Central precocious puberty is a condition where an individual will experience the onset and progression of the biological changes that -- from childhood to adulthood in reproductive capacity at an inappropriately early age.

Q. How do you diagnosis a child who comes to you with precocious puberty?

A. A child who is referred for concerns of precocious puberty is first recognized by objective physical changes that occur within the body related to puberty occurring at an age that is abnormal for what we know about normal development.

For a female, this is any pubertal change occurring younger than eight years of age and mostly manifested in the first stages as breast development, changes in linear growth.

And for males, it would be testicular enlargement before nine years of age also accompanied by increased growth and other signs of androgen production.

Q. So you mentioned observing physical characteristics.

Are there other sorts of objective factors you can look at, for example, in lab work to try and diagnosis a child with precocious puberty?

A. So the presentation becomes apparent by physical changes that occur. And in the field of endocrinology -- and this is not unique to the condition of central precocious puberty. It applies to nearly all of the conditions that we treat that we rely upon objective biological measures to assess the functioning of the endocrine system.

For the condition of precocious puberty, there are some patients that have elevated sex steroid hormone levels that are being produced in areas of the body that are not being regulated by the normal centers in the brain that control pubertal development. That would be gonadotropin independent precocious puberty.

The condition that we're talking about in relation to the use of GnRH agonist relates to abnormalities in the signaling within the pituitary gland within the brain. We can objectively measure this by testing for the levels of those gonadotropin hormone, LH and FSH. We can also objectively measure the resulting sex steroid hormone production that is simulated by those gonadotropin hormones.

THE COURT: Doctor, you're using on words that

my court reporter is having trouble catching up with. Can you slow it down just a notch so -- we're fine on your pace until we get into technical terms, and then she's having trouble catching up. So if you'll be mindful of when you're using words like you just used a moment ago. If you can pronounce those more slowly, she can pick them up.

THE WITNESS: My apologies.

THE COURT: No apology. I just -- you know what you're saying, but we're trying to catch up. Thank you.

THE WITNESS: Very good.

So the question was what -- how do we diagnosis central precocious puberty. We measure hormones from the pituitary gland, LH and FSH. LH refers to a luteinizing hormone and FSH refers to follicle stimulating hormone.

These are two hormones that are made in the pituitary gland that signal to the gonads. In males, it lead to production of testosterone. In females, it lead to the production of estrogen and all of the functioning of those gonads.

We also have objective measures of the effects of those sex steroid hormones, either testosterone or estrogen, their effects on bone maturation. We have objective measures, if we have growth data available, to look at the acceleration of growth velocity, and we can

look at the peripheral effects of those sex hormones.

The testosterone as an androgen will lead to virilization, which can be manifested in a number of ways. And estrogen -- the primary observable effect of estrogen is breast development, but there are other objective biological changes, including changes to the primary sex organs, the vaginal mucosa, that we can document that that child was undergoing these physiologic changes at an abnormally early age.

BY MR. JACOBS:

Q. So when you would prescribe GnRH agonist to treat a child that you diagnosed with central precocious puberty, what is the goal of that treatment?

A. The goal of treatment -- really to understand what we're trying to achieve we need to understand what the risks are of going through puberty at an abnormally early age. As I said, the sex steroid hormones are going to lead to growth acceleration. They're going to get taller faster. Most parents and children are not bothered by that, but they don't recognize that in the process of growing too quickly, their bones are maturing too rapidly and they're going to complete their linear growth at -- prematurely. And even though they have initially tall stature, they're going to end up with short stature. Many times, depending on the age of onset, significantly short

stature that may be to a degree that it can impact their functioning in adult life.

Another challenge of abnormal early puberty is that the children will have those biological changes at a state where their developmental process is not sufficient for them to be able to manage those biological changes.

The process of puberty by definition is related to developing reproductive competency. And to have a fertile kindergartener presents many problems when a child is not able to handle the changes that are going on in their body because they've not had the developmental progression that normally occurs during the adolescent years.

This can present in very practical ways. For example, the challenges of menstruating when you're in kindergarten can be very problematic. The sexual advances that may be made by older classmates when a child is not able to be able to make that decision about engaging in sexual activity because of the immaturity of their development.

Q. So I think you just walked us through whatever the -- about the consequences of having precocious puberty.

So what are the goals of treating central precocious puberty with GnRH agonist?

A. The goal is to be able to allow that child to have that pubertal development enter the normal quiescence that

is present at that age, meaning that, at that time of life, normally there are active signals from the brain that suppress the secretion of those gonadotropin hormones. We try to restore them to that natural state that they would have normally if they did not have that disease condition.

We try to preserve their final adult height. So by suppressing the signals from the pituitary gland and suppressing the production and action of those sex steroid hormones, our goal is to be able to slow the rate of bone age advancement so that they can achieve maximal height.

We also try, for example, in females to prevent them from progressing to the point of having menarche, which is the onset of menstruation, until the normal age. I said the lower limit of normal pubertal development is typically eight years of age in females, nine years of age in males. The normal lower limit of menstruation for females is ten years.

So we try to get them to an age where that, if they were to progress in puberty to the point of having menses, that they would be -- it would be occurring at an age with their peers that did not have central precocious puberty.

Q. So when you're -- when you're treating a patient for central precocious puberty with GnRH agonist, is there a point or an age at which you start to think it's time to

take them off of that? And can you explain how you make that decision?

A. Yes. With the goals that I have outlined as far as preservation of adult height and the suppression of puberty to allow that development to occur at a normal age, we try to get them to an age where their peers would be the experiencing this. So, for example, we try to make sure that the females that have this condition have their development suppressed until the age where -- of ten years for having menses because there are children that do not have central precocious puberty that will begin at that point in time.

There are dangers in carrying out this intervention too long because the delay could have adverse effects by suppressing the normal changes. So what we try to do is -- again, this is true for all areas of endocrinology -- weigh relative risks versus relative benefits. And our goal is to have the maximal benefit we can have on height without having adverse effects about abnormally suppressing puberty.

We do not induce a condition where puberty is delayed. We merely want to allow them to get to the age of the lower limits of normal for pubertal development.

Q. So you mentioned the risks of delaying puberty. Could you explain what the risks -- what those risks are?

A. There are several risks with delaying puberty too long. The biggest concern that we have is the effects on bone marrow density. We know that the process of puberty and the sex steroid hormones that are produced during that puberty are critically important for the accrual of maximum bone density. This is a crucial stage of life because individuals, after achieving their peak bone density through the rest of their life, will have gradual loss of that density. So if they begin -- or they reach a peak bone density that is low, they are at much greater risk of having severe bone disease, osteoporosis, later in life.

So we also recognize that there are elements of the biological changes related to puberty that coincide with the psychosocial changes that occur during adolescence. Again, it's important to recognize that puberty is described in terms of the biological changes leading to reproductive capacity occurring at a time of a child's life where there are very, very important psychosocial changes that are going on in their development from childhood to adulthood in other areas of interacting with their peers, with their parents, in society at large.

Q. You mentioned osteoporosis later in life being a risk of this. When you say "later in life," what sort of time frame should we think about?

A. So what we worry most about, it's a progressive loss over time. So the lower your bone density is at the time that you reach your early 20s and the rate at which you lose bone density over time can vary. It is well established with very rigorous research studies that that correlates with -- in late adulthood. So we're talking decades later. And there is no way that we know of that, if you fail to achieve that bone -- maximum bone density, that you can make up for that later in life. The only intervention that you may be able to use is to delay the rate of decline of that bone density.

So the age at which it presents depends upon the severity of the -- of the failure to achieve maximal bone density, but it's a time point in terms of years and actually decades before we would see the full manifestations and, to be clear, osteoporosis to the degree that it will cause pathologic fractures and we know that the risks that that has later in life.

Q. So we've been talking about some risks. I want to specifically ask about the risks posed by GnRH agonist just from the drug itself.

Can you describe what those are?

A. So the -- again, understanding how these drugs work within the body, the name actually helps one to understand how they're working. So there are signals at higher rate

centers that signal. So gonadotropin-releasing hormone, or GnRH, signals to the pituitary gland to lead to the secretion of LH and FSH. Those signals are normally present in a pulsatile fashion, meaning that there are short bursts of GnRH that lead to simulation of the receptors in the pituitary gland that lead to the production of those hormones.

Paradoxically, when you administer that same stimulus continually rather than in a pulsatile manner, rather than simulating the gland, it will suppress it. The effects of suppression are not immediate. The initial administration of the medication is going to actually stimulate the gland until the suppression phase occurs.

We can evidence this in many ways. When we clinically treat with this class of medications, if the patient is not taking the medicine consistently, we will actually see the opposite effect.

Depending on how far an individual has progressed through puberty, the effect of this class of medications is going to lead to a fall in the sex steroid hormone levels. It is known that that fall in sex steroid hormone levels can have significant psychological effects. In fact, it is present in the label of the product that it can lead to mood changes, including depression. One can think of this in a similar way that -- in a condition that

people are more familiar with of postpartum depression, but it's the same mechanism that is occurring, is that the rapid changes in the sex steroid hormone levels can lead to those adverse effects.

The medication itself very recently has -- and this is actually important to recognize that all medications that we give have relative risks and relative benefits. Sometimes we don't fully understand all of the risks until much later.

There is a new recognition, for example, that giving puberty blockers can lead to an increase of pressure in the brain, a condition known as pseudotomb -- pseudotumor cerebri. It's not a tumor, but it leads to increase of a pressure in the head that's usually clinical recognized by changes in the back of the eye, the nerves in the back of the eye becoming blurred, but it actually can adversely affect one's vision as well in addition to the causing a severe headaches.

These are known effects from the medications themselves. And then there are the effects of the -- that are secondary to the effects of the medication in their changes to the sex steroid hormone levels.

Q. When you prescribe a GnRH agonist to a patient, just practically speaking, how are those sorts of drugs administered?

A. So these medications, again, the goal is to be able to have sustained delivering of the normal signals that would stimulate the pituitary gland to lead to suppression. They're usually given as injections.

The first products that were used were -- required monthly injections of the medications. There are new formulations that allow one to fill that every three or six months. There's forms of the medication that can be delivered by an implant that is placed under the skin that will deliver the medication for over a year. There is a very short acting version of this that actually can be inhaled through the nostrils that requires a daily administration.

These medications, when given in the manner that they are prescribed leading to sustained delivery of that stimulation, then will lead to the suppression of the pituitary function.

Q. When you're prescribing and administering GnRH agonist to treat central precocious puberty, does anything change due to strictly whether your patient is male or female?

A. So at the level of the pituitary gland and the higher signaling from GnRH to the release of LH and FSH, those signaling processes are the same in males and females. So the effect of giving the puberty blocker is identical when

it is given to a male as when it is given to a female in the -- both the intent and the effect of suppressing the secretion of those gonadotropin hormones.

Q. I guess to wrap that up, say you had a male patient and a female, patient both with central precocious puberty. Assume that they weigh approximately the same and you're administering a GnRH agonist. Would you use a different dose between them or no?

A. The exact same medicines are given to males and females in the various ways that they can be offered and the dosing is given in the same manner as based on weight.

Q. We've been discussing the use of GnRH agonist to treat central precocious puberty. I'd like to switch gears slightly.

What is your understanding of how GnRH agonists are administered for the treatment of gender dysphoria?

A. So the administration of the medication is the same meaning that the forms of the medication and the way it's delivered by subcutaneous injection or implant is the same, but there are many, many differences between the use of this medication to suppress normally timed puberty compared to the suppression of abnormally early puberty.

Q. And earlier we were discussing risks associated with delayed puberty. Could you explain whether the extent to which any of those risks are also applicable in the

context of using GnRH agonist to treat gender dysphoria?
A. So the question of what are the risks of suppressing normally timed puberty, there is data that I can refer to that we know very well how that can effect an individual, and really in an adverse way. But there are many questions that aren't answered because this has not actually been studied rigorously for the effects of suppression of normally timed puberty.

In relation to the duration of treatment that I earlier discussed, it is very relevant to the question of interruption of normally timed puberty. This is a very different time in an individual's life. There are reasons -- or there are effects of the pubertal process, including bone density, that are critical in that phase of life.

When you interrupt that at that stage of life when the body is already signaling to go through puberty, to suppress that can have very significant effects on final stature, on bone density. Those are well established.

