EXHIBIT 66

1 IN THE UNITED STATES DISTRICT COURT
2 FOR THE MIDDLE DISTRICT OF ALABAMA
3 NORTHERN DIVISION
4
5 BRIANNA BOE, et al.,)
6 Plaintiffs,)
7)
8 UNITED STATES OF AMERICA,)
9 Intervenor Plaintiff,) Civil Action No.
10 v.) 2:22-cv-184-LCB
11 HON. STEVE MARSHALL, in his)
12 official capacity as)
13 Attorney General, of the)
14 State of Alabama, et al.,)
15 Defendants.)
16 The deposition of ARON JANSSEN, M.D.,
17 called for examination, taken pursuant to the
18 Federal Rules of Civil Procedure of the United
19 States District Courts pertaining to the taking of
20 depositions, taken before KRISTIN C. BRAJKOVICH, a
21 Certified Shorthand Reporter, CSR. No. 84-3810, of
22 said state, at Suite 3800, 110 North Wacker Drive,
23 Chicago, Illinois, on the 12th day of April, A.D.
24 2024, at 9:00 a.m.

1 PRESENT:
2
3 KING & SPALDING LLP,
4 (10 North Wacker Drive, Suite 3800,
5 Chicago, Illinois 60606,
6 1-312-995-6333), by:
7 MR. BRENT P. RAY,
8 bray@kslaw.com, and
9 MS. KATHERINE VESSELS,
10 kvessels@kslaw.com,
11 appeared on behalf of Plaintiffs;
12
13 UNITED STATES DEPARTMENT OF JUSTICE,
14 (150 M Street NE,
15 Washington, DC 20002,
16 1-202-598-0083), by:
17 MR. JAMES FLETCHER,
18 james.fletcher@usdoj.gov,
19 appeared via Zoom on behalf of
20 Intervenor Plaintiff;
21
22
23
24

1 PRESENT (Continued):
2
3 COOPER & KIRK,
4 (1523 New Hampshire Ave., N.W.,
5 Washington, DC 20036,
6 1-202-220-9621), by:
7 MR. JOHN D. RAMER,
8 jramer@cooperkirk.com,
9 appeared on behalf of Defendants.
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23 REPORTED BY: KRISTIN C. BRAJKOVICH,
24 CSR No. 84-3810.

1 I N D E X

	WITNESS	EXAMINATION
3	ARON JANSSEN, M.D.	
4	By Mr. Ramer	5

5
6 E X H I B I T S

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1 (WHEREUPON, the witness was duly
2 sworn.)
3 ARON JANSSEN, M.D.,
4 called as a witness herein, having been first duly
5 sworn, was examined and testified as follows:
6 EXAMINATION
7 BY MR. RAMER:
8 Q. Good morning, Dr. Janssen. My name is
9 John Ramer. I represent the defendants in this
10 case, and I know you have been deposed before.
11 It's going to be the typical drill.
12 I'll ask you questions, ask for verbal
13 responses. We'll try not to talk over one another.
14 If at any point you need a break, let me know. I
15 just ask that you answer any pending questions.
16 And I'm otherwise going to try to shoot for a break
17 on the hour.
18 If you don't understand any of my
19 questions, please just let me know. Otherwise,
20 I'll assume that you understood them. Does that
21 make sense?
22 A. It makes sense.
23 Q. Dr. Janssen, are you an expert?
24 A. I'm an expert in some things, yes.

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1 Q. In what field or fields are you an
2 expert?
3 A. I'm a child adolescent psychiatrist and
4 an expert in the field of transgender mental
5 health.
6 Q. Anything else?
7 A. Suicide, anxiety, systems of care
8 delivery.
9 Q. Anything beyond those?
10 A. I would say those are kind of most of my
11 areas of expertise.
12 Q. And you are testifying in this case as
13 an expert, correct?
14 A. Yes.
15 Q. And you do not intend to testify about
16 material beyond the opinions that you have offered
17 in your reports, correct?
18 A. That is correct.
19 Q. And you have been deposed as an expert
20 before, correct?
21 A. Yes.
22 Q. And did you give truthful testimony
23 during those depositions?
24 A. I did.

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1 Q. And you testified at a hearing in Texas
2 last year, correct?
3 A. The terminology, I might not get
4 100 percent correct if it was a hearing or a court,
5 whatever it was. I testified, yes.
6 Q. And did you give truthful testimony at
7 that proceeding?
8 A. I did.
9 Q. And what did you do to prepare for this
10 deposition?
11 A. I reviewed my reports, and I continue to
12 stay up-to-date on the extant literature.
13 Q. And did you review any documents in
14 particular?
15 A. Just my reports that I had submitted.
16 Q. And did you speak with anybody in
17 preparation for this deposition?
18 A. Only our lawyers.
19 Q. Anybody else?
20 A. No.
21 Q. And, Dr. Janssen, where do you practice?
22 A. I practice here in Chicago. I'm an
23 associate professor of child and adolescent
24 psychiatry at Northwestern University and vice

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1 chair of clinical affairs at the Pritzker
2 Department of Child and Adolescent Psychiatry at
3 the Ann and Robert H. Lurie Children's Hospital of
4 Chicago.
5 Q. As part of your clinical practice, do
6 you practice as part of a multidisciplinary clinic?
7 A. I do, yes.
8 Q. And what kind of providers are in that
9 clinic?
10 A. It depends upon the clinic in question.
11 Relevant to the work that I'm doing that lends
12 itself to my expertise in transgender health, our
13 gender clinic includes psychiatrists,
14 psychologists, social workers, adolescent medicine
15 physicians, endocrinologists.
16 Q. And how many other -- or how many
17 psychiatrists or psychologists are at part of the
18 clinic?
19 A. I would have to go through my -- the
20 roster to give you an exact number. I don't have
21 it off the top of my head.
22 Q. Is it fewer than ten?
23 A. Yes.
24 Q. And are you -- as a -- let me back up.

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1 Is it fair to refer to psychiatrists and
2 psychologists as mental health professionals?
3 A. Yes.
4 Q. As a mental health professional, what is
5 your role in the clinic?
6 A. I served multiple roles in the clinic.
7 As the psychiatrist, my primary role in this clinic
8 is seeing youth with co-occurring mental health
9 conditions that require medication management or
10 more complex care.
11 Q. And you said that you were an expert in
12 child and adolescent psychiatry. How do you define
13 who is a child and who is an adolescent?
14 A. There are multiple different definitions
15 that we might use. The distinction is going to be
16 more important, depending upon what the question
17 is. Generally speaking, as somebody who trained in
18 adult psychiatry and child and adolescent
19 psychiatry, there's some diffuse definitions that
20 mix between childhood, adolescence, and adulthood.
21 Q. In this field, is it fair to say that a
22 child is somebody who is pre-Tanner Stage 2?
23 A. In the context of making a diagnosis of
24 gender dysphoria and that there is gender dysphoria

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1 in children and gender dysphoria in adolescents,
2 that differentiation is based upon pubertal status,
3 but there are different processes for evaluating
4 cognitive development that are different from
5 Tanner staging.
6 Q. And for adolescents, in terms of making
7 a diagnosis, do you have a line between an
8 adolescent and an adult?
9 A. Making a diagnosis of what?
10 Q. Gender dysphoria.
11 A. The technical definition of the
12 diagnosis of gender dysphoria includes adolescents
13 and adulthood. Really, it's more based upon the
14 individual that you are assessing in terms of their
15 capacity to understand the various processes, their
16 ability to provide accurate information, family
17 involvement, et cetera.
18 Q. Okay. For purposes of today, when I
19 refer to child or children, let's assume that I'm
20 referring to pre-Tanner Stage 2 patients. Does
21 that make sense?
22 A. That makes sense, and if I am confused
23 about it later, I will clarify.
24 Q. And for adolescents, if I'm referring --