The -- there are many other effects that are not well investigated but could potentially have effects because of the absence of the sex steroid hormones during a time when they would normally be present.

Q. In the plaintiffs' experts have claimed that the effects of GnRH agonist, when used in the course of treating gender dysphoria, are reversible.

What is your opinion on that?

A. The question of reversibility of using the puberty blockers, on one level, the suppression of the signals from the pituitary gland when the drug is removed are expected to resume. So this is the same basis for which when we treat central precocious puberty, when we withdraw the administration of the GnRH agonist, that within months to at most a year -- usually it's within several months -- that signaling within the pituitary gland will resume.

That part is reversible to the best of our knowledge. Although I will add that we have not rigorously studied this in the suppression of normally timed puberty.

But there are many other aspects of that by its very nature is not reversible, and -- to name just a few of the many.

As I mentioned earlier, there is a developmental process of adolescence that occurs at the same time as the physical changes that occur during puberty which is a biological process. If one blocks normally timed puberty, you are altering the normal association of the biological changes that occur together with the developmental stages of adolescence. That is a temporally dependent process and it is impossible to turn back time.

So once you've blocked puberty, even if you allow the signaling from the pituitary gland to resume, you cannot

buy back the time when that physical process has been disrupted at a time that it would normally occur in that stage of an individual's life.

There are other changes. The changes with bone density can be partially reversed with puberty being allowed to proceed. But the best evidence that we have to date is that -- that that deficit is not fully made up and, again, it pertains to how long these medication are administered. And so there is a concern and data to back this up in published literature that, even though bone density will increase with the administration or allowing puberty to progress either naturally or artificially, that those deficits not reversible as well.

Because this is a relatively new use of this class of medications that has never been rigorously studied to the degree that we don't have the information yet for its effects in the interruption of normal puberty in relation to what we know about the blocking of puberty when it occurs abnormally early.

Q. So the plaintiffs' experts have claimed that when gender dysphoria patients who have been prescribed GnRH agonists move on to taking cross-sex hormones, that this effectively initiates an opposite sex puberty.

Can you explain your opinion as to whether that is true?

A. The claim that is being made in that argument is looking at the desired phenotypic changes related to the effects of the sex steroid hormones, meaning that one is looking for virilization by the administration of testosterone to a female or a feminization by administering of estrogen to a male.

What is not recognized by many who make that claim is that the administration of the sex steroid hormones differ by the sex of the individual, the effects of that. It is not identical to give testosterone to a male as it is to give it to a female, nor is it the same thing to give estrogen to a male versus female. And there is a scientific basis that we know very well as to why that is.

The differences between males and females occurs in every nucleated cell of the body. There is genetic programming that differs between males and females. This is a process known as epigenetics, meaning that there are modifications of the DNA itself that alter the expression of genes when exposed to the same stimulus. So if you give testosterone to a male, the physical -- or the physiologic effects of giving that testosterone, even in the measurement at which genes are turned on and turned off, will differ as to whether it is being given to a male or a female.

This has been well documented in scientific studies.

And, for example, there's over 6,000 sex differentially expressed genes between males and females. If you look at what proteins are being made, what signals are going on in the body in response to hormones, they differ drastically.

So it is quite erroneous to infer from the phenotypic changes that occur, the appearance of that individual, that is -- that what is going on in the body is the same.

The other component of that question as far as inducing puberty in the opposite sex is that the whole purpose of puberty biologically speaking, not limited to human beings, but across the animal kingdom, is in relation to reproductive capacity. And an individual -- a male given estrogen is not going to be able to function in that reproductive process as a female, nor is a male going to be able to participate -- a female going to be able to participate in the male function by merely getting testosterone.

We're looking at changes in the appearance of the individual, but we are not inducing puberty as it is understood by scientists and have always -- has always been understood by scientists in relation to what puberty means.

Q. You mentioned gender incongruence earlier in the context of explaining your understanding of gender dysphoria is. Are you familiar with the term "desistance"

being used in the context of gender incongruence?
A. The term "desistance" refers to individuals that have had this experience of their gender identity that is discordant with their sex later and desiring to have those changes occur to allow their body to appear according to their gender identity rather than their sex, later essentially desiring to reverse those changes. And so that's what the term is understood to mean.
Q. Are you aware of scientific literature that bears on the question of whether administration of GnRH agonist effects whether a minor's gender incongruence persists or desists over time?
A. So one of the arguments for using puberty blockers in individuals that experience gender dysphoria -- and, again, there are several claims that are often made. One is that it provides a pause button to arrest pubertal development to allow a child to have more time to explore their gender identity.

The experience in the published literature of individuals that are treated with puberty blockers demonstrates that the vast majority, nearly the 98 percent of all individuals get puberty blockers, will go on to get cross-sex hormones. There are concerns among the scientific community that this is not just a pause button but actually is directing an individual to pursue those

later stages of the affirmation approach and that it's not a neutral intervention.

The data that is cited to challenge that -- again, the -- there is much that could be said about the literature, but that experience of 98 percent going on to cross-sex hormones differs, meaning that it's almost -- almost universal that they will go on to desire these later stages interventions is very different than the experience of -- again, that has been publish in the literature prior to the adoption of this approach where the vast majority in fact did not that have persistence of their sex discordant gender identity.

Q. Shifting gears just a little. Have you ever prescribed a GnRH agonist to treat a mental health or psychological condition?

A. Well, I will refer you back to the role of a pediatric endocrinologist is to treat diseases of the endocrine system. So we're looking at treating physical disease. I am not aware of, outside of the question of intervening in the area of gender dysphoria, where this approach is used to treat any other condition other than the biological diseases that we talked about.

Q. A similar question. Have you ever prescribed GnRH agonist to a minor due to that patient feeling distressed about the coming onset of puberty?

A. I have never administered a GnRH agonist for that purpose. I do see children that present to my clinic frequently with concerns about pubertal development, and I've never recommended a GnRH agonist to alleviate that anxiety whether it comes from the parent or the child.
Q. Based on your knowledge of the field, are you an outlier in that approach among pediatric endocrinologists?
A. Again, aside from this current discussion on the affirmation approach for the treatment of gender dysphoria, it has -- this is unique in its application in any other condition that we encounter in pediatric endocrinology.

And as far as my colleagues that -- I think that there are many that share my concern about how it's being used in the treatment of gender dysphoria.
Q. Shifting gears to a new or the next medication. Are you familiar with spironolactone?
A. Yes.
Q. Can you explain what that is?
A. Yeah. Spironolactone is a drug. Its primary function had been for the treatment of blood pressure and heart failure. It's a mineral -- mineralocorticoid antagonist. It is known as potassium sparing diuretic. But in relation to the field of endocrinology, it also has the effects in blocking the action of androgens. So it's

an androgen receptor blocker.
Q. When you say "androgen," could you explain what an androgen is?
A. So androgens are hormones that lead to virilization. Testosterone is a prime androgen, but there are many others in the body that have androgen effects, so leading to hair growth, acne, body odor, those changes that occur.
Q. Are those often colloquially referred to as male hormones?
A. Correct. Androgens are male type hormones.
Q. Do you in your clinical practice ever prescribe spironolactone?
A. It is not a prime medication that we use, but the major area in endocrinology is in the treatment of polycystic ovarian syndrome where females will undergo virilization due to excess androgen production and generally coming from the ovary.
Q. So in the course of diagnosing a patient with polycystic ovarian syndrome, are their objective markers, say, on blood work that you would verify?
A. So the diagnosis of polycystic ovarian syndrome is a clinical diagnosis based upon the physical evidence of virilization or androgen effects, insulin resistance, and irregular periods. But there are objective biological measures to assess those androgen levels, most notably

free testosterone levels are elevated, meaning that the normal protein that binds testosterone is lowered, called sex hormone binding globulin. So there are objective measures of elevated free testosterone.

There are objective measures of disregulation of those signals from the pituitary gland, the LH and the FSH, to compliment the clinical diagnosis by looking at the degree of virilization that is present in that patient.

Q. We've been discussing -- I'll abbreviate PCOS in female patients. Do you ever prescribe spironolactone to your male patients?

A. I do not prescribe spironolactone. I'm trying to think if there is any exception. For an endocrinologic purpose, the answer would be no.

I will add that the intent of giving spironolactone is addressing the virilization, but the condition itself recognizes that those elevated androgen levels have effects within the body that go beyond the undesired appearance of virilization.

The whole condition of poly cystic ovarian syndrome is recognized to have adverse effects on fertility, to have adverse effects on metabolic health and risks of having cardiovascular disease. There is a whole field of medicine that has investigated the serious physical

consequences of the elevated androgen levels in affected females. And it's an example of the difference between males and females.

The levels that we're talking about of androgen exposure in females is of an order of magnitude different than we would see in other conditions, for example, where we would have, for example, an androgen secreting tumor which could affect both a male and a female leading to vastly different levels of those androgens in the body.

So the amounts of the androgens normally differ markedly between males and females and the metabolic consequences of those elevations in androgens differ between males and females as well.

Q. Just make sure I got the clear answer to the previous question. Is there ever a time as a pediatric endocrinologist where you would prescribe spironolactone to a male patient, a minor male patient?

A. The reason I paused before answering is that there are indications, for example -- there are adrenal hormones that can be made and there are diseases that can actually influence the amount of potassium and sodium in the body. This is a class of medication that is often used to elevate potassium levels. It actually can cause -- if it's not regulated, can actually cause dangerously high levels of potassium, and someone needs to monitor for it.

So there may be indications where spironolactone is given for the purposes of electrolyte balance, but not specifically related to androgen production.

Q. You can correct me if I'm wrong with this, but I think I understand you to mean that you would not prescribe spironolactone to a male patient with a primary goal of blocking androgens. Is that what you were meaning?

A. So independent of its current application to this question of gender dysphoria, the answer is no.

Q. Thank you.

Just on that, you mentioned treating males with spironolactone maybe for electrolyte balancing reasons. In the course of diagnosing and treating that problem, would you be relying on objective markers, say, blood work to guide you?

A. Most certainly we would have the objective measure of the sodium and potassium levels. We also have a means to measure the androgen levels that are being produced. And there are many tests that we have to do this in a very precise and comprehensive manner.

The steroid hormone levels are often measured either in the basal stage or in a stimulated state where we actually can look for abnormalities in the production of these hormones in the adrenal conditions that I spoke of.

Q. Similar question that I asked about puberty blockers. Have you ever prescribed spironolactone to treat a mental health condition or a psychological condition of a minor?
A. I have not. Again, aside from the use in the affirmation approach to gender dysphoria, it is -- it is not used to treat a psychiatric condition.
Q. But is it also true outside of your personal practice in the field of pediatric endocrinology generally?
A. I would say that the virilization that occurs in the female patients is undesired, but the primary purpose is to restore that individual to a state of health, meaning it is not to treat the mental health issues; it's to be able to allow the body to be restored to its normal state.
Q. Thank you. I want to shift gears past that and moving on to sex hormones.
So do you ever prescribe testosterone to minors in your clinical practice?
A. Yes.
Q. And for what conditions would you prescribe testosterone?
A. There are a few conditions. One is gonadal failure, which can either be primary or secondary, meaning that there may be damage or a nonfunctioning testes in a male or there may be abnormalities in the pituitary signaling telling the testes to work. There are also individuals --

males that are born with a small phallic size, and we will administer testosterone to lead to phallic growth.

Q. For those conditions you were discussing, what are some of the objective criteria that you would use in diagnosing and treating those conditions?

A. So the condition of either primary or secondary hypogonadism can be objectively assessed by measuring the levels of testosterone or derivatives of testosterone or the sex steroid hormones that are used in the production of testosterone and objectively measuring LH and FSH levels. So we can objectively measure the functioning of the pituitary gland and the gonad through biochemical tests.

Q. When you're prescribing testosterone, do you monitor the testosterone levels of the patient when they are undergoing treatment?

A. The answer is yes.

Q. Why would you do that?

A. It's very important -- so in the initiation for those that fail to go through puberty, we generally do this in a gradual method to slowly increase testosterone levels to coincide with the normal rise of testosterone that occurs with normal puberty. We also want to avoid excess of testosterone in that individual because we know very well that too high of testosterone levels can have very serious

adverse effects. This can also be measured -- one of the effects of the testosterone is to elevate red blood cell counts and it can lead to a very serious elevations outside the normal range if you over dose of that medication.

We also see effects on blood pressure, on lipids, on rage, for example, and in males priapism, which is having a painful erection that doesn't go away.

Q. You mentioned using testosterone to treat a delayed puberty. Is that a condition -- would you only use it to treat delayed puberty in males or would you also use that in females?

A. It is only used in the treatment of delayed puberty in males. There are two ways that it is given. One is - probably the most common reason to give it is for somebody that has delayed puberty of a constitutional nature, meaning that they have the capacity to go through puberty normally, but it has not been triggered at the normal age.

In that case, we'll give very low doses of testosterone to, essentially -- we like to refer to it as priming the pump. We give them low doses for a period of three or four months and then look for then the initiation of normal puberty.

There is a subset of patients that, when you attempt to use it for stimulating puberty for constitutional

delay, they end up having the inability to go through puberty normally most often because they don't have the signals in their brain, the LH and FSH. It's a condition known as hypogonadotropic hypogonadism. And they will require ongoing therapy with testosterone. That is reserved for males.

THE COURT: Mr. Jacobs, what are you looking like on time?

MR. JACOBS: We got a long ways to go.

THE COURT: Then we're going to take a break. Court will be in recess for about 15 minutes.

(A recess was taken at 10:08 a.m. until 10:21 a.m.)

THE COURT: Thank you for the break.

BY MR. JACOBS:

Q. All right. So Dr. Hruz, we were discussing treatments of delayed puberty. And just to clarify something, you've mentioned in relation to testosterone a normal range. I just wanted to ask, are there accepted ranges of, for example, testosterone by endocrinologists that you want to see in patients? Can you explain that?

A. Yes. So there are very well established normal ranges in both males and females for testosterone levels and they can be stratified out as to the time of life and Tanner stage of development. And so the answer is yes.

Q. When I say a supraphysiological level of

testosterone, would you understand that to mean above the normal range for where that particular patient is at in the Tanner stages?
A. Yes.
Q. And in your practice of prescribing testosterone, is there any reason that you would ever intentionally have a patient reach supraphysiological levels of testosterone?
A. In the normal course of practice, the answer is no because of the recognition of the adverse effects that can occur with that. Again, the practice of endocrinology is directed toward restoring the body to its state of natural health and to avoid the adverse effects of disruption of the normal endocrine system.
Q. You may have briefly touched on this earlier. You mentioned different testosterone ranges for different patients. Are there different normal ranges of testosterone for males and females?
A. Yes. That is correct. Testosterone levels -- so it is important to recognize that both males and females make both estrogen and testosterone, but at very different levels. So the ranges are very different for the sex hormones between males and females.
Q. You don't have to give an exact number but assuming there are post-pubertal teenagers, could you just compare the levels of testosterone you might expect to see in a

male versus the levels of testosterone you might expect to see in a female assuming everyone is healthy and normal?
A. So it's almost an order of magnitude different. Now, it's important to recognize that the sex steroid hormone levels will vary for females over the course of a month, for males the time of the day. So there are differences between morning and evening testosterone levels, but the ranges that one sees in a female are a fraction of the percent that are seen in males.
Q. And do those -- again, assuming, say, teenagers post puberty, everything is healthy, would the normal ranges for females and males overlap? And by that, is the high end of the range of normal female testosterone lower than the low end of the range for a male?
A. There is a clear distinction between the normal levels of testosterone in an adult male compared to an adult female. It is not equivalent. In fact, when you get testosterone levels into the range that we would typically see in a male, one would be looking at conditions like the PCOS that we spoke of earlier.
Q. So when talking about treating delayed puberty in hypogonadism using testosterone, are there objective criteria that you would measure to determine whether the treatment is going successfully?
A. There are clear both biochemical and clinical

indicators of successful treatment of hypogonadism in males, and the same could be said for -- for gonadal failure for -- in females. The same could be said for successful treatment with a puberty blocker. Objective measures looking at the sex steroid hormone levels that are achieved and the physical objective changes that occur in the body in response to that sex steroid hormone being delivered.

Q. When you're in a situation of delayed puberty that you described as priming the pump, did you mean to say that -- excuse me.

When you're treating delayed puberty, one form of that was a temporary administration of testosterone. Did I understand that correctly?

A. Correct. So the condition of constitutional delay is where one has all of the machinery to be able to go through puberty, but the onset that was puberty is delayed. The way that we normally treat that is to give about 50 milligrams of IM testosterone monthly for three to four months, and then we'll see them back at the six-month time point, and then we will assess the levels of the pituitary hormones, LH and FSH, and the testosterone level that that child has.

We can also look objectively at the testicular size with the onset of puberty. The first sign of the onset

puberty is testicular enlargement. Somebody that has had constitutional delay and is treated with this low dose of testosterone for three to four months, when seen in follow-up, will have both increase in testicular size, measurable gonadotropin levels in the pubertal range, and rising testosterone levels indicating the success in initiating that puberty and that there is not a need for ongoing testosterone therapy.

Q. And in a situation like you just mentioned where constitutional delay appears to be resolved, why would you not continue to administer testosterone following that?

A. Again, the practice of endocrinology is directed toward restoring health. Once puberty has been initiated and is progressive, there is no need to administer ongoing testosterone therapy. The normal signals present within the body by design with the pituitary gland signaling to the testicles would continue with maturation of the gonad leading to reproductive capacity.

Q. So what would the risks or side effects be if you did continue to administer testosterone to a male in that situation with resolved delayed puberty?

A. The question as to the adverse effects of continuing testosterone for somebody that has normal function of the pituitary gland and their gonad, it is necessary to have the signaling that occurs from the pituitary gland in that

pulsatile manner that I previously discussed. That is going to be necessary for -- for sperm production and for normal functioning of that gonad. If one bypasses the signaling from the brain and gives testosterone for an extended period of time, you are going to suppress that normal function of the testes.

We often see this in older children and adults that are using testosterone to increase lean body mass and is demonstrated the adverse effect of doing that in that their testicular size is decreased, their sperm counts are significantly decrease, it induces a state of infertility, and that is not in agreement with the practice of endocrinology where our goal is to restore health.

Q. Suppose you had a patient come in, it's an adolescent male, who's presenting with severe body image issues. He was distressed about not having much muscle mass.

Would you ever prescribe testosterone for the purpose of increasing that patient's muscle mass?

A. So if I understand the question of a child that has gone through normal puberty, has normal levels of testosterone, but is dissatisfied with their body appearance. Most, if not all, practitioners would consider it malpractice to be inducing increased lean body mass for the desires of that individual. It is because of, one, the lack of necessity, but also the adverse

effects of giving that extra testosterone to induce that phenotypic change.

I will add that it's the reason why testosterone is a controlled substance.

Q. I want to ask a couple of questions about administering testosterone to female patients. Is there ever an indication in your clinical practice to prescribe testosterone to a female child or adolescent?

A. Testosterone -- I'm not aware of any indication where we would give testosterone to a female.

Q. And what are some of the risks that prescribing testosterone to female children or adolescents would pose?

A. Well, the effects of the testosterone or any androgen would lead to virilization. There is -- again, depending on the levels achieved, there could be very serious adverse effects with that. There is not really an indication for -- outside of this question of the gender affirmation approach, for inducing virilization in a female for any purpose other than, again, the gender affirmation.

Q. I want to shift a little bit and talk about estrogen.

Do you prescribe estrogen to minors in your clinical practice?

A. Yes.

Q. And for what conditions would you prescribe estrogen?

A. Estrogen can be given to females for the same types of indications in males of either constitutional delay or hypogonadism and -- which could be either primary or secondary, meaning that, due to a defect in the presence or function of the ovaries or a defect in the structure and function of the pituitary gland, there are individuals that have conditions in which they experience premature ovarian insufficiency where the ovaries become inactive over time, both genetically and through environmental incidents.

Q. Are there objective criteria that you would look at when you're diagnosing and treating patients with those types of condition?

A. The same as when we're talking about the treatment of males, we can measure estrogen levels, we can look for the effects of the estrogen as well. So measuring -- depending on the condition that we're treating, measuring the gonadotropin levels, the LH or FSH, the estradiol levels, and then we also look at the physical response to the intervention.

Q. You use the term "estradiol." Could you just explain what you mean by that?

A. Just like there are many different forms of androgens in addition to testosterone, there are many different forms of estrogens that can be measured in the body.

Estradiol is the main hormone that we follow and measure in females that we treat with estrogen.

Q. When we're discussing estrogen here today, is that mostly interchangeable with the term estradiol?

A. The estrogens can be given in a number of different forms, but the physical marker that we usually use in clinical practice is estradiol. We do have situations where one is exposed to either endogenous or environmental estrogens -- that's one of the causes of precocious puberty -- where we will measure other forms of estrogens, a form known as phytoestrogens, to our comprehensively look at the various forms of the compounds that have the effects of the estrogen. But for the purposes treating hypogonadism, we will generally follow estradiol levels.

Q. What are some of the medication risks that are associated with estradiol?

A. So, again, all medications that we give have risks and benefits. The effects of estrogen -- the most well-recognized are increased risk of stroke, thromboembolic stroke, clotting. It can have effects on blood pressure. It has effects on bone as well, as far as estrogen is actually the hormone that leads to closure of the growth plates that arrests further growth throughout the rest of life.

So there are also effects of estrogen on various

tissues of the body, some that are known, for example, in stimulating cancer risk. There are also protective roles of estrogen in other tissues.

Q. Have you ever prescribed estrogen to treat a mental health or psychological condition in your practice?

A. I have not. The only indication for estrogen that has debated -- it's a very ethically charged question about effecting final stature in an individual. There are some that advocate for a developmentally disabled children that are never able to ambulate, they have to be carried from one location to another, that -- that allowing them to be taller is a disadvantage. And there are some of my colleagues that would advocate giving estrogen to that -- actually, that's not answering your question because you asked about a mental condition.

Mental condition. It is given for people that are worried about being too tall. And, again, it's an ethically controversial topic and many of my colleagues, because of the risks of giving it, it is not used. It was used about several decades ago and we don't use that treatment any further.

Q. Suppose you had a female minor patient seeing you. This patient has body image issues and is very distressed about having smaller breasts than she would like to, maybe this patient read on the Internet somewhere, if she had

higher estrogen levels, she might grow largest breasts.

Would you ever prescribe estrogen for the purpose of increasing breast size in a patient like this?

A. Well, breast size varies markedly in any one individual, and the data that's available of giving extra estrogen can actually adversely affect the shape and contour of the breast, so it would have adverse effects. But the desire -- the request by a patient to have that estrogen administered for that purpose is not something that would be done in endocrine practice.

Q. So what about male patients, is there ever an indication in your clinical practice for prescribing estrogen to male children or adolescence?

A. The only discussion is in the area that I just mentioned as far as stature. But most males don't present with concerns about tall stature, so it would be reserved for those developmentally disabled children.

Q. What are some of the risks of prescribing or administering estrogen to male children or adolescents?

A. So the same effects that we see in females would be present, including an increased risk of stroke. Again, emphasizing that the administration of estrogen to a male is not the same thing as giving it to a female. In fact, there are concerns that the risk is even higher in individuals that receive that estrogen.

Q. Now I want to talk about in the course of treating gender dysphoria. You have child, adolescent who takes puberty blockers to suppress puberty, following that is given cross-sex hormones. Are there any additional concerns or increased risks for patients in this situation that are separate and apart from using those drugs in isolation?

A. It is important to consider the combined effects of a puberty blocker followed by cross-sex hormones by virtue of the fact that nearly all of the individuals that have been studied that have received the puberty blockers go on to get cross-sex hormones. In addition to the effects that we've already mentioned by the hormones themselves, the most significant adverse effect of that approach is to render an individual to be sterile.

The reason for that is that you are exposing -- so by giving the puberty blocker, you're preventing the gonad from normally maturing. And then exposing it to a hormone that it does not normally see causing structural changes to that gonad that, by the best evidence that we have available, will prevent that individual from having fertility later in life.

Q. So aside from fertility, has there been any discussion of the effect of puberty blockers followed by cross-sex hormones on sexual function?

A. There are certainly -- so the -- there are very serious concerns about the effects of the cross-sex hormones on normal sexual function and preventing -- for example, when you're giving a male estrogen, which is suppressing endogenous testosterone levels, the ability to have a normal physiologic responses to lead to, for example, orgasm is going to be impaired.