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1 let me start again.
2 When I'm referring to adolescents today,
3 I'll be referring to Tanner Stage 2 up to age 19.
4 Does that make sense?
5 A. Sure.
6 Q. Do you personally diagnose patients with
7 gender dysphoria?
8 A. Yes.
9 Q. Do you or the other mental health
10 professionals at your clinic see all of the
11 patients at the clinic who are being considered for
12 pubertal suppression?
13 A. The work flow for our clinic is that all
14 of the patients considered for puberty suppression
15 are seen by a mental health professional within our
16 clinic. They are not always the treating provider
17 of mental health care but do assessments in that
18 role.
19 Q. Can you explain the distinction between
20 the treating provider and the assessor?
21 A. Sure. For example, there are some kids
22 who have co-occurring mental health disorders that
23 require therapeutic interventions. Some of those
24 therapeutic interventions are done by mental health

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1 professionals in the community and in our clinic,
2 but all patients who are evaluated are done so in a
3 multidisciplinary way that includes a mental health
4 professional.
5 Q. And that assessment is done by mental
6 health professionals in your clinic; is that right?
7 A. Correct.
8 Q. And is the same true for patients who
9 are being considered for cross-sex hormones?
10 A. Yes.
11 Q. Have you ever practiced in Alabama?
12 A. No.
13 Q. Are you aware of any gender clinics in
14 Alabama?
15 A. I know of the existence of one at the
16 University of Alabama, but I'm not familiar with
17 its workings.
18 Q. And is that the University of Alabama
19 Birmingham, sometimes shortened to UAB?
20 A. I have seen it written as UAB, so I
21 assume that is the case.
22 Q. Have you ever been to that clinic?
23 A. No, I have not.
24 Q. Do you have any firsthand knowledge of

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1 that clinic's practices?
2 A. No.
3 Q. Do you personally recommend that
4 patients receive puberty blockers as a treatment
5 for gender dysphoria?
6 A. When that is medically indicated, yes.
7 Q. And is the same true for cross-sex
8 hormones?
9 A. When it is indicated, yes.
10 Q. And is the same true for surgeries?
11 A. When it is indicated, yes.
12 Q. The purpose of recommending these
13 interventions is to reduce gender dysphoria,
14 correct?
15 A. Correct.
16 Q. And so one would judge the efficacy of
17 those interventions based on their ability to
18 reduce gender dysphoria, correct?
19 MR. RAY: Object to form.
20 BY THE WITNESS:
21 A. The measurement of the severity of
22 gender dysphoria is one outcome that we would be
23 tracking as a result of these interventions. We
24 also want to understand functioning, quality of

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1 life, impact on co-occurring mental health
2 conditions, general wellness, a sense of comfort,
3 et cetera.
4 BY MR. RAMER:
5 Q. If an intervention improves quality of
6 life but does not reduce gender dysphoria, is the
7 intervention an effective treatment for gender
8 dysphoria?
9 A. That sounds like a hypothetical. That
10 is not something that I have encountered in my
11 clinical practice, so I'm not sure how to answer
12 that question.
13 Q. Well, I guess take it as a hypothetical.
14 If hypothetically an intervention improved quality
15 of life but did not reduce gender dysphoria, is
16 that treatment an effective treatment for gender
17 dysphoria?
18 MR. RAY: Object to form.
19 BY THE WITNESS:
20 A. It depends upon how we are measuring
21 efficacy and what the discussions that you have had
22 with your patients and families have been. Here is
23 what our goal is. If we have achieved that goal,
24 that treatment is generally effective.

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1 I have just never seen in practice that
2 we see significant changes in quality of life that
3 are not also paired with improvements in severity
4 of gender dysphoria.
5 BY MR. RAMER:
6 Q. Have you ever seen that in a study?
7 A. Not that I recall, but I can't recall
8 all of the details of every study that I have read.
9 Q. When did you first begin treating
10 minors -- sorry.
11 When did you first begin treating
12 children and adolescents with gender dysphoria?
13 A. In my residency training was when I
14 first had exposure to and had treatment
15 relationships with gender-diverse young people.
16 Q. And in approximately what year was that?
17 A. Probably that would be 2008, 2007,
18 somewhere in there.
19 Q. And when was the first time you
20 diagnosed a child with gender dysphoria?
21 A. I could not recall off the top of my
22 head the very first time I made that diagnosis.
23 Q. Do you know what year it would have
24 been?

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1 A. Sometime between 2007 and 2011.
2 Q. And is the same true for diagnosing
3 adolescents with gender dysphoria?
4 A. The same would be true, yes.
5 Q. When was the first time you recommended
6 that a patient receive puberty blockers as a
7 treatment for gender dysphoria?
8 A. Well, I first started my gender clinic
9 after completing my fellowship in 2011, so it's
10 likely that 2011 was the first time I had made that
11 recommendation independent of any supervisors.
12 Q. And is the same true for cross-sex
13 hormones as a treatment for gender dysphoria?
14 A. Yes.
15 Q. Is the same true for recommending that a
16 minor -- sorry. Let me restart.
17 Is the same true for recommending a
18 child or adolescent to pursue a social transition
19 as a treatment for gender dysphoria?
20 A. The same is likely true, yes.
21 Q. Have you ever recommended that an
22 adolescent patient receive surgery as a treatment
23 for gender dysphoria?
24 A. I have, yes.

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1 Q. What kind of surgery?
2 A. The majority of the surgeries that I
3 have assessed for and made the recommendation for
4 for somebody under 18 is for top surgery or chest
5 masculinization surgery.
6 Q. Have you ever recommended any other
7 types of surgery for an adolescent as a
8 treatment --
9 A. Yes. Very likely, yes.
10 Q. And what other types?
11 A. Vaginoplasty.
12 Q. Do you recall the age of the patient
13 that you recommended?
14 A. If I'm remembering correctly, 17.
15 Q. And was it only one?
16 A. From my recollection, yes.
17 Q. Approximately how many of your patients
18 are minors who have been diagnosed with gender
19 dysphoria?
20 A. That is a hard question to know off the
21 top of my head. I would really have to go back and
22 review because many of the patients that I started
23 seeing as minors, I continue to see and are now
24 adults. But between the 300 and 500 folks that I

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1 have seen with gender dysphoria, probably
2 80 percent of them are children or adolescents.
3 Q. Do you have patients who are diagnosed
4 with gender dysphoria during childhood?
5 A. Yes.
6 Q. Do you have patients who are diagnosed
7 with gender dysphoria during adolescence?
8 A. Yes.
9 Q. In your clinic, which instance is more
10 prevelant?
11 A. Diagnosis in adolescence is more
12 prevalent, but that is, in part, due to the format
13 and structure of the clinic.
14 Q. What do you mean by that?
15 A. So our clinic is a multidisciplinary
16 clinic, and one of the options that is provided to
17 patients that allow for -- that lead to patients
18 seeking out our care is access to the medical and
19 surgical interventions, which are not interventions
20 that are appropriate for or indicated for
21 non-adolescents. When I was working in New York in
22 my clinic, it was a clinic that was situated within
23 the department of psychiatry, it was mental health
24 focused, so I saw more youth or children at that

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1 point than I do here in my clinic in Chicago.
2 Q. And I'm sorry if my question was
3 unclear. I guess I was trying to ask about when
4 the patients were diagnosed with gender dysphoria
5 as opposed to just the makeup of your clinic. Does
6 that make sense, or is the answer the same?
7 A. The answer is the same, but I can
8 clarify, which is to say that many people get a
9 diagnosis when they are seeking care. And so they
10 do not receive a diagnosis, even though the
11 symptoms may have been present, until that care has
12 been sought, so it would not be surprising that
13 most people are getting a diagnosis of gender
14 dysphoria in adolescence, even though many of them
15 have had symptoms from early childhood that had
16 been impairing. Does that make sense?
17 Q. Yes. And what is your basis for knowing
18 that they would have had symptoms from childhood?
19 A. The initial step of care is a
20 comprehensive evaluation that includes an
21 assessment of early childhood symptoms.
22 Q. If I use the phrase "natal male," you
23 can assume that I'm trying to describe the same
24 thing that someone else might describe as a male

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1 assigned at birth. Does that make sense?
2 A. Yes.
3 Q. And the same thing for natal female and
4 female assigned at birth. Does that make sense?
5 A. It does.
6 Q. Of your patients, do you know
7 approximately how many are natal males and how many
8 are natal females?
9 A. No. I would have to go back and review
10 my records.
11 Q. Do you have any estimate?
12 A. No, I don't.
13 Q. Is it 50/50?
14 MR. RAY: Object to form.
15 BY THE WITNESS:
16 A. I don't have an estimate.
17 BY MR. RAMER:
18 Q. Although you can't recall the precise
19 ratio now, has the ratio been stable throughout
20 your years of treating minors for gender dysphoria?
21 A. I'm not exactly sure the question that
22 you are asking. And I don't want this to sound
23 evasive, but it really depends upon the milieu in
24 which you are practicing. So in early childhood,

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1 as an example, you are going to typically see more
2 natal males in your terminology who are presenting
3 for care than natal females.
4 And in a multidisciplinary clinic where
5 medical interventions are part of the primary
6 reason for seeking care, you are typically going to
7 see a more 50/50 or more predominant natal female
8 split. So my exposure to the ratios of patient
9 populations that I'm seeing is going to be more
10 dependent upon the milieu of practice as opposed to
11 some demographic change or prevalence change over
12 time.
13 Our clinic in Chicago has more -- as an
14 entirety of the clinic, more assigned females at
15 birth or natal females than natal males. I don't
16 recall off the top of my head what my ratio is.
17 Q. Outside of the clinic, have you ever
18 conducted a study that observed an increase over
19 time in the ratio of natal females to natal males?
20 A. I have not personally conducted any
21 study on that.
22 Q. Have you ever authored an article that
23 observed an increase over time in the ratio of
24 natal females to natal males?

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1 A. I would have to go back and read
2 everything that I have read, and I have read a lot
3 over the years. Certainly, it has been commented
4 on in the literature that in the gender clinics
5 that have been tracking patients over time, that
6 they have seen an increased rate of natal females
7 presenting for care.
8 Q. Do you agree that the reasons for
9 variations in that ratio remain unknown?
10 A. Unknown is a bit of a tricky word for
11 me. That implies that there's two categories,
12 known and unknown. We know some things. We don't
13 know everything about the ratio change.
14 Q. Do you think that we know enough to make
15 informed decisions about why the ratio is changing?
16 A. I think we have enough to generate
17 hypotheses that are testable through the process of
18 peer-reviewed science.
19 Q. And once you test a hypothesis, what is
20 the result?
21 A. The result -- I mean, in all of academic
22 medicine, we are never really satisfied with a
23 result, which is why in generally every systematic
24 review or study that is looking at the literature,

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1 one of the recommendations is, we need more
2 research. Because we don't like a period in
3 science; we like an ellipses or a comma. There's
4 always more to learn, so we want to make sure that
5 we are continuously evolving our capacity to be
6 able to provide the best and up-to-date information
7 to the patients as they make decisions about their
8 care.
9 Q. What hypothesis do you think explains
10 the change in the ratio?
11 A. From my read of the literature and my
12 experience working with these patients, at least a
13 healthy chunk of the reason that we are seeing an
14 increase in this rate is that there's access to
15 treatment that didn't exist before.
16 Q. So the idea is that this has always been
17 the ratio and it's just being revealed more now?
18 A. The best evidence that I have seen, is
19 that the ratio of transgender adults between
20 assigned females at birth and assigned males at
21 birth, so natal males and natal females, has
22 generally always been 50/50. And that has not
23 changed. What has changed is who is presenting for
24 care, not who exists in the world.

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1 Q. Does that 50/50 ratio hold for children?
2 A. In the large national samples we have,
3 there have not been anything that I would say is
4 quality, in terms of looking at identity rates in
5 childhood. What we have is the diagnosis of gender
6 dysphoria, which is a different thing all together,
7 but it's hard to say. We don't know for sure, but
8 it's likely to hold up in childhood because gender
9 identity is a staple phenomenon. And if it's 50/50
10 in adulthood, it's most likely to be 50/50 in
11 childhood.
12 Q. You don't think that there's a greater
13 proportion of natal males to natal females in the
14 childhood group?
15 A. Historically in the clinics that have
16 done work with gender-diverse youth, if we look at
17 the 1990s and early 2000s, the predominant folks
18 who were presenting for care prior to puberty were
19 natal males, and those ratios changed from site to
20 site and over time it reduced. That speaks to a
21 complex phenomenon, which I'm happy to get into
22 but --
23 Q. Minority stress?
24 A. It's less about who exists as a

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1 transgender or gender-diverse child and who
2 presents for care.
3 Q. When you first began recommending that
4 adolescent patients receive cross-sex hormones as a
5 treatment for gender dysphoria in 2011, did you do
6 so for individuals who identified as nonbinary?
7 A. I would have to review my notes to know
8 for sure.
9 Q. Is there any reason to think that you
10 would not have done so for an individual who
11 identified as nonbinary?
12 A. The terminology has changed and evolved
13 over time, and how patients self-identified is
14 certainly given now in terms of the words that are
15 used. So whether a patient used gender nonbinary
16 or gender queer or some other term, I would have to
17 go back and see.
18 The population of patients that I was
19 seeing early on, I was not seeing a lot of gender
20 binary folks, but the diagnosis of gender dysphoria
21 requires that there is an incongruence between the
22 assigned sex at birth. And one's gender identity
23 does not require that you have a binary identity in
24 order to make the diagnosis.

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1 Q. And my question is not so much as a
2 factual matter what you were doing in 2011. It's
3 more as a matter of theory. Was there any reason
4 you would not have recommended cross-sex hormones
5 to an individual who did identify as nonbinary back
6 in 2011?
7 A. I mean, there are reasons to not
8 recommend gender-affirming hormones for folks who
9 are nonbinary and folks who are transgender. It's
10 an individualized assessment that has a set of
11 criteria that need to be met in order for you to
12 make that recommendation.
13 So on the individual basis, there are a
14 number of reasons why you would not make that
15 recommendation, but just on the whole of being
16 nonbinary is not one of those reasons.
17 Q. And the same is true for puberty
18 blockers?
19 A. Correct.
20 Q. And the same is true for surgery?
21 A. Correct.
22 Q. And the same is true for social
23 transition?
24 A. Correct.

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1 Q. When you first began recommending that
2 adolescent patients receive cross-sex hormones as a
3 treatment for gender dysphoria, did you ever
4 recommend cross-sex hormones for a patient who did
5 not previously undergo pubertal suppression?
6 A. Yes.
7 Q. When you first began recommending that
8 adolescent patients receive cross-sex hormones as a
9 treatment for gender dysphoria, did you ever
10 recommend cross-sex hormones for a patient who did
11 not identify as transgender until adolescence?
12 A. I would have to go back and review my
13 notes, but that is not an uncommon process for
14 there to be some sense of differentness in
15 childhood but come to a recognition of a
16 transgender gender identity with the distress that
17 often comes with puberty.
18 Q. So you would not have deemed someone who
19 did not identify as transgender until adolescence
20 as ineligible for cross-sex hormones; is that
21 right?
22 A. Correct.
23 Q. When you first began recommending that
24 adolescent patients receive cross-sex hormones as a

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1 treatment for gender dysphoria, did you require
2 that those individuals also receive psychotherapy?
3 A. No, I did not. They were required to
4 have a mental health evaluation, and some required
5 psychotherapy as a part of the process, but it was
6 not a requirement for all patients.
7 Q. Is the same true for puberty blockers?
8 A. Yes.
9 Q. And the same is true for surgery?
10 A. Yes.
11 Q. And the same was true for social
12 transition?
13 A. Yes.
14 Q. When you first began recommending that
15 adolescent patients receive cross-sex hormones as a
16 treatment for gender dysphoria, did you use age
17 limits?
18 A. I mean, the short answer is no. The
19 guidelines have always been meant to be applied
20 flexibly, so there were not hard age limits that
21 were utilized.
22 Q. And is the same true for other medical
23 interventions?
24 A. Correct.