The converse of giving testosterone to females -- in adults, it actually is used in low doses to stimulate sexual desire, but it's very different in the way that it's being used in the affirmation approach. The levels are much higher than what we would recommend in the adult field of endocrinology.

Q. So are there other endocrine treatments for children and adolescents that you're aware of that take a minor who has otherwise normal fertility prospects and results in either reduced or impaired fertility or even sterilization?

A. Well, one could argue that the administration of -- for the purposes of contraception is intended to impair fertility, but there's a unique situation that that is occurring in the treatment of affirmation for gender dysphoria. The difference is that the intended goal is to disrupt that normal function, which is contrary to the entire remainder of the field of endocrinology that is

directed toward restoration of health rather than disruption of sexual function and the normal processes within the body.

It is important to recognize that, prior to the initiation of the cross-sex hormones with or without puberty blockers, that the sexual function of that individual is completely in tact. So there is no abnormality in the biological function of that individual prior to the initiation. In all other conditions that we approach we are addressing diseases or defects in the normal functioning of the body in terms of its endocrine system.

Q. So you mentioned contraceptives as one example of impaired fertility. Specifically as to sterilization, are you aware of any endocrine treatments given to minors that have as an effect permanent sterilization?

A. Endocrine, no. There are many treatments that we do to treat other conditions unrelated to endocrinology that have a consequence of inducing sterility in the area of oncology, for example.

There are endocrine tumors where we're -- it's required. Again, this is a defect in the normal appearance of the body and function of the body in which it's necessary to have an intervention that -- that as a consequence leads to infertility, but it is directed

toward treating the tumor that is present that is life threatening.

This is a unique situation in the affirmation approach to apply it for this purpose.

Q. You mentioned something about oncology. Were you referring to cancer treatments?

A. That's correct.

Q. Can -- aside from what you mentioned about a life-threatening endocrine tumor or cancer treatments, do any other sterilizing consequences of endocrine treatments or other treatments you're aware of for minors come to mind?

A. There is not a single other condition, other than this affirmation approach that I'm aware of, that that intervention is done in a way to have that effect because of -- for somebody that has a normally functioning endocrine system prior to the initiation.

Q. By that effect, you mean sterilization?

A. The effect of sterilization by administering hormones, correct, or surgery.

Q. Shift gears just a little bit. Are you familiar with the clinical practice guidelines that are published by the Endocrine Society?

A. Yes. I'm very familiar with the Endocrine Society guidelines.

Q. Is that -- is that something that you make use of in your own practice?
A. In general, practice guidelines can be very valuable, in the practice of medicine in general, to allow a practitioner to pull from the growing volume of scientific studies that are done in any particular condition.

Clinical practice guidelines, however, are only that. They are guidelines and they are highly dependent upon the quality of the evidence that is used in the generation of those guidelines. It's well understood that there are some very good guidelines that are in place and there are some that are very poor. There's also very much recognized that, in the practice of medicine, there have been many guidelines that were based upon poor quality evidence that later, when higher quality evidence was generated, resulted in a complete opposite recommendation being made.

Q. So we mentioned the Endocrine Society guidelines. Are there other published guidelines that you use in your practice other than the Endocrine Society?
A. There are many. The American Diabetes Association has guidelines. Each of the professional organizations in the treatment of polycystic ovarian syndrome, there are various guidelines.

It's very interesting that, when one looks at some of

the guidelines even within a particular condition, that many times the recommendations will differ depending on which specialty generated the guidelines. So there are many caveats to the generation of clinical practice guidelines.

In my practice as pediatric endocrinologist, as a physician scientist, but as a physician, all physicians aim to use the highest quality of evidence in making clinical decisions about how to care for their patients. And we do recognize that there is a utility in guidelines in properly understood and utilized.

Q. So are you familiar with the grade system of evaluating evidence?

A. Yes, I am.

Q. Is that a system that the Endocrine Society guidelines makes use of in its --

A. The Endocrine Society makes a heavy use of the grade system in the generation of other guidelines, yes.

Q. Are you familiar with what it means when a grade system labels a recommendation as being based on low or very low quality evidence?

A. So the grade system was generated specifically to provide an objective assessment of the quality of evidence that is used in the generation of clinical practice guidelines. And they rate in the grade system high

moderate, low, or very low quality of evidence to make an assessment about the reliability. In that designation, by definition, the different categories differ in the likelihood that the recommendations are going to change as new information becomes available.

The high quality recommendations in the grade system mean that it's unlikely that the recommendations are going to change as new information becomes available. In contrast, very low evidence means that it's very likely that the recommendations are going to change as new information becomes available.

So it's very important to recognize that the grading system -- grade that is used in the Endocrine Society guidelines is assessing the quality of the evidence that is used in making those recommendations, the confidence that one has that one is making prudent guidelines for the practitioner, and the likelihood that, as new information becomes available, that the guidelines will change.

Q. Are you familiar with the Endocrine Society's recommendations relating to the treatment of gender dysphoria?

A. Yes, I am. There was -- the initial guidelines by the Endocrine Society came out in 2009 and they were revised in 2017.

Q. And are you familiar with the level of evidence that

the grade system assigns as supporting those recommendations related to gender dysphoria treatment?

A. The question of the level of evidence by the grade system in the Endocrine Society guidelines is a major area of concern as I looked at the data. And it's important to recognize that nearly all of the recommendations that are made in those Endocrine Society guidelines are based upon low or very low quality evidence. There's only one recommendation that even rises to the level of moderate evidence, and that is for adverse effects of the intervention.

So while it's not a unique situation to have low quality evidence, it's necessary to recognize that low quality of evidence in being able to take what is being put together in those guidelines as to the most prudent course of action for the effected patients that one is going to encounter in practice.

Q. You said it's not unique. In pediatric endocrinology, are there other recommendations made by the Endocrine Society guidelines that are based on low or very low quality evidence outside of gender dysphoria that you're aware of?

A. Well, so in every guideline -- so it's important, when you go through the guidelines, there are many -- in most guidelines, it's not a single recommendation; it is a

series of analysis of the various questions related to the clinical condition. And in most guidelines, you're going to encounter some of the recommendations that are based upon low quality evidence and usually the phrase that -- and the terminology that we suggest, not that we recommend, recognizing that it's an unsettled area.

One encountering a patient in practice isn't all that's left of the option of walking away. One needs to act in a prudent way based upon what evidence is available. However, the strength of which one puts forward the recommendations is rather unique in this area of gender dysphoria.

Other conditions, for example, that I'm aware of that are very relevant in the treatment of pediatric endocrine diseases -- I'll give an example. The congenital adrenal hyperplasia -- congenital adrenal hyperplasia. That's abbreviate CAH. Those guidelines have been generated and they have actually been revised like the gender dysphoria guidelines.

In reviewing them, about half of the recommendations have moderate quality evidence. A very different scenario than what we see in the endocrine practice guidelines. Another difference that we see in other guidelines is that, when we're confronted with low quality evidence, there is a recognition of being more tentative in how

definitively we present the recommended course of action.

There's a risk/benefit analysis that is made in the treatment of all conditions. It is based upon the quality of evidence that is present and the relative risks of intervening or not intervening in a particular way. The higher the risk, the lower the quality of evidence, the more caution that is used in advocating for one particular course of treatment. And I would say it's rather unique as I've encountered in my career with the degree of poor quality evidence and strength of recommendations that are being made are vastly different than the other guidelines that I'm aware of.

Q. Now, I want to shift to talking about this research related to gender dysphoria. So we've been discussing all these various endocrine disorders and we've been discussing some objective criteria that go into diagnosing those conditions.

Based on your knowledge of what a diagnosis of gender dysphoria entails, are there similar objective criteria that are used in making a diagnosis of gender dysphoria?

A. So I shared in many of your prior questions about how there is objective biological evidence and objective clinical evidence that one has in making a diagnosis. For the condition of gender dysphoria, there is not a single biological measure that one can use to assess the accuracy

of that designation independent of the patient's report of gender dysphoria. It resides solely within the expressed identity and desires of the individual themselves, and there's not any test that we can do to be able to test the accuracy of that -- that condition.

Q. I want to talk about the body of research concerning use of GnRH agonist and cross-sex hormones to treat gender dysphoria.

Are you familiar with that body of research?

A. I have been actively investigating that body of literature for the past ten years, so I'm very familiar with the studies that have been done. There is a growing number of studies. The more frequently referenced studies are the ones that I've given most attention to, but I continue to review and critically assess the literature in this field, yes.

Q. So we've had prior testimony in the case that's talked about the differences between longitudinal study and cross-sectional study and random control style. So I don't want to ask you to completely retread that ground. But could you briefly describe the differences in what those types of studies are used to show and what they can show?

A. Certainly that -- you know, looking at the evidence and the different studies that are done, they have varying

levels of reliability. They have different -- I mean, all studies have various strengths and limitations. If properly understood and applied, they can provide useful information. Many times, the lower quality studies are merely a means to generate a novel hypothesis that will then direct the conduct of a trial that will actually allow one to get better information about a cause/effect relationship.

The lowest level of evidence is always case reports or experts' opinions. Those are based upon not really science. It's just a general experience. And, again, in that area, they can be useful for generating a novel hypotheses.

Next up on the pyramid of quality of evidence would be, for example, some of the cross-sectional studies that are done where you take a look at a condition at one point in time. That is allowing -- can allow one to infer associations, but by it's very nature is not able to assess a causal relationship between cause and effect.

The highest part of that evidence-based pyramid is going to be the randomized controlled trial where it's carefully controlled in all aspects of the study with the exception of the independent variable that is being investigated in that trial.

Q. So we're clear, can a longitudinal study or a

cross-sectional study establish cause and effect relationship?

A. So any cross-sectional study by its nature is not assessing the precise cause and effect. It merely can tell you an association.

There are some types of longitudinal studies that can infer improperly designed and controlled. If it's a randomized longitudinal study, one can infer that the difference between the treatment arms are related in a causal nature. If it's not controlled, if it's not randomized, there are always recognized that are -- can be unrecognized variables that actually led to the effect and, therefore, it is an association not a causal relationship.

Q. Have there been any random controlled trials that examine whether GnRH agonists provide benefits to treat minors with gender dysphoria?

A. I'm not aware of any randomized control trial to address the question of GnRH agonist therapy for gender dysphoria.

Q. Same question as to the use of cross-sex hormones for gender dysphoria, any randomized control trials?

A. Correct. To my knowledge, there has never been a randomized control trial looking at the efficacy of cross-sex hormones in gender dysphoria.

Q. Have there been cross-sectional or noncontrolled longitudinal studies examining those two treatments?
A. Yes. I am aware of a handful of studies that have been done of a longitudinal nature with -- again, the studies that I've read have very serious limitations and weaknesses, but they have in a noncontrolled manner followed cohorts of patients. In fact, one of the largest studies going on in the NIH right now is longitudinal analysis where, essentially, the hypothesis is we have no idea what's going to happen, but we're going to follow these patients over time to find out what's going to happen. That could be considered a longitudinal study. It's not a rigorous way to do science -- it is not a rigorous way to do science and it really in the end is going to be unable to answer the question that is needed to be answered in this area.
Q. I want to talk about a few of the specific studies that have come up in this case and, specifically, that were brought up by the plaintiffs' expert witnesses.
Are you familiar with the 2011 longitudinal study that was conducted by de Vries and others that measured mental health outcomes after receiving puberty blockers?
A. Yes. I'm very familiar with that study.
Q. What is your assessment of that study?
A. It's an important study to discuss because it's often

used as the gold standard for the rationale for this affirmative approach. It's important to recognize the -- how that study was conducted and how the patient population in that study was generated to properly interpret the effects of using pubertal blockade in minors.

It was very carefully selected, the patients that were enrolled into that study. They, in fact, excluded patients that had significant psychiatric comorbidities which are very, very prevalent in the current population that is presenting to the gender clinics here in the United States. So, essentially -- and, you know, that study had about 70 patients. They had 70 patients, not about 70. They had 70 patients in them. And part of the intervention that was done was to provide psychological support. And because it was designed in that way, the patients throughout the trial period had ongoing psychological contact with psychologists and psychological support. Any conclusions about the -- because it was a -- it didn't have a controlled population that received all of the care except for the puberty blockers. That's how a properly controlled trial is designed. That it's not possible to infer from the outcome how much of the benefit that was observed in that study was related to the psychological intervention, how much of it was related to

the fact these patients were higher functioning to begin with, and how that translates to the current population that is being -- for which this affirmation approach is being applied.