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1 Q. When you first began recommending that
2 adolescent patients receive puberty blockers as a
3 treatment for gender dysphoria, did you require
4 that those patients also subsequently receive
5 cross-sex hormones?
6 A. No, there's no requirement for that.
7 Q. And there never was; is that right?
8 A. There has never been a requirement.
9 Deciding whether or not to pursue gender-affirming
10 hormones is a different decision, and it's a
11 different assessment process than the decision
12 whether to start puberty-blocking agents.
13 Q. And the same is true for an adolescent
14 patient who is receiving cross-sex hormones with
15 respect to subsequently receiving surgery, correct?
16 A. Every patient and family makes an
17 individualized plan.
18 Q. When you first began recommending
19 puberty blockers as a treatment for gender
20 dysphoria, what evidence were you relying on?
21 A. I was relying on the evidence from the
22 peer-reviewed literature.
23 Q. Can you explain what literature?
24 A. Sure. The best data that we had came

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1 from primarily the Dutch and Toronto clinics that
2 had followed these patients longitudinally over
3 time.
4 Q. If I refer to the Dutch protocol, do you
5 understand in this field that I would be referring
6 to the protocol used by the researchers in the
7 Dutch clinic?
8 A. Yes. I visited the Dutch clinic as a
9 part of preparing for my clinic to open, and so I
10 understood what their processes were at the time.
11 The word "Dutch protocol" has been used in
12 different ways by different people to describe
13 different things, so when I talk about the Dutch
14 protocol, I'm talking about my personal experience,
15 having seen the clinic, which is different than how
16 it has often been referred to in popular press in
17 particular.
18 Q. Is the protocol that you are referring
19 to different from what they described in their
20 studies?
21 A. No. What they described in their
22 studies is an accurate description of the Dutch
23 protocol.
24 Q. So in your opinion, in 2011 there was

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1 sufficient evidence to conclude that giving
2 adolescents puberty blockers was effective for
3 treating gender dysphoria, correct?
4 A. As a scientist, I hate concluding
5 anything, but the preponderance of the evidence
6 suggested at the time that it is safe, effective,
7 and appropriate intervention.
8 Q. And you were recommending that
9 intervention?
10 A. I was, yes.
11 Q. And the same -- I'll just ask.
12 And, in your opinion, back in 2011,
13 there was sufficient evidence to conclude that
14 giving adolescents cross-sex hormones was effective
15 treatment for gender dysphoria, correct?
16 A. Yes.
17 Q. At that time, do you think that we had a
18 full understanding of the impact of these
19 interventions from a medical perspective?
20 A. I don't think that we will ever have a
21 full understanding of the impact of any medical
22 intervention ever. There's always more to learn
23 and more to study. We have more data now than we
24 did then. I anticipate in ten years, we'll have

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1 even more data and more understanding.
2 Q. Does the data now matter, if you already
3 reached the conclusion that it was -- the evidence
4 was sufficient to actually recommend these
5 treatments for real patients?
6 A. It would matter if the data that has
7 been subsequently published contradicted what led
8 to those conclusions in the first place.
9 Q. Back in 2011, if someone had said to you
10 that little is known about the long-term effects of
11 hormonal interventions in minors with gender
12 dysphoria, what would you have said to them?
13 A. I would say, Can you define "little"?
14 Q. How would you define it, if somebody
15 said, Do we know a lot, do we know a little? What
16 would you have said back in 2011?
17 A. I would say back in 2011, we had similar
18 amounts of data for this intervention as we had for
19 many other interventions that we routinely use in
20 childhood and in child mental health.
21 Q. Can you provide some of those examples?
22 A. Sure. The data on most interventions in
23 childhood is sometimes scant, so as an example,
24 getting information from parents about their

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1 children's childhood and how symptoms developed in
2 childhood, there's virtually no evidence to support
3 that as an intervention or as a part of the
4 assessment process.
5 It does not mean that it's not
6 appropriate. It's pretty common sense, that we
7 want to get a historical view of a child over time,
8 but there's no published literature on that. So we
9 can't say, if you ask that question, What is the
10 long-term effect of asking parents about childhood
11 symptoms or childhood evaluations? We don't have
12 an answer for that. But, nevertheless, this is the
13 bedrock of the field that I work in.
14 Q. When you say "we don't have an answer
15 for that," can you just explain why we don't have
16 an answer for that?
17 A. Because there have not been studies to
18 look specifically at that question.
19 Q. Why haven't there been?
20 A. In part, because many of the benefits
21 are self-evident.
22 Q. Could you elaborate on what you mean by
23 that?
24 A. Yeah. So and a part of doing an

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1 evaluation on a child, an adolescent, or an adult,
2 and as somebody who is trained in all three, one of
3 the advantages that those of us who train in child
4 and adolescent psychiatry have over adult
5 psychiatrists is that we actually have training in
6 early childhood assessment.
7 But gathering a clear history of early
8 childhood symptoms, early childhood behaviors,
9 early childhood engagements, early childhood
10 relational patterns helps us understand and predict
11 some of these over time.
12 Q. Sorry. I guess my question was, Why do
13 we not have studies about the long-term effects?
14 And did I understand your answer to be, Because the
15 benefits are self-evident?
16 A. The benefits of gathering a full
17 developmental history are self-evident and have
18 always been a part of the mental health field.
19 Just because something has not been studied does
20 not mean that it's not effective. That is the
21 point I'm trying to make. Does that make sense?
22 Q. I think so. Do you think that there's a
23 lack of studies assessing the long-term effects of
24 hormonal interventions in minors with gender

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1 dysphoria because the field is so new?
2 A. No. I think there are longitudinal
3 studies that have looked at long-term exposures to
4 gender-affirming hormones over time. There have
5 been cohorts that have been studied upwards of 20
6 to 30 years at this point that had exposures to
7 this in childhood, and there have always been adult
8 transgender patients who have accessed care in some
9 form or another in childhood that patients -- that
10 folks have followed.
11 And there's also really strong
12 longitudinal data, particularly coming out of
13 northern Europe in the adult population.
14 Q. What study are you referring to that has
15 20 to 30 years' data for children or adolescents?
16 A. The Dutch cohort has been followed for
17 at least 20 years.
18 Q. Do you know how large that cohort is?
19 A. It started with 40 to 70 patients, from
20 my recollection, but I would have to look at the
21 studies to be certain.
22 Q. Are there any studies with a larger
23 cohort that follow patients for 20 years or more?
24 A. The studies that are funded now are

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1 certainly hoping to do that with much larger
2 numbers.
3 Q. But, currently, the answer is no?
4 A. Currently, there's a lot of adult
5 studies that have significantly more than those
6 patients.
7 Q. Back in 2011, do you agree that patients
8 and families had to weigh risks and benefits of
9 these interventions with only limited available
10 evidence?
11 A. I would disagree, I think, with the
12 premise of that question. Every decision that you
13 make in terms of medicine requires a discussion of
14 the risks, benefits, and alternatives that are
15 known and a discussion of potential unknown risks,
16 benefits, and alternatives.
17 Q. So what premise are you disputing?
18 A. I don't know the word "limited" and what
19 that refers to in this context.
20 Q. Do you think there are interventions for
21 which we have more available evidence than others?
22 A. Yes.
23 Q. Do you think there are interventions for
24 which we have limited available evidence?

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1 A. Yes.
2 Q. Back in 2011, do you think that the
3 intervention of pubertal suppression for gender
4 dysphoria had only limited available evidence?
5 A. Again, it requires a comparison group.
6 Limited as compared to the evidence for statins and
7 cholesterol reduction, yes. Limited in terms of
8 the impact of Zoloft on generalized anxiety
9 disorder, maybe not.
10 Q. Back in 2011, if someone had said that
11 the long-term consequences of social transition for
12 prepubertal children raises potential concerns,
13 would you have agreed with them?
14 MR. RAY: Object to form.
15 BY THE WITNESS:
16 A. So it really is going to depend upon the
17 context. As a child and adolescent psychiatrist
18 and somebody who works in this field, I'm having
19 individualized discussions that review risks,
20 benefits, and alternatives. Concern to me is that
21 it's a meaningless word. Concern, I have concern
22 in positive ways, I have concern in negative ways.
23 So if the question is negative impacts
24 of social transition, that is a separate question

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1 than thinking about long-term concerns.
2 BY MR. RAMER:
3 Q. If someone had said that there are
4 negative impacts of social transition, would you
5 have agreed with them?
6 A. I would not because it's not supported
7 by the literature or my personal experience working
8 with patients who have socially transitioned.
9 Q. Do you think there's any concern that
10 prepubertal children who have socially transitioned
11 may feel boxed in to their affirmed gender
12 identities?
13 A. That has not been my experience working
14 with youth who have socially transitioned.
15 Q. How do you know?
16 A. Because I talk to them about it and I
17 ask them about it, and I have had patients who have
18 stopped socially transitioning.
19 Q. Because they were feeling boxed in?
20 A. No, because they felt their identity
21 resolved in a way that was aligned with their sex
22 assigned at birth as opposed to misaligned with
23 their sex assigned at birth.
24 Q. When you say that you ask them about it,

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1 would you ever expect a patient to say,
2 Dr. Janssen, I feel boxed in by my social
3 transition?
4 A. I would not anticipate that they would
5 use that language, but I would ask about it as a
6 part of our assessment of the intervention. With
7 any intervention that we are recommending, one of
8 the goals that we have is to assess the efficacy of
9 that intervention. Have there been any anticipated
10 benefits that you were hoping for? Have there been
11 any unanticipated consequences that you had not
12 imaged? How has that been for you? What is that
13 like? Is it the right decision?
14 All of that is continuously reassessed
15 as a part of this process.
16 Q. If a social transition is affecting the
17 patient's understanding of gender though, would the
18 patient even be aware?
19 A. I don't know what you mean by
20 "understanding of gender."
21 Q. What do you understand us to have been
22 talking about when we are talking about being boxed
23 in?
24 A. It really is an individual experience,

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1 and it could mean a lot of things to a lot of
2 different people, which is why in the abstract it's
3 very hard to have a discussion about it. If I have
4 a patient who sits here and says, Yeah, I am very
5 confident. I was assigned female at birth. I'm
6 very confident in my male identity. Sometimes I
7 wish I could wear a dress every once in a while.
8 Does that mean boxed in? They have never used that
9 language, but that is going to be a discussion that
10 I have that is very individualized to that one
11 patient and that one clinical encounter. In the
12 abstract, I just don't know what that means.
13 Q. Do you think the concept of a social
14 transition increasing the likelihood of persistence
15 is completely unsubstantiated?
16 A. The data that we have primarily comes
17 from a Steensma study out of the Dutch clinic that
18 looked at factors that impact persistence and
19 desistance. Persistence and desistance is very
20 specific in terms of how it's defined, and it's
21 been misused in many, many ways because there is a
22 specific definition to persistence, which is that a
23 child who has a diagnosis of gender dysphoria in
24 childhood who passed Tanner Stage 2 of puberty,

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1 when their body begins to develop, no longer meets
2 criteria for that diagnosis. That is the
3 definition of desistance. It's been used to
4 describe a whole bunch of other things, but in this
5 article by Steensma, factors that affect
6 persistence. People -- children who presented to
7 care and having already socially transitioned were
8 more likely to be in that persistent group, where
9 they had the diagnosis in childhood, and by the
10 time they hit adolescence and puberty, Tanner
11 Stage 2, they continued to meet criteria for the
12 diagnosis.
13 When I talked with Tomas about this and
14 in the literature itself, the theory is not that
15 social transition caused persistence of gender
16 identity but more likely that the kids who had more
17 severe distress, more clarity around identity, were
18 more likely to be in that persistent group and were
19 also the kids who were more likely to have socially
20 transitioned prior to initiation of care at the
21 clinic.
22 Q. By "Tomas," did you mean Steensma?
23 A. Correct.
24 Q. Do you think that there is any chance

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1 that social transition might cause persistence?
2 A. I think that is a testable hypothesis,
3 and it's not been one that has been borne out by
4 the literature thus far.
5 Q. When we have been discussing the Dutch
6 protocol or the Dutch clinic, the main research
7 from that are the two de Vries studies, correct?
8 A. There's been a -- they are a very
9 productive group, so there's been much more than
10 the two de Vries studies. Those are the ones that
11 have certainly got the most attention.
12 Q. Do you agree that there are limitations
13 to all of those studies?
14 A. There's limitations to every study, yes.
15 Q. What are the limitations in those
16 studies?
17 A. I wish it had been a bigger cohort. I
18 wish there had been more clear measurements of
19 functioning and quality of life. I wish at the
20 time that we had measurements of body congruence.
21 I wish we had more clear measurements of family
22 acceptance rates.
23 Q. Why do you wish it was a bigger cohort?
24 A. Bigger is almost always better in terms

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1 of these kinds of studies. The larger cohort you
2 have, not only does it support the intervention
3 more effectively, but you are also powered to
4 differentiate subgroups within your study
5 population to understand, are there some subgroups
6 that benefit more from this intervention or others.
7 Q. And did you mention measurements of body
8 congruence?
9 A. I did, yes.
10 Q. What do you mean by that?
11 A. Well, certainly from the Chin study,
12 body congruence seems to predict some of the
13 benefits on mental health that come with
14 transition, so alignment with the body,
15 satisfaction with the body. I think if we had a
16 clear understanding of that from 20 years ago, it
17 would have helped. More is always better, even if
18 it would not have changed the conclusions or the
19 interventions.
20 Q. In the de Vries studies, did they not
21 measure body congruence?
22 A. In the de Vries studies, from my
23 recollection -- and, again, unless I had it in
24 front of me, I don't want to comment on specifics

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1 of the study, and so I'm commenting from my
2 recollection of working with them over time.
3 They used what was then called the body
4 image scale, which has some -- which is not the
5 most effective tool, in my opinion.
6 Q. Why is it not the most effective tool?
7 A. It was not designed for this population
8 specifically.
9 Q. What was it designed for?
10 A. I don't recall the specifics of the
11 origin of the body image scale, so I could not tell
12 you.
13 Q. But you know it was not designed for
14 this?
15 A. Yes.
16 Q. And is the body image scale different
17 from the UGDS?
18 A. Yes. The Utrecht Gender Dysphoria Scale
19 is upright.
20 Q. Do you think that is a valid measurement
21 for gender dysphoria?
22 A. I think it's a valid measure. I think
23 there's probably refinements in it that would
24 improve its utility, but it's what we had at the

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1 time.
2 Q. What kind of refinements would improve
3 its utility?
4 A. Language that is more up-to-date,
5 ability to characterize more nonbinary identities
6 in distress.
7 Q. Okay. Switching gears a little bit.
8 You helped author the WPATH, that is W-P-A-T-H,
9 Standards of Care 8, correct?
10 A. Yes.
11 Q. If I refer to those as the SOC 8, will
12 you know what I'm referring to?
13 A. I will.
14 Q. Can you tell me what the SOC 8 are?
15 A. The standards of care are a document
16 that compiles the most recent and up-to-date
17 literature in the field of transgender health to
18 make evidence-based recommendations for care.
19 Q. Are all of the individuals who helped
20 author the SOC 8 experts in the field of
21 transgender medicine?
22 A. No. Because there were also sections on
23 the law, other sections that involve things outside
24 of medicine.