Q. So in your opinion, does this study provide reliable quality evidence that GnRH agonists provide benefits to gender dysphoria patients?

A. By the very nature by which that trial was conducted, at best it can provide a rationale for doing further studies that could show that there is either benefit or not of this intervention. But it does not answer the question about whether the administration of puberty blockers is the solution to the problem and whether alternative approaches that don't carry the same risks relative to purported benefit, namely whether psychological intervention alone may have the same or superior benefit.

Q. So move on to the next study. Are you familiar with the 2020 cross-sectional study by van der Miesen and others that measured some patients who received puberty blockers and some who did not?

A. Yes. I'm familiar with that study.

Q. What's your assessment of that study?

A. Again, it's important to recognize that that was a cross-sectional analysis where they had three different

populations of study subjects. One was patients that were presenting to the gender clinic that had not received any intervention. There was a second set of subjects that had undergone the intervention. And there was a third population that they had that were controls randomly selected from another population. So by its cross-sectional nature, it cannot establish a causal relationship between cause and effect.

There were notable differences between the different study populations. One of the most notable was there was a time or an age difference between those that were starting and finishing. There was also the same limitation as far as the degree to which the patients that were claimed to have benefit, whether it was due to the intervention itself or whether it was due to the psychological approach. By the way the study was designed, it was not able to answer that.

So, again, it is a great illustration of the limitation of that type of cross-sectional analysis and where the conclusions that have been made cannot be reliably validated because of that study design.

Q. Same question that I asked you before. In your opinion, does this study provide quality, reliable evidence that puberty blockers provide benefits to gender dysphoria patients?

A. It does not answer the question of whether patients have benefit. At best it provides a rational for engaging in the higher quality controlled trials that need to be done to actually assess whether there is true benefit from the intervention itself and not from another factor in that cohort.

Q. So move on to the next study. Are you familiar with Dr. Turban's 2020 article in *Pediatrics* that compared patients who had access to puberty blockers and those who didn't? Are you familiar with that study?

A. I'm very familiar with that paper, yes.

Q. What is your assessment of that study?

A. I could probably spend an hour going through all of the limitations weakness of that study. In fact, I did do this to my students. I illustrated for them the problems with that paper and conclusions that were made based upon the evidence that was presented.

I can begin by mentioning that the whole study was based upon the 2015 US Transgender Survey, which has a number of limitations and weaknesses and a biased -- bias -- recruitment bias, study subject bias, and other irregularities.

The assessment that was made -- again, it was a cross-sectional study. It was retrospective surveying these individuals for events that happened in the past,

after telling them that the whole purpose of that study was to be able to uncover injustices that were occurring because of the inability to get that form of intervention.

But all of that aside, if you look at the actual data that's present in the paper, the conclusion was that, if you had wanted to get puberty blockers and got them or did not get them, how does that affect your lifetime suicidality. What it failed to even mention was the fact that whether or not you were prescribed puberty blockers might have had significant effect -- or be based upon differences between those two cohorts, for example, in other psychological comorbidities.

More than that, if you look at the actual data in the paper itself, there was no statistical difference in prior year suicidality. So that lifetime suicidality was the measure that they reported, but the paper claims data that shows that at the time that the study was conducted within the past year, there was no statistical difference between those that did and did not get puberty blockers. It's a great example of failure to recognize study limitations, weaknesses, biases, and making conclusions that are not supported by the actual data in the paper.

Q. How was that study received in the field?

A. It received widespread acclaim. In fact, it was rated by *The Journal of Pediatrics* the paper of the year

in the year that it was published. The media headlines repeatedly claimed that puberty blockers prevented suicide. The authors of the paper themselves did not say that. They said there was an association with lifetime suicidality without any mention of the fact that current year suicidal ideation remained unchanged.

I actually wrote a letter to the editor which was not published, but contacted the editor as to the basis as to why it received that claim in the journal, and was told that it was based upon popularity, not upon scientific rigor. This is great example of the damage that can be done when there is a lack of recognition of the low quality of evidence that is present in making conclusions that are not supported by that evidence.

Q. So in your opinion, does this study provide reliable, quality evidence that puberty blockers provide benefits to gender dysphoria patients?

A. This study does not provide that data. The answer is no.

Q. So plaintiffs' experts, they claim that there is no evidence showing a statistically significant -- scratch that.

Plaintiffs' experts claim that the body of literature doesn't have a statistically significant showing that puberty blockers worsen mental health outcomes for gender

dysphoria patients.

Can you give your opinion as to that claim?

A. Well, it's a very interesting claim to support an intervention that has very serious risks to the effected patient to say that there is no statistically demonstrated worsening. There are many problems with the literature. This is what I found repeatedly when I reviewed this literature critically.

Again, approaching this as a physician scientist, you know, all of science is conducted with a certain level of rigor. And the way we conduct science is to develop a hypothesis as to whether there is a difference between intervention or not. And we begin actually with something called the null hypothesis. That is how science should be conducted, when you begin from a state of assuming that there is no difference and then you look for evidence to disprove that null hypothesis.

Many times in the literature that has been published in this field of gender dysphoria, they will make claims that when one does not see a difference, it's due to lack of statistical power. Yet the same investigators that make those claims, when they don't support a difference, will make a claim that in the same degree of uncertainty that it pertains to the beneficial effect that we can have confidence in that result.

The reason why that many of the studies don't show -- and there's another component of this that we should discuss as well. The difference between statistical significance and clinical significance. I'll actually illustrate this in another one of the Turban papers. This was one that was done in JAMA Open Network on cross-sex hormones.

That there was a conclusion that was made about suicidality after receiving cross-sex hormones in that -- so used the same 2015 survey with all of the weaknesses that are present in subjects and bias and -- but -- and it was retrospective and cross-sectional. But looking at the data itself for the outcome of suicidality having covered desired -- or have you had suicidal ideation, they reported a difference, not recognizing that the clinical significance of having suicidal ideation is vastly different than having a suicidal plan or actually attempting suicide or being hospitalized for a suicide attempt. And to report as the conclusions of the paper that suicidality is different but failed to recognize that there was no statistically significant difference following that intervention in those that actually acted upon that desire is really problematic.

So we have to look at both the statistical limitations of studies. And this is a very rampant in

this literature, that many of the trials that are done are based upon small sample sizes, and particularly when they try to do longitudinal analysis. There is a large number of dropouts in the studies, people that are lost to follow-up that, when a final analysis is, done you have so few patients that you are not able to detect statistical differences because of methodologic limitations.

But even if one grants that, that the purpose of giving a puberty blocker or giving a cross-sex hormone to a child is intended to prevent them from committing suicide, if you fail to demonstrate that there is a difference in the intervention, that there is no difference, that is of significance and of high significance in assessing whether one is going to proceed with that intervention.

Q. On the survey data that you mentioned, the US National Transgender Survey, you stated you had several criticisms with that data. Are there others in the field who have shared similar criticisms of that data?

A. In deed, there have. And, you know, some of them are so obvious that, in talking to colleagues, raising to the level of needing to publish a paper to be able to point out all of the weaknesses in the study has become necessary because in the discussion that that is not actually adequately covered.

There are -- there is a very good review by DeAngelo and colleagues that go through the limitations of the 2015 US Transgender Survey. Dr. Michael Biggs in the UK has written about some of the study methodologic limitations that are written on that. Normally, it's -- in other areas of medicine, one would recognize the limitations to the study. The study authors themselves would acknowledge the study weaknesses and would be a necessity to publish a separate paper pointing out all of the limitations of the study.

But it's quite interesting and important to recognize that everything that I have shared this morning is not -- is shared by other respected members of the relevant scientific community that recognize these very, very significant and serious limitations in the way the research is being conducted with a failure to acknowledge those limitations in making conclusions about how one is going to take that data that has been obtained and how to apply it to clinical practice.

THE COURT: Mr. Jacobs, you're going to have to slow him down. I'm not sure I've been able to.

MR. JACOBS: Okay. I'm sorry.

BY MR. JACOBS:

Q. I'll work with you on that.

A. I'll take a deep breath before I start and try to do

that midway through.

Q. If you see my hand raised like this, that will be a signal when you're looking at me to slow the pace. Okay.

So we've been -- so we've been discussing thus far some of the research on puberty blockers specifically. Now I want to move on to some of the research discussing cross-sex hormones that have been discussed by the plaintiffs' experts in this case.

Are you familiar with the 2019 longitudinal study by Allen and others that looked at suicidality following cross-sex hormones?

A. Yes. I'm aware of that study.

Q. What is your assessment of that study?

A. Well, it was a longitudinal study, but the serious limitations in that analysis, one, it was a very small patient population. I think there were about 47 patients in that cohort. There was no controlled group. There was no consideration of other things that happened in addition to the administration of cross-sex hormones, and, namely, provision of psychological support over the integral that they were following over time. And because of that, to be able to make a conclusion that this demonstrates that the administration of cross-sex hormones was the reason for any changes that were observed in psychological functioning, is stepping beyond what the data can say.

Again, in the way that that study was conducted, it could have been designed in a different manner that would have allowed one to be able to get that causal relationship between intervention and effect. But, unfortunately, it was not done in that manner and, therefore, it cannot be used as the evidence that one would like to say that this is a beneficial approach in the treatment of gender dysphoria.

Q. When you say, could have been designed in a better way, how could it have been designed in a better way?

A. If one was -- and this is the way really all science should be conducted, is that, if one is -- you want to compare your experimental intervention in comparison to a patient population that has everything identical except for that intervention, or some trials are conducted with two different interventions that are compared side by side.

That would allow one to assess, because in that study design followed longitudinally, one could infer and actually accurately conclude that the only difference between the outcome in psychological functioning was that you received cross-sex hormones and thus, because that was the only difference present, that that was the reason for that difference. That was not done in the Allen study and, therefore, you cannot make that conclusion.

Q. So in your opinion, does the Allen study provide quality, reliable evidence that the administration of cross-sex hormones provides benefits to gender dysphoria patients?
A. The answer is no. At best, it will provide a rationale for conducting the properly designed study to answer that question.
Q. So are you familiar with study that came out in 2022, earlier this year, by Green and others that measured suicide attempts and access to cross-sex hormones?
A. Yes.
Q. What is your assessment of that study?
A. Again, that study has many of the same weaknesses that I've already mentioned. Again, it's quite pervasive in the literature in general.

As opposed to the Allen study, which is a very small sample size, this was a large cohort of patients but it suffered many of biases or potential biases in patient recruitment. It was a convenient sample that was recruited over the Internet and it was a cross-sectional analysis which, again, because of the limitations, at best can demonstrate correlations but it cannot by its design establish a cause and effect.
Q. When you say "convenient sample," could you explain what that term means?

A. Certainly. So there are rigorous ways to look at an entire population or a subset of a population that encompasses all of the differences that are present in that group. Those are the best studies. The best studies of those nature in the area of gender dysphoria that I'm aware of are the ones that are done -- that were done in adults in Sweden where they have a probability sample where they have the entire population. So there is no bias in the patients that are being selected to enter into that study.

A convenient sample is when you take a subset of patients that are identified by what's called nonprobability, meaning that it doesn't represent the entire population, and enter that base survey where you invite participants to fill out a survey and you advertise that on social media sites that are directed toward people that have one particular desire in the outcome of the study is highly -- has the high potential for bias.

It is the recognition of these study limitations, including that convenience sampling methodology, that leads to the designation of these being very low quality evidence in the grade system.

Q. Just to sum up that study, in your opinion, does the 2022 Green study provide quality, reliable evidence that cross-sex hormones provide benefits to gender dysphoria

patients?
A. I would say no because of the very serious limitations of that study by design.
Q. There are a few studies that the plaintiffs' experts have claimed show benefits of the administration of cross-sex hormones over a longer period of time in the some of the other studies in the literature.
So are you familiar with Dr. Turban's study that came out in 2022 earlier this year that was a cross-sectional study comparing mental health outcomes between those who had access to hormones and those who didn't?
A. I believe you're referring to the JAMA Open Network paper. So that was -- again, that was a study that I mentioned earlier based upon the 2015 US Transgender Survey with all of the limitations.
I'm happy to share even more detail of the limitations in the way that, by it is very nature, again, with how the sample population was recruited, that it was retrospective cross-sectional, did not have controls. All of those limitations were present in that study that prevent one from making reliable conclusions about a cause-and-effect relationship between receiving cross-sex hormones and psychological functioning with all of the additional caveats of the data itself that I mentioned earlier.