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1 Q. Are all of the individuals who helped
2 author the SOC 8 chapters related to medicine
3 experts in the field of transgender medicine?
4 A. I was involved in two of the chapters,
5 the child and adult mental health chapters. There
6 were experts -- all of the folks who were involved
7 in the drafting of those two chapters were experts
8 in the field of transgender health.
9 Q. You are unable to say that authors of
10 the other chapters are experts in the field of
11 transgender medicine?
12 MR. RAY: Object to form.
13 BY THE WITNESS:
14 A. Based upon the criteria for selection of
15 authors, that would be my assumption, but I was not
16 involved in the other chapters, so I could not tell
17 you specifically every person who was involved.
18 BY MR. RAMER:
19 Q. So you think there's a chance that
20 people were drafting chapters of the SOC 8 related
21 to medicine who were not experts in the field of
22 transgender medicine; is that correct?
23 MR. RAY: Object to form.
24

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1 BY THE WITNESS:
2 A. I would not say that that is correct.
3 In previous depositions, it has been asked of me
4 that patients or family members who were involved
5 in the process were not experts, and I think that
6 there are individuals who have expertise outside of
7 medicine that allow us to refine our medical
8 knowledge in such a way that we understand how it
9 can be best applied in a community-based setting.
10 Q. Are the listed authors of the adolescent
11 chapter in the SOC 8 experts in the field of
12 transgender medicine?
13 A. I was a member of the child chapter, not
14 the adolescent chapter.
15 Q. I understand. I'm asking, are the
16 listed authors of the adolescent chapter of the
17 SOC 8 experts in the field of transgender medicine?
18 A. I would be happy to review those list of
19 authors, if you have it, and let you know. I don't
20 recall off the top of my head every author on the
21 adolescent chapter.
22 Q. Are you offering opinions based on
23 recommendations made in the adolescent chapter of
24 the SOC 8?

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1 A. I'm making recommendations as an expert
2 in the field of transgender health. The WPATH
3 standards of care represent one piece of the extant
4 literature in the field, not the entirety of my
5 utilization of the literature to make
6 recommendations.
7 Q. So you are unable -- sorry.
8 As you sit here, you cannot say the
9 listed authors of the adolescent chapter of the
10 SOC 8 are experts?
11 MR. RAY: Object to form.
12 BY THE WITNESS:
13 A. The folks that I know who are on the
14 adolescent chapter are experts in the field. I
15 don't have the entire roster of every author in
16 front of me, so I can't say with certainty that all
17 of the authors are. However, in order to be a
18 member of the committee that writes this, you had
19 to have a degree of expertise.
20 BY MR. RAMER:
21 Q. Are the SOC 8 evidence-based guidelines?
22 A. They are.
23 Q. Every part of the SOC 8 is
24 evidence-based?

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1 A. The format of the SOC 8 is that there
2 are statements and then supporting text that
3 provides context to those statements. All of the
4 statements that were included were evidence-based
5 statements. The context and the text descriptions
6 around those statements did not necessarily go
7 through that same process that the other statements
8 did.
9 Q. What makes a statement evidence-based?
10 A. Because they were based upon the review
11 of the literature.
12 Q. When you say "based upon the review of
13 the literature," what do you mean by that?
14 A. It means reading and reviewing all of
15 the peer-reviewed scientific evidence that existed
16 in support of the options for interventions for
17 transgender patients, individuals with gender
18 dysphoria, and making recommendations based upon
19 the summarization of that extant literature.
20 Q. So by the authors reading the literature
21 and then summarizing it and making recommendations,
22 your view is that makes those recommendations
23 evidence-based; is that right?
24 A. The subsequent stage after generation of

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1 the statements was to go through a Delphi process
2 in which there are several rounds of revisions
3 using experts in the field to support or reject the
4 various proposed statements. The Delphi process is
5 an evidence-based process for building consensus
6 around clinical topics.
7 Q. Do you think that there's a distinction
8 between statements that are evidence-based and
9 statements that are consensus-based?
10 A. Expert consensus is a form of evidence.
11 There's overlap in that Venn diagram, but it's not
12 a circle.
13 MR. RAMER: When -- actually, we are probably
14 at a good -- we have been going for about an hour.
15 Is now a good time to stop and go off the record?
16 THE WITNESS: Sure.
17 MR. RAY: Take about a ten-minute break or so?
18 MR. RAMER: Yeah, that works for me.
19 (WHEREUPON, a recess was had.)
20 BY MR. RAMER:
21 Q. Dr. Janssen, could you please state what
22 your role was in helping draft the SOC 8?
23 A. I was an author as a part of the adult
24 mental health chapter and the child chapter.

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1 Q. I'm going to hand you what has been
2 marked as Janssen Exhibit 1 that says Chapter 7,
3 Children, at the top. And your opposing -- or your
4 counsel has copies.
5 (WHEREUPON, a certain document was
6 marked Janssen Deposition Exhibit
7 No. 1, for identification.)
8 BY MR. RAMER:
9 Q. Is this the Children chapter that you
10 helped draft?
11 A. Yep.
12 (WHEREUPON, a certain document was
13 marked Janssen Deposition Exhibit
14 No. 2, for identification.)
15 BY MR. RAMER:
16 Q. And I'm now going to hand you what has
17 been marked as Janssen Exhibit 2. It says, Chapter
18 18, Mental Health at the top, and is this the
19 mental health chapter that you helped draft?
20 A. Yes, it is.
21 Q. How did you come to be an author for
22 these two chapters?
23 A. I don't actually know what the specifics
24 were on the WPATH side. I submitted an application

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1 with my CV, experience, publications, and from what
2 I recall, the chapter leads worked with the editors
3 of the document in selecting the authors to
4 participate.
5 Q. And do you recall who the chapter lead
6 was for the Children chapter?
7 A. Amy Tishelman.
8 Q. And do you recall who the chapter lead
9 was for the Mental Health chapter?
10 A. Dan Karasik.
11 Q. Can you provide just an overview of the
12 drafting process?
13 A. Sure. I can talk about the drafting
14 process for the two chapters, which generally
15 involved weekly or bimonthly hour-long meetings
16 over the course of several years in which we
17 reviewed literature, posed questions, had vigorous
18 debates, reviewed the statements, re-reviewed the
19 statements, drafted text, redrafted the text, over
20 and over again over a long period of time.
21 Q. And those weekly or biweekly meetings,
22 were those in person?
23 A. These were virtual.
24 Q. And in addition to those meetings, how

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1 did you and your co-authors typically communicate
2 with one another throughout the drafting process?
3 A. It really depended upon the person.
4 Primarily, I would assume e-mail, but we met
5 frequently enough that a lot of the meat of the
6 discussion happened in the actual meetings.
7 Q. And so returning to Exhibit 1, the
8 Children chapter, how did you select the articles
9 that are cited here?
10 A. The articles cited were the ones that
11 were used to generate the statements and were
12 selected based upon applicability, quality of
13 evidence.
14 Q. And was it just a function of you and
15 the co-authors selecting the studies that you
16 thought were applicable?
17 A. It was reviewing all of the studies that
18 we are aware of that had been published on the
19 specific topics that we were in charge of making
20 recommendations for.
21 Q. When you say "all of the studies that
22 you were aware of," how do you maintain awareness
23 of studies?
24 A. Me personally or the field at large?