Q. Just make sure I'm asking about the correct study. Did Dr. Turban publish a study earlier this year? I think it was PLOS One. Is that how you say the name of that journal?
A. I may have the journal incorrect. I may have the journal incorrect.
Q. But the discussion you just had --
A. It was in reference to that paper, correct.
Q. In your opinion, does that paper provide quality, reliable evidence that cross-sex hormones provide benefits to gender dysphoria patients?
A. It does not provide that evidence. So the answer is no.
Q. So are you familiar with a 2014 study by de Vries and others that examined puberty blocker access five to seven years over that time period?
A. Yes. I'm familiar with that study.
Q. What is your assessment of that study?
A. So that is a follow-up of that 2011 study where there were initially 70 patients that were followed prospectively after receiving pubertal blockade. The follow-up actually encompassed 55 patients. So there were 15 patients that were lost or not included in that secondary analysis. The reason for disqualification is there are many reasons why they couldn't be tracked or

they didn't fulfill their criteria for the study.

But it has the same limitations that was present in assessing the original 2011 study. It was a very selected patient population that is not representative of the population. It had a predominance of males desiring to appear female rather than females desiring to be a male, which is the predominant effect that we're seeing now presenting to gender clinics. It were -- individuals that had -- ones -- because it took the extension of the original study, it was a selected -- patients where those were excluded from the study that had the psychological comorbidity that was present, so they're higher functioning to begin with. And then throughout the study, they received ongoing psychological support.

For the same reasons in the short run, by having a longer study does not obviate the limitations of that study in making a conclusion that can be applied to the gender clinics that are operating here in the United States.

Q. So does that 2014 de vries study in your opinion provide reliable, quality evidence that puberty blockers benefit gender dysphoria patients?

A. It does not provide the answer that one is seeking as to whether the risk versus benefit of the affirmation approach, including puberty blockers, is warranted. At

best, it provides a basis for conducting the proper studies that need to be done to assess -- to answer that question.

Q. So the last couple of studies that were discussed by the -- in Dr. Turban's testimony in this case I think had to do with surgery outcomes. Are you familiar with the 2018 cross-sectional study by Olson-Kennedy and others that examined top surgery patients?

A. Yes, I -- if you're referring to that study, I'm familiar with that study, yes.

Q. What's your assessment of the science behind that study?

A. Well, there are a number of interesting aspects of that study. Most notably, is that the scale that they used to assess the intervention itself was a novel scale that had never been validated by the lead study author. And there are many reasons why in these types of studies it's important to have that test validation before one uses that and makes conclusions. But it had the -- it was a convenient sample that -- and then the other concern is the length of follow-up.

It's important to recognize that, if you are assessing one's level of dysphoria or anxiety or difficulty with the appearance of one's body and there is an expectation that you're going to have benefit by

altering the appearance of the body, even before one conducts the experiment, there would be a rationale to believe that that immediate effect would be fulfilled. The question is, does it solve the problem? Does it address the underlying issue at hand that led to the dysphoria? And is the risk of that intervention mitigated by the purported benefits?

The length of follow-up was not sufficient to be able to establish that as addressing the problem. It used a sample population that had potential for bias. It was a small sample set. And it used a scale that really had not -- has not been validated in the way that we would for other types of similar types of studies.

Q. So your in your opinion, does that 2018 paper provide quality, reliable evidence that top surgery provides benefits to gender dysphoria patients?

A. The answer is no because of all of the limitations and the failure to conduct the trial in a way that could answer the question.

Q. So are you familiar with the study that came out in May of this year by Tang and others that measured post-surgery regret? It was a Kaiser study. Does that sound familiar?

A. Yeah, the Kaiser study. What they were trying to assess in that paper was looking retrospectively through

their medical records for those that had had the surgery.

So there is a couple of interesting observations from that study. The first, it's quite notable the age of which these patients were identified. The mean age was 16 years. There were ten patients that were about 12 to 13 years of age that had bilateral mastectomies performed on them, which many now -- this has come out even in the publishing discussion about the concerns about surgical interventions in young children.

The timing of follow-up is similar to the Olson-Kennedy study in that the follow-up was a mean about two years, some as short as three months. And, you know, not really assessing the question as to whether they addressed the underlying cause of the dysphoria or whether it provided lasting benefit in way that would justify the risk involved in performing that intervention.

Q. So in your opinion, does the study provide quality, reliable evidence that top surgery provides benefits to gender dysphoria patients?

A. No. There is not evidence from that study that long-term benefit can be achieved from that intervention.

Q. Let's shift gears. Well, I'll wrap up with this. So we've discussed quite number of studies specifically. I think your testimony is -- I won't summarize your testimony.

Aside from the studies that we've discussed here today, are you aware of any studies in the literature that in your opinion provide quality, reliable evidence that either puberty blockers or cross-sex hormones provide benefits to gender dysphoria patients, specifically minors?

A. Because of the major methodological limitations and weaknesses of the extent published literature in the field of gender dysphoria, one cannot make a conclusion that this is justified as a safe and effective long-term solution to gender dysphoria in consideration of the significant risks and unsubstantiated long-term benefits.

Contrary to that, there is a major deficit in even the willingness to address the question of the benefit of psychological intervention, at least as this question is considered within the United States.

As I said, there are studies that indirectly give evidence as hypothesis generation that psychological interventions can have significant benefit in this patient population and that the question is, if that alone without embarking upon cross-sex hormones and puberty blockers can achieve the benefit that one is seeking without the risks associated with cardiovascular effects, weight, stature, stroke, and all of the other things -- infertility.

I am aware of studies that -- for example, that show

that -- even though they're not randomized, that if you compare psychological intervention alone versus puberty blockers and psychological interventions, both groups showed benefit. I'm thinking of a Costa study in particular. It was as small sample. And it's being dismissed because, again, lack of statistical significant, but it is a piece of evidence that needs to be considered in generating novel hypotheses and designing properly-designed studies with controls that can assess that question as to whether psychological intervention is really the basis for which benefit can be achieved in this patient population.

Q. You mentioned the Costa study. By the Costa study, are you referring to the 2015 article by Costa and others publishing in the *Journal of Sexual Medicine*?

A. That is my recollection. It was directly a study where patients either immediately received puberty blockers or that was delayed and they were followed up over time and assessed psychological function.

Q. So you're aware that Dr. Turban served as an expert witness in this case for plaintiffs, correct?

A. Yes, I am.

Q. Are you familiar with Dr. Turban's work in this field?

A. I am very familiar with his work and -- because many

of the things that he has stated in conclusions from his paper that others have -- have shared in the media, it's very important to recognize the quality of the research that he has done, the contribution to the field in light of the major weaknesses that we've already discussed.

Q. Has there been -- you mentioned weaknesses. Has there been criticism of Dr. Turban's work in this field in terms of research and advocacy?

A. There is -- again, as I stated earlier, that the way that science is conducted -- now, one -- when one conducts scientific investigation, it is impossible that bias does not exist. But properly done, one recognizes one's biases and one designs an experiment that allows one to minimize those biases, that one looks at the data objectively with the lens that has been established for the normal conduct of science. That means that one recognizes what is one's starting scientific premises, that foundation that is not provable by science that leads to the generation of a hypothesis about an intervention that may have benefit, and to design an experiment to determine whether that benefit is achieved and in relation to what potential risks may be present.

If you look at the way that the studies -- and I will reference not the data itself because one can accept that there was a need early on in the study of a new condition

where there is not a demonstrated solution, that the starting point is these lower quality studies to be used and recognized with their limitations and then to take that data and then apply it with more rigorous studies.

If you look at the way the papers that Dr. Turban and others have published, by merely reading the conclusions that are made in the paper, that scientific process of disproving the null hypothesis is not what is apparent from that discussion. Rather, by dismissing data that does not correlate with the hypothesis, it is equivalent to beginning with a conclusion and then looking for the data to support that conclusion. That is a vastly different way of doing science and it's a danger to all of science, and one needs to recognize those dangers.

So it goes beyond the methodological weaknesses which can be recognized, acknowledged, and accepted to higher levels of concern about the way this is being presented in the media and by the public and most importantly by the patients that are desperately looking for relief of their suffering.

A patient that is not aware of these limitations and is being told that we have understood the condition in its evolution and the proper treatment based upon the quality of evidence that is available does not provide the benchmark that we use in all other areas of medicine.

Q. So related question to a portion of that discussion, are you familiar with the term clinical equipoise?
A. Yes, very familiar.
Q. Could you just briefly explain what that term means?
A. The discussion of equipoise means that, in order to be able to engage in a scientific investigation, there needs to be a question that remains unanswered. One would not conduct a study if one already knew the outcome, putting patient study subjects at risk, or engaging in the cost and the logistics of doing that study.

This is another area that is very important in the discussion of this condition of gender dysphoria, that it is frequently claimed erroneously that one has achieved the answer to the question of how to best address gender dysphoria and, therefore, it is not ethical to conduct the trials that need to be done.

On the basis of the limitations that we've already discussed and growing evidence that the patients that have been subjected to this affirmation approach are continuing to suffer, that many of them are recognizing a decade or later that they were not helped in the way that they expected, that our -- our questioning intervention that was done by the level of scrutiny that's occurring in other areas of the world like Europe where the discussion is now gaining attention about the many, many questions

that remain. It is erroneous to say that we have identified the best or an effective solution that maximizes benefit and minimizes risk in the alleviation of suffering from gender dysphoria.

Quite the contrary. There are major, major questions that remain. There was a lack of attention to alternative hypotheses, different scientific premises, and most notably, a failure to recognize the potential for benefit by psychological interventions. Again, as I mentioned, in Europe they are recognizing this now and are giving priority to the psychological interventions in this patient population recognizing that this is still highly experimental, unproven. At best we can take the evidence to develop novel hypotheses and design the properly -- the proper studies that need to be done.

Q. So just to tie this up. In your opinion, is there equipoise with respect to the question of treating gender dysphoric minors with puberty blockers?

A. There remains a question as to whether this is a -- the risks outweigh the benefits and whether alternatives exist and it still is an area that needs scientific investigation.

Q. Maybe a better way to phrase it is that the plaintiffs' experts in this case argue that there is a lack of clinical equipoise as to the use of puberty

blockers to treat gender dysphoria.

Do you agree or disagree with that assertion?

A. I disagree with their conclusion.

Q. Same question with cross-sex hormones. Plaintiffs' experts argue that there is a lack of clinical equipoise for the use of cross-sex hormones to treat gender dysphoria.

Do you agree or disagree with that statement?

A. I disagree with that assertion.

Q. So in your opinion, does the state of the current body of scientific literature ethically preclude random controlled trials being conducted concerning the treatment of gender dysphoric minors with puberty blockers?

A. We need to do the higher level studies based upon the uncertainties that we have. So that I think to conclude that we don't need to do randomized trials, I disagree with that assertion.

Q. Is your answer the same with respect to cross-sex hormones?

A. Yes.

Q. You mentioned briefly some of the ongoing discussion outside of the United States in Europe. Can you give an overview of what's been happening in that area outside of the United States?

A. I most certainly can. I'll just limit my comments to

Sweden, Finland, and the United Kingdom, but also recognizing that other European countries that have been engaged in the affirmative model for a longer period of time than in the United States. When these countries looked at the available evidence to truly look at evidence-based recommendations rather than here in the United States where one takes an eminence-based recommendation, meaning using the purported authority of medical societies that don't represent the entire society, but rather small subsets of the entire society, to make conclusions -- when they've actually looked at the data, they have uniformly concluded exactly what I shared with you this morning about the major limitations and weaknesses of the available studies, the fact that this remains an experimental protocol.

In fact, Sweden -- the Karolinska Institute in Sweden has suspended delivering affirmative care outside of research studies. In all of these countries, they're now prioritizing psychological interventions. They are acknowledging that more research needs to be done. This is the way that the field of medicine normally operates; that we -- when we're faced with low-quality evidence, many uncertainties and questions, it's not that we don't seek answers to those questions, but we proceed with the utmost of caution. That is what is going on.

The most recent -- the Cast review in the UK came to exactly the same conclusions that I have made in my reading of the literature over many years and many of my colleagues and those that have written on this area that, despite the claims that are being made about the efficacy of the affirmation approach, the evidence itself is insufficient to make that conclusion.

Q. You mentioned the Cast review. Could you explain what that is?

A. So the health system in the UK undertook -- led by Dr. Cast. They actually published two reports NICE, the national health care organization. One on puberty blockers and one on cross-sex hormones. And the conclusions of that study really looking at the available evidence concluded that the data was insufficient to be able to have an answer to the benefit of this approach.

It actually followed in step with the publication of their experience, essentially, a follow-up. Many times in science where you have this initial report based upon limited studies, you look to find corroborating results from another study. This was a paper by Carmichael that came out in the UK where, essentially, they were not able to confirm the beneficial effect that was seen in the de Vries study that we discussed earlier. And there are theories or hypotheses as to why the data looks very

different in that report versus the original Dutch cohort. And much of that relates to the way that these patients were enrolled in the study and the lack of the same rigor and including the patients in that outcome.

So based upon that, the whole delivery of care to individuals that have gender dysphoria is in -- is being reconsidered and reprogrammed to be able to acknowledge what we don't know and to seek to find the answers to what needs to be found within that desire to treat these patients with gender dysphoria.

Q. You mentioned the Carmichael paper. Are you referring to the 2021 study that was -- that observed pubertal suppression in 12- to 15-year olds that was published in PLOS One?

A. Correct.

Q. A few minutes ago you mentioned I think the term that you used was the eminence method or something similar.

Could you explain just briefly what you meant by that term?

A. So we -- in the field of medicine, we like to make our decisions based upon scientific evidence. There is another way of looking at how to make decisions based upon the prestige or the recognition of an authoritative body. And it's not to say that, if the -- the body that has the prestige is basing their recommendations on quality

evidence. It could be trustworthy to accept what is being said. But it's a world of difference to take it on the authority of an organization without looking at the actual evidence. It is repeatedly stated in the conversation on the treatment of gender dysphoria that multiple professional organizations have all concluded that this is the prudent approach. Now --

THE COURT: You're going to have to slow him down or I'm going to stop him.

MR. JACOBS: I apologize, Your Honor. Let's pause for minute so the court reporter can catch up.

THE COURT: That's about the seventh time I've had to ask, and it's not going to work.

MR. JACOBS: I apologize, Your Honor.

THE COURT: I don't know what else to do.

BY MR. JACOBS:

Q. You can go on.

A. So addressing the question of eminence, meaning accepting the authority of a professional organization, in contrast to evidence looking at the actual data that is used to support the recommendations is vastly different. And having a larger number of eminence-based directives does not obviate the concern with the lack of quality evidence.

Q. So when you're -- when we're talking about the

eminence method in the United States in the context of gender dysphoria, what are the organizations that people would be referring to?

A. Well, the -- they -- the authority of the American Medical Association, the American Academy of Pediatrics, and WPATH are all used to make this eminence-based argument. It goes further that many of the claims that are made is that the -- let's take the example of the American Academy of Pediatrics.

One is given the impression that the entire body that belongs to the American Academy of Pediatrics has made that conclusion. What has failed to be recognized that that policy was the generation -- was generated by a very small subset of individuals; that one could question whether they have conflicts of interest; one can question whether they have included representative views from the entire organization; and whether they have in an unbiased way critically evaluated the scientific literature as is now being done in these other European countries.

Q. So shifting gears just a little. In a clinical setting, how does a physician go about determining whether recommending a particular treatment to a patient is ethical or unethical?

A. So in the area of -- in general in medicine, one always needs to consider the relative risk and the

relative benefit of any intervention that we recommend. And the decision about to treat a patient in a particular manner requires assessment of the relative differences. The higher the risk, the higher that one is going to need to have the evidence or the safeguards in place for being -- for embarking upon that intervention. So there are ethical considerations based upon both safety and efficacy.

Q. So if a physician, say, is trying to decide whether to begin offering a treatment that he's never offered before, would he have some sort of duty to review or familiarize himself with the relevant scientific literature about that treatment?

A. So the answer is yes, that there is an obligation for the clinician to be aware of the intervention that they're proposing and the evidence that's available for that. It is recognized that the volume of literature that has been generated in the field of medicine is growing exponentially; that there are varying -- as we discussed, the quality of the data of varies vastly, and when one draws upon clinical practice guidelines to help inform decisions, it does not take away the responsibility of the practicing physician to recognize the quality of the evidence that is being used, and when things do not go as planned, the treating physician is responsible for that

adverse outcome. And one cannot rely upon an uncritical, blind acceptance of policy statements to justify an adverse effect that could have been recognized if one had done due diligence in recognizing the weaknesses of the data.

Q. So if the physician is considering offering this new treatment, does review the evidence, and the physician isn't convinced that the treatment is likely to provide benefits to his patients that justify the risks, is it ethical for the physician to begin offering that treatment?

A. It is highly unethical, unprofessional, and irresponsible to embark upon a treatment which the treating physician has deemed not justified by a careful assessment of risk and benefit.

Q. Is it ever part of your clinical practice to recommend either puberty blockers or cross-sex hormones for gender dysphoria patients?

A. I have not administered hormones for that purpose, precisely because my assessment of the available literature and the data that we have does not justify the risk with concerns about benefits. So my assessment of risk and benefit would make it unethical, unprofessional for me to be able to intervene in that way.

Q. Are you the only pediatric endocrinologist in the

United States who feels this way?
A. Most certainly not.
Q. Do most pediatric endocrinologists in the United States offer or recommend puberty blockers and cross-sex hormones to treat gender dysphoria?
MR. STRANGIO: Objection. I don't think they laid a foundation for his expertise on what all pediatric endocrinologists do.
THE COURT: Sustained.
MR. JACOBS: I'll withdraw it.
THE COURT: I'm sure he can answer all don't because he knows he doesn't, but --
MR. JACOBS: I'll withdraw the question and move on to something else.
BY MR. JACOBS:
Q. So move on to talking about disorders of sexual development. Can you explain what a disorder of sexual development is?
A. Yes. Disorders of sexual development are conditions in which infants are born where the normal process of sexual differentiation into male and female primary sexual organs does not occur in a manner that leads to male and female phenotypes types. The best example is, when a child is normally born, by looking at the appearance of the external genitalia, a parent or a physician can

correctly identify the sex of that individual 99.98 percent of the time by the appearance of the external genitalia.

In a very rare subset of individuals, 0.02, percent the answer to the question is that there is ambiguity so that the question cannot be answered.

Q. When you say "correctly identify the sex," what do you mean by that?

A. Recognizing what we mean by sex in relation to the normal function of males and females in the reproductive process as to having testes versus ovaries, having X and Y chromosomes versus X and X chromosomes, to be able to participate in the reproductive process as either male or female.

Q. You mentioned patients with ambiguous genitalia. What type of care do you provide to those patients?

A. It's very important, when we're faced with ambiguity, an individual that has a disorder of sexual development, first, to understand, if we can, what is the reason for the ambiguity presenting itself because many of the conditions that lead to the ambiguity are the result of medical conditions that can be life-threatening or have serious effects on later functioning in life.

So the role of the endocrinologist and the treating team is to understand what is the sexual anatomy both

internal and external, what is the genetic composition, what is the hormone profile of androgens versus estrogens that are present in that individual, and to ascertain what is the best course of treatment to address the condition that led to that ambiguity.

Q. Do you ever offer surgical interventions for patients with disorders of sexual development?

A. In the routine care of patients that have DSDs, we do indeed. In the newborn period, reserve surgeries for those abnormalities that are going to affect the health of that individual; meaning that, if there is an abnormality in the ability to excrete urine, if there is a connection between the urethra and rectum, things that will cause harm to the patient in that newborn period. We do not perform surgeries to alter the appearance of the genitalia solely for that purpose.

Q. When you say "solely for that purpose," what do you mean by that?

A. Meaning, in this -- this is the field of those that are involved. And I've been treating children with DSDs for a quarter century, 25 years. When I first trained, it was felt that one needed to make a definitive conclusion about the sex of that individual in the newborn period to allow that child to thrive later in life.

We have discarded that approach and opt not to do

surgeries to change the appearance of the genitalia because of the many uncertainties about the function of that individual, and do not believe -- or we believe that the most cautious approach is the best approach, to wait before intervening and to gather the information that often will not become apparent until later in life.

That has been a change over the last several decades. It's a much more cautious approach than in the past. Quite the opposite is being done in the area of gender dysphoria. But I think for the reasons that we are cautious in recognizing that we don't always know the answer and that we have recognized that there is not -- that there is a need to have more time to explore the outcomes over time.

THE COURT: Mr. Jacobs, how much longer do you have on your direct?

MR. JACOBS: I'm getting to my sum up section, Your Honor. So maybe five minutes, maybe ten if it takes a little bit longer than that.

THE COURT: I'm sorry. Your sum up?

MR. JACOBS: I'm almost done. Yeah, just concluding the testimony is what I mean.

THE COURT: All right. Go ahead.

MR. JACOBS: So I apologize if there is a little bit of repetitious in this, but just to get out --

THE COURT: I mean, I'm going to have his transcript. I don't need you to summarize what he's told us, if that's what you're planning on doing.

MR. JACOBS: I don't think so, Your Honor.

BY MR. JACOBS:

Q. Based on your review of the available evidence, Dr. Hruz, is there a similar risk/benefit profile for prescribing GnRH agonists to treat precocious puberty in minors and using GnRH agonists to treat gender dysphoria in minors?

A. So gender dysphoria and central precocious puberty are different conditions with a different risk/benefit profile, and one cannot conflate those two diseases.

Q. As a pediatric endocrinologist, would you consider those two things the same treatment as in GnRH agonist for precocious puberty versus GnRH agonist for gender dysphoria? Would you consider those two things to be the same treatment or different treatments?

A. One is treating different conditions with the same class of medication.

Q. Based on your review of the available evidence, is there a similar risk/benefit profile for treating delayed puberty in boys with testosterone and providing testosterone to girls for gender transition?

THE COURT: Sounds like a summary to me. He's

already testified to the last two questions in depth and for hours.

MR. JACOBS: If it's clear to Your Honor, that's good enough for me.

THE COURT: Thank you.

MR. JACOBS: If I can have just one moment, Your Honor.

THE COURT: Sure.

BY MR. JACOBS:

Q. So if I could just go back to clarify one thing.

You mentioned the difference in inclusion criteria between the de Vries studies on puberty blockers and the Carmichael study. You mentioned there was a difference.

Can you explain exactly what the difference was?

MR. STRANGIO: Objection. I think that mischaracterizes the testimony.

BY MR. JACOBS:

Q. I'll ask this way.

Was there a difference in the inclusion criteria for the de Vries studies concerning pubertal blocker and the Carmichael study concerning puberty blockers?

A. The difference between the Carmichael study and the de Vries study is that, in the de Vries, there was a much more rigorous stratification and inclusion criteria that was applied to that patient population that has shifted

over time. And by the time the Tavistock center began their program, there was not the same degree of attention to the psychiatric comorbidities as far as inclusion or exclusion criteria.

MR. JACOBS: Pass the witness Your Honor.

THE COURT: We're going to break for lunch until 1:30. 1:45.

(A recess was taken at 12:18 p.m.)

* * * * *

REPORTER'S CERTIFICATE

I, Valarie D. Flora, FCRR, TX-CSR, AR-CCR, certify that the foregoing is a correct transcript of proceedings in the above-entitled matter.

Dated this the 8th day of December, 2022.

/s/ Valarie D. Flora, FCRR

United States Court Reporter

(Proceedings continuing at 2:02 p.m.)

THE COURT: We're back on the record.

Go ahead, sir.

MR. STRANGIO: Thank you.

CROSS-EXAMINATION

BY MR. STRANGIO:

Q. Good afternoon, Dr. Hruz. My name is Chase Strangio. I'm one of the attorneys with the plaintiffs. It's good to see you again. So you are not a psychiatrist. Right?