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1 Q. You personally.
2 A. Me personally, I have Google Scholar
3 alerts set up and review several of the journals.
4 (WHEREUPON, a certain document was
5 marked Janssen Deposition Exhibit
6 No. 3, for identification.)
7 BY MR. RAMER:
8 Q. I'm now going to hand you what has been
9 marked as Janssen Exhibit 3. It says, Appendix A,
10 Methodology at the top. Does this appear to be
11 Appendix A to the SOC 8?
12 A. It does.
13 Q. And does this appendix discuss the
14 methodology used to create the SOC 8?
15 A. It does.
16 Q. On the first page of this chapter, which
17 says, S247 at the top, in the left column, first
18 paragraph, third sentence. I'm just going to read
19 it and ask if I read it correctly. It says,
20 Evidence-based guidelines include recommendations
21 intended to optimize patient care and are informed
22 by a systematic review of evidence and an
23 assessment of the benefits and the harms of
24 alternative care options. Did I read that

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1 correctly?
2 A. You did.
3 Q. For the Children chapter, did you or
4 your co-authors seek a systematic review of
5 evidence?
6 A. It depends upon what you mean by
7 "systematic review."
8 Q. What do you understand the term
9 "systematic review" to mean in the field of
10 reviewing medical literature?
11 A. There's at least two, if not more,
12 definitions of systematic review. There's a
13 systematic review which typically follows a
14 predetermined format. There are various different
15 predetermined formats that can exist for a
16 published scientific or systematic review versus a
17 more colloquial systematic review, which involves
18 review of the extant literature, between when SOC 7
19 was published and when the SOC 8 was published.
20 Q. And this refers to a systematic review
21 of evidence, so let's assume it's referring to the
22 first type of systematic review that you referenced
23 and --
24 A. I don't know if that is fair to assume

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1 that that is correct.
2 Q. So you think that this sentence is
3 potentially using the phrase "a systematic review
4 of evidence" in a colloquial sense?
5 A. The editors of the document, so the
6 primary three or four -- I'm trying to remember
7 now -- editors of the document were the ones who
8 created the methodology, so you would have to ask
9 them about their specific use of this term and what
10 they meant for it.
11 Q. And so as drafters of the Children
12 chapter, did you perform a systematic review?
13 A. In a colloquial sense, certainly. We
14 reviewed all of the extant literature that we had.
15 We ran into the problem with a systematic review in
16 a more formalized sense for many of the
17 recommendations in childhood because of what I had
18 mentioned earlier in terms of a lack of publication
19 around the importance of involving a parent in the
20 evaluation of a child as an example.
21 Q. For the mental health chapter, did you
22 or your co-authors conduct a formal systematic
23 review?
24 A. I don't actually recall. We did a

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1 review of all of the extant literature that had
2 been published on the topic since the last revision
3 of the SOC 7. I don't recall if Dan had led a more
4 formalized systematic review process or not.
5 Q. Who do you mean by "Dan"?
6 A. Dan Karasik, the chapter lead.
7 Q. So same page, right column, fifth bullet
8 down. It refers to using the involvement of an
9 independent body from a reputable university to
10 help develop the methodology and undertake
11 independent systematic literature reviews where
12 possible. Do you see that?
13 A. I do.
14 Q. How does one determine whether a
15 systematic literature review is possible?
16 A. I would not be testifying here as an
17 expert in study design or methodology. Karen
18 Robinson was the evidence review lead who was, if
19 I'm recalling correctly, at Johns Hopkins. You
20 would have to ask her in terms of what those
21 specific criterion are.
22 Q. But you did not conduct a formal
23 systematic review for the Children chapter because
24 there were not enough studies, correct?

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1 A. I was never going to be in a position to
2 conduct the formalized systematic review. That was
3 not the role of the authors on the chapter.
4 Q. No, but earlier we were discussing, did
5 you perform a formal systematic review, and please
6 correct me if I'm misunderstanding. I thought you
7 said you did not conduct one because part of the
8 problem was that there were not studies that were
9 relevant to the particular statements; is that
10 right?
11 A. I apologize, and I'm getting into
12 semantics. We reviewed in a systematic way all of
13 the extant literature on the impacts of gender care
14 on childhood in preparation for the writing of this
15 chapter. It did not go through the noncolloquial
16 systematic review process, as led by the expert
17 from Johns Hopkins, to the best of my recollection.
18 It does not mean that we did not do it.
19 Q. When you say "it does not mean that we
20 did not do it," what is the "it"?
21 A. "It" being a systematic review of the
22 literature that existed in the time between the
23 publication of the Standards of Care 7 and then the
24 Standards of Care 8.

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1 Q. And when you say "a systematic review"
2 in your answer just now, you are using it in the
3 colloquial sense, correct?
4 A. Correct.
5 Q. So still first page in Exhibit 3, left
6 column, second full paragraph. Last sentence in
7 the paragraph, it refers to community members
8 completing conflict of interest declarations. Do
9 you see that?
10 A. I do see that.
11 Q. Did you complete a conflict of interest
12 declaration?
13 A. To the best of my recollection, I did.
14 I do them all of the time as part of being in
15 academic medicine, so the specific memory of doing
16 this one comparatively to the several that I have
17 to do every year is not something that I can recall
18 with specificity.
19 Q. So you don't recall whether you reported
20 any conflicts?
21 A. I did not report any conflicts because I
22 did not have any conflicts.
23 Q. This next paragraph in Exhibit 3, about
24 halfway down, there's a sentence that I'll just

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1 read it and ask if I read it correctly. It says,
2 Consensus of the final recommendations was attained
3 using a Delphi process that included all members of
4 the Standards of Care Revision Committee. Do you
5 see that?
6 A. I see that.
7 Q. Could you explain what that is?
8 A. The Delphi process?
9 Q. Yes.
10 A. Again, I'm not testifying as an expert
11 in study methodology, but, in general, a Delphi
12 process is an evidence-based way of finding
13 consensus around medical guidelines.
14 Q. So you are not offering an opinion about
15 the significance of the Delphi process to the
16 SOC 8; is that right?
17 A. I don't recall with 100 percent
18 certainty if that was a part of the declaration.
19 I'm happy to review my declaration to see if that
20 is something that I commented on.
21 Q. But you are not an expert on the Delphi
22 process?
23 A. I'm not an expert in the study design.
24 Q. Does study design include using a Delphi

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1 process?
2 A. Study design involves the psychometric
3 validation of a Delphi process and the statistical
4 power of the Delphi process. It does not involve
5 utilization of the Delphi process or understanding
6 of how to use the Delphi process in establishment
7 of consensus-based guidelines.
8 Q. Can you explain the utilization of the
9 Delphi process in the drafting of SOC 8?
10 A. Yeah, in a very basic sense. The
11 statements are generated. They are provided to an
12 expert panel to review, accept or reject. From
13 those initial edits, the statements are pared down
14 and refined to send to the experts to review a
15 second time. Those that have a broad degree of
16 consensus, and this document, as you noted in your
17 paragraph that you read, 75 percent was required as
18 a threshold for allowing the statement to be
19 included.
20 Q. When you referred to the expert panel
21 just now, are you referring to the individuals who
22 voted in the Delphi process?
23 A. Correct.
24 Q. Do you know who voted?

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1 A. The individuals who voted, from my
2 recollection, were the guideline steering
3 committee, the chapter leads, and the chapter
4 authors.
5 Q. Would you agree that everyone who voted
6 in the Delphi process was an expert in the field of
7 transgender medicine?
8 A. An expert of some type or another, yes,
9 to my recollection.
10 Q. Was the Delphi process required to
11 approve everything contained in the chapter?
12 A. The Delphi process was required to
13 approve the statements.
14 Q. So returning to Exhibit 1, the Children
15 chapter, on the third page of the chapter, which is
16 S69, am I correct in understanding that the Delphi
17 process was used to approve the statements that are
18 in the box on this page but not the supporting text
19 throughout the chapter?
20 A. That is correct.
21 Q. Did you vote in the Delphi process?
22 A. Yes.
23 Q. Did you vote on the statements for other
24 chapters?