A. That is correct.

Q. And you are not a psychologist?

A. Correct.

Q. And you are not a surgeon?

A. Correct.

Q. And, as a pediatric endocrinologist, your charge is to treat, as I understand it, hormone-related disease?

A. Correct.

Q. And you have never diagnosed any person with gender dysphoria. Correct?

A. Correct.

Q. And you have never treated a patient for gender dysphoria. Correct?

A. Not for gender dysphoria, correct.

Q. And you currently work at the Washington University in St. Louis. Is that correct?

A. I currently work at Washington University, yes.
Q. And you are affiliated with the St. Louis Children's Hospital?
A. Yes.
Q. And the St. Louis Children's Hospital has a transgender center. Is that correct?
A. Yes.
Q. And, at the transgender center, the doctors treat adolescent patients with gender dysphoria with puberty blockers and cross-sex hormones. Is that correct?
A. Yes.
Q. And you believe that treatment of gender dysphoria in adolescents with puberty blockers should be limited to the setting of a carefully controlled and supervised clinical trial. Is that correct?
A. I believe that it is properly done under the setting of an experimental protocol, yes.
Q. And by experimental protocol, you mean a carefully controlled and supervised clinical trial?
A. With all of the requirements for rigorous research, undergoing review by an IRB board with all of the safeguards to protect the subjects for that study.
Q. And that would be, considering all of those caveats, a carefully controlled and supervised clinical trial?
A. There are many ways to design the trial, but it needs to be

set up under that paradigm, yes.
Q. Okay. And, in your practice, you very frequently prescribe medications off label. Is that correct?
A. Yes.
Q. And that is a very common practice in the area of pediatrics?
A. It is necessitated by the fact that many of the drugs that we use have not been specifically tested in children.
Q. So it's a common practice in pediatrics?
A. It is a common practice in all of medicine with the caveat that anyone who prescribes off label is required to carefully weigh the relative risks and benefits of using that drug off label, accept the responsibilities for that.
Q. Understood. And on direct you testified that you don't do surgeries on infants with disorders of sex development for purpose of changing the appearance of genitals, of their genital characteristics. But you are aware that some doctors in the United States do do that. Right?
A. I am very much aware of the conversation that is going on nationally. I would say that as an approach to treating DSDs as a whole that what I shared in my testimony is accurately reflecting what most programs that have DSD programs abide by.
Q. But some don't abide by that.
A. Well, I don't have knowledge of every program.
Q. But some could. But some could do that?

A. I have no knowledge.
Q. Okay. So you don't know?
A. I only know of the programs that operate under the paradigm that I outlined.
Q. Understood. Are you familiar with an organization called the Alliance Defending Freedom?
A. Yes.
Q. And the Alliance Defending Freedom is also known as the ADF. Right?
A. Yes.
Q. And you traveled to the ADF's Arizona offices in 2017 for a meeting about the types of healthcare at issue in this case. Right?
A. I don't recall the specific dates, but I did travel there, yes.
Q. And, approximately, would you say that it was in that range of that year?
A. Again, I would have to look at the dates. But I did travel to ADF, yes.
Q. And you traveled there for two separate meetings at the ADF offices related to the treatment of gender dysphoria in adolescents. Is that correct?
A. Yes.
Q. And Mark Regnerus was at at least one of the ADF meetings you attended?

A. Yes.
Q. And so was Dr. Patrick Lappert?
A. Yes.
Q. I want to just ask you just a few questions about your CV and publications. Just for clarity, it's Defendants' Exhibit 3. So, according to your CV, you published four articles and one book chapter about transgender people and gender dysphoria. Is that right?
A. If that's what's listed on my CV, yes.
Q. Is there other publications beyond what are listed on your CV?
A. There is a recent book that was published that wasn't included on that CV.
Q. And what's that book?
A. *Sexual Identity*.
Q. And the earliest of those was published in 2017. Is that correct?
A. I would have to look at the exact date, but that sounds about right.
Q. And that first article of yours addressing gender dysphoria was published in *The New Atlantis*. Right?
A. Yes.
Q. And *The New Atlantis* is not a peer-reviewed scientific journal. Correct?
A. It is editorially reviewed.

Q. But it's not a peer-reviewed scientific journal. Correct?
A. It depends on how you define peer reviewed. It was extensively reviewed by editors in the process of putting this together.
Q. When you were describing your publications, you said most of them are published within peer-reviewed top tier journals in your field. Would you consider *The New Atlantis* one of those?
A. In the category of *Diabetes* or *Nature Communications*, it is not considered in that same category, no.
Q. And you also published two articles about gender dysphoria in *The National Catholic Bioethics Quarterly*. Correct?
A. Yes.
Q. And *The National Catholic Bioethics Quarterly* is published by the National Catholic Bioethics Center. Right?
A. Yes.
Q. And those two articles were published in 2018 and 2019 or thereabouts?
A. It sounds about right. I would have to look at the dates.
Q. But it's probably correctly listed on your CV.
A. Correct.
Q. And the last of your four articles about gender dysphoria was published in *The Linacre Quarterly*. Is that correct?
A. Yes.
Q. And *The Linacre Quarterly* is a journal of the Catholic Medical Association. Correct?

A. It is -- that is the publisher, yes.
Q. And the book chapter that's listed in your CV that you wrote on this topic was published in a book entitled *Transgender Issues in Catholic Healthcare* in 2021. Is that correct?
A. Yes.
Q. And that book was published by the National Catholic Bioethics Center, the same organization that publishes the journal that published two of your articles. Is that correct?
A. Yes.
Q. And then, in 2017, you received a certification in healthcare ethics from the National Catholic Bioethics Center in Philadelphia, Pennsylvania. Is that correct?
A. Yes.
Q. And in its brief statement on transgenderism, the National Catholic Bioethics Center that we've been discussing states that "Gender transitioning insists on affirming a false identity and, in many cases, mutilating the body in support of that falsehood." Is that correct?
A. I would have to review what they have written.
Q. Let's pull up that document to see if it helps refresh your recollection.
We will eventually have it on the screen in front of you is my understanding.
A. If it saves time, I can just accept that it does indeed say that.

Q. Okay. Does that sound consistent with your understanding of their position?
A. I don't know what their current position is.
Q. Does that sound consistent with -- well, if you want to go to the top, just to confirm, does this look like the brief statement on transgenderism from the National Catholic Bioethics Center?
A. That is in the format of their publications, yes.
Q. And then I think at the very top, above human anthropology and gender, "Gender transitioning insists on affirming a false identity and, in many cases, mutilating the body in support of that falsehood."
A. I read that, yes.
Q. And does that sound consistent with your understanding of their position at least in winter of 2016?
A. This is what they have written, yes.
Q. And do you agree with the statement that gender transitioning affirms a false identity and, in many cases, mutilating the body in support of that falsehood?
A. There are many ways to interpret that statement and many of the words that are used. I think the word "mutilation" is appropriate when defined as changing the body in a way that takes away normal functioning. And the question actually as to identity is a very important question that I considered very early on in my investigation of this area. It's the basis of

the scientific premise for the affirmative approach. And that's an anthropological question, not a scientific question.

Q. Understood. I'm going to move on from that.

You've written or joined a friend of the court, or amicus briefs, in several cases in federal courts. Is that correct?

A. Yes.

Q. In 2017 you joined an amicus brief in a case called *Grimm versus Gloucester County* at the United States Supreme Court. Is that correct?

A. Yes.

Q. And that case, just to refresh your recollection, was an appeal of a lower court's decision that school districts are required by law to treat students in accordance with their asserted gender identity instead of their biological sex. Is that correct?

A. That was my understanding, yes.

Q. And that brief concluded by saying "that conditioning children into believing that a lifetime of impersonating someone of the opposite sex, achievable only through chemical and surgical interventions, is a form of child abuse." Is that correct?

A. I do recall that, yes.

Q. And you joined that brief. Correct?

A. I did. And I've said previously that I would not have chosen that wording. But to convey the message that was being

said in that brief, I represented the assessment at that time.
Q. In 2018 you submitted a brief in the case called *Doe versus Boyertown* at the United States Supreme Court?
A. Yes.
Q. And your brief asked the court to review a lower court decision holding that school districts are authorized by law -- school districts are authorized by law to treat students in accordance with their asserted gender identity instead of their biological sex?
A. That is my recollection, yes.
Q. And your brief said that school policies that treat children who experience gender atypical thoughts or behavior as if they belong to the opposite sex would help the child to "maintain his or her delusion but with less distress by, among other aspects, requiring others in the child's life to go along with the charade." Is that what the brief said?
A. I am very much aware of word choices and how people have had conversations about being bothered by the language.
THE COURT: Doctor, I think the question was is that how the brief was worded?
THE WITNESS: Yes.
BY MR. STRANGIO:
Q. And in 2020 you signed on to an amicus brief in *Meriwether versus Hartop*? Do you recall that?
A. Yes.

Q. And that brief was in support of a professor who objected to Shawnee State's requirement that faculty and staff address students according to the student's preferred form of address, including the use of the student's preferred pronoun? Is that correct?
A. As best I can recall at this time, yes.
Q. And in that brief, you said the following: "The popular notion regarding, quote, gender identity that says a person has a, quote, boy mind in a girl body is not true. If it is supposed to be taken even more or less literally, it is an idea that should be summarily dismissed."
A. That is what it said there. And I'm happy to talk about the science that supports that statement.
Q. No, thank you. Just a moment.
Just one final question. So you mentioned your book, *Sexual Identity*?
A. Correct.
Q. And that has a subtitle, "The Harmony of Philosophy, Science and Revelation"?
A. Correct.
Q. And it was published by Emmaus Road Publishing?
A. Emmaus.
Q. Excuse me. I'm sorry. Emmaus Road Publishing. Emmaus Road Publishing is a religious publisher. Correct?
A. I would have to look. It does publish books on that topic,

yes.

MR. STRANGIO: I pass the witness.

REDIRECT EXAMINATION

BY MR. JACOBS:

Q. Dr. Hruz, I think you testified you attended a couple of meetings at ADF in 2017. Did I hear that right?

A. Yes. Well, two meetings. I don't think they were both in 2017.

Q. But the first meeting you attended, was that in 2017?

A. Again, I don't recall the exact date. I was at two meetings.

Q. Is it common throughout your career for you to attend professional conferences with others in the field?

A. Yes.

Q. And did you begin investigating treatments related to gender dysphoria before or after the first time you attended an ADF meeting?

A. Five years prior to that meeting I began my investigation into that, the question of gender dysphoria.

Q. The book that you were discussing, *Sexual Identity*, in what capacity did you contribute to that book?

A. I wrote one chapter specifically on the topic of the science, so that was my role.

THE COURT: On the topic of what?

THE WITNESS: The biology of sex.

MR. JACOBS: I don't have any further questions, Your Honor.

MR. STRANGIO: No further questions.

THE COURT: You are free to go, sir.

MR. JACOBS: With that, Your Honor, defendants will rest.

THE COURT: So, in keeping with what I understood to be a joint request to submit posttrial briefs, for lack of a better summary, have y'all discussed the timing of that?

MR. JACOBS: Your Honor, we haven't reached a conclusion as to that. We discussed it a few days prior. But I think, if the Court would like us to, we can confer after, maybe advise via email if we can come to an agreement on scheduling.

THE COURT: I only anticipate that y'all would be more informed as to a realistic date than I would, meaning if y'all can agree on one, it would probably be easier on everyone at least at that end of the room. So I don't propose to force feed a date on you unless you just can't come up with one together.

MR. JACOBS: I think we'll come up with an agreement. We just haven't had a chance.

THE COURT: Fair enough. I don't need it today because I have my mind -- I've handicapped the date in my mind that y'all might come up with, and I'm not going to suggest it for fear that it's wrong. But it wasn't by the end of the week or even the end of next week. If y'all can just let me know

when you can agree on what that basically briefing schedule would be, that would be great, so I'll know what to expect.

Ms. Cooper?

MS. COOPER: I agree. That's fine with us.

THE COURT: Suits you?

MS. COOPER: Yeah.

MR. JACOBS: I don't think we have anything else.

THE COURT: We're adjourned.

(Proceedings concluded at 2:21 p.m.)

REPORTER'S CERTIFICATE

I certify that the foregoing is a correct transcript from the record of proceedings in the above-entitled matter.

/s/Elaine Hinson, RMR, CRR, CCR Date: December 7, 2022.
United States Court Reporter