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1 A. Yes.
2 Q. Can you describe how you would vote as a
3 practical matter. If that is not clear -- can you
4 describe how you did it?
5 A. There was an online portal. The
6 specifics beyond that, I cannot recall. There was
7 a space to approve, disapprove, provide comments,
8 but I don't recall. It was several years ago at
9 this point, so I don't recall the specifics of what
10 that portal looked like.
11 Q. Did you ever leave comments in the
12 Delphi process?
13 A. I did. I don't remember the specific
14 comments that I did, but I did make comments, yes.
15 Q. And when you were voting, was it an up
16 or down vote, or was there some sort of grading as
17 well?
18 A. My recollection is that it was a --
19 actually, I don't remember.
20 Q. Did you vote on the statements in the
21 eunuch chapter?
22 A. I don't recall not voting on any of the
23 chapters, but I don't remember specifically voting
24 for or against the specific statements in the

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1 eunuch chapter right now.
2 Q. I would like to return to Exhibit 3, the
3 Appendix A, Methodology, and still on the first
4 page of the appendix, which is S247, the right
5 column, second bullet from the top refers to the
6 inclusion of diverse stakeholders. Do you see
7 that?
8 A. I see that.
9 Q. Do you know what that is referring to?
10 A. From my understanding, it's referring to
11 experts in the field that have lived experience.
12 Q. Experts in the field who have lived
13 experience?
14 A. From my understanding, yes.
15 Q. Did you have any diverse stakeholders in
16 your chapter drafting process?
17 A. Well, I would make the argument that all
18 of us in the chapter drafting process were diverse
19 stakeholders who represented a multidisciplinary,
20 multi-continental group of experts that have
21 experience working with transgender and
22 gender-diverse youth.
23 Q. Do you think that is what this bullet is
24 referring to?

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1 A. I did not write this bullet, so I can't
2 tell you what the thought process was for including
3 it.
4 Q. I'm not asking you about the -- to go
5 inside the mind of the person that drafted this.
6 I'm asking your understanding as an author of the
7 SOC 8, do you think that where this is referring to
8 inclusion of diverse stakeholders, it's referring
9 to the group of individuals that you just
10 described?
11 MR. RAY: Object to form.
12 BY THE WITNESS:
13 A. As somebody who is not involved in the
14 formalization of the processes involved in
15 selecting people for the various chapters, I can
16 only make a guess. One change between SOC 7 and
17 SOC 8 was that historically people with lived
18 experience were not a part of the process, and
19 having individuals with lived experience, people
20 with gender dysphoria, people with -- children with
21 gender dysphoria who have expertise in the field
22 provides an extra layer of understanding and
23 context that allows us to make more refined
24 statements appropriately for the patients that we

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1 are working with.
2 BY MR. RAMER:
3 Q. For the Children chapter, was there
4 anyone with lived experience who helped draft the
5 chapter that is not listed as an author?
6 A. We had one person who was the parent of
7 a transgender child who ran an organization in the
8 UK supporting transgender youth.
9 Q. What was that organization?
10 A. It was called Mermaids.
11 Q. And what was that individual's role in
12 the drafting process?
13 A. She was a chapter author similar to the
14 other chapter authors in the field.
15 Q. So I would like to move ahead --
16 sticking with Exhibit 3, move ahead to page S250,
17 and the right column and Section 3.9. And the
18 first sentence after that says, Once the statements
19 passed the Delphi process, chapter members graded
20 each statement using a process adapted from the
21 grading of recommendations, assessment, development
22 and evaluations (GRADE) framework. Do you see
23 that?
24 A. Yes.

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1 Q. Did you do that?
2 A. Did we grade our statements? We did.
3 Primarily, the chapter authors working with the
4 leads were in charge of the nitty-gritty of that
5 process.
6 Q. And you were a chapter author, correct?
7 A. Yes.
8 Q. Can you describe how that grading
9 process worked?
10 A. From my recollection -- and, again, this
11 is my recollection, that we reviewed the
12 evidentiary support for the statements that we were
13 making and that the chapter leads, in discussion
14 with the editors, made that final determination
15 through some process that I was not privy to, as I
16 was not a chapter lead for either of these.
17 Q. Can you kind of just walk me through how
18 you would grade the evidence, as this is
19 discussing?
20 A. Again, this is separate from kind of the
21 acronym GRADE process. How I would grade it in my
22 role as being an author on the chapter was
23 reviewing the specific scientific studies that we
24 were discussing as a part of the process of

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1 developing and discussing as a committee the risks
2 or the pros, the cons, the limitations and the
3 benefits of the various study designs and whether
4 or not to include it as a part of the
5 recommendation process or not.
6 Q. When you say that you are assessing the
7 various study designs, what do you mean?
8 A. I mean, is it a case report with one
9 patient. Is it a cohort study? Is it a randomized
10 controlled trial? What is the value of the study?
11 What are the limitations of the study? What is
12 missing from the study?
13 Q. What is the significance of the various
14 study designs that you just referenced of
15 randomized controlled trial, cohort study, or case
16 study?
17 A. Simply to provide context to the type of
18 study that was done.
19 Q. Did you assess the studies for bias?
20 A. We did.
21 Q. How did you do that?
22 A. As a part of becoming a -- in my field,
23 I can only talk about my field as a physician, as
24 somebody who went through adult psychiatry training

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1 and child psychiatry fellowship, learning how to
2 critically review scientific literature is
3 something that we are taught over the course of
4 many years.
5 Q. Is it mostly a function of you reading
6 the study and determining whether you think that
7 there's a high degree of bias or not?
8 A. That is a part of it, but part of being
9 able to ascertain bias is expertise in
10 understanding of the field. I, as somebody who is
11 an expert in transgender health, have more capacity
12 to pick out things that might be missing or things
13 that might be biased in studies in my own field
14 than picking out bias in a study on ECMO in PICU
15 patients. The capacity to pick out bias and
16 analyze studies in an effective way is benefitted
17 by individuals who have clinical and personal
18 experience working with the patient populations
19 that are being studied.
20 Q. Can you provide an example where that
21 expertise would be beneficial in assessing the bias
22 of a study?
23 A. I would probably defer to a specific
24 study. If you would like me to look at a specific

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1 study, I'm happy to read it and kind of show how I
2 would go through that process.
3 Q. I guess the -- what I'm struggling with
4 a little is, my understanding is -- correct me if
5 I'm wrong. Assessing bias in a study has to do
6 with the design of the study, right?
7 A. Not completely, no.
8 Q. What am I missing?
9 A. So assessing bias involves not just the
10 design of the study, how the authors are funded,
11 what is included but what is excluded, what are the
12 patient populations, how are they selected, how are
13 they reported on, how is the text describing what
14 they are reporting on generated, are there funding
15 sources that are questionable, and do the authors
16 provide any sorts of conflict of interest
17 disclosures that make you question whether or not
18 the studies are valid.
19 Q. Are there tools that are used to assess
20 bias in individual studies?
21 A. I'm not -- I don't know.
22 Q. Have you ever heard of the Cochran
23 Methods Group?
24 A. I have heard of them, but I'm not

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1 familiar with those processes.
2 Q. Okay. So then how did you -- I guess,
3 sorry. So you did not use any tools to assess the
4 bias of the studies in your chapter; is that right?
5 A. I did not use a tool to assess bias in
6 those studies in my chapter.
7 Q. Did anyone review -- let me ask it this
8 way.
9 Once the authors settled on the grading
10 of the statements, did anyone review that grading?
11 A. There was a review process that I was
12 not privy to. The chapter leads worked with the
13 editors, from my recollection, to assign the final
14 recommendations.
15 Q. So, basically, you lost visibility on
16 the grading process once it went up to the chapter
17 lead?
18 A. I would say that is accurate, yes.
19 Q. Among you and your co-authors, were
20 there ever disputes about the grading?
21 A. There were discussions and robust debate
22 about what to include, but I don't recall
23 specifically if there was dissent around specific
24 statements being graded.

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1 Q. Going back to Exhibit 1, the Children
2 chapter, and to page S69. Since you lost
3 visibility on the grading process, as you say, were
4 you surprised about the final statements in the
5 chapter?
6 A. I was not.
7 Q. And looking at this box on page S69, it
8 looks like the statements 7.1 through 7.14 are all
9 we recommend; is that right?
10 A. Yes.
11 Q. And now going back to Exhibit 3, the
12 Methodology appendix, and going to S250, right
13 column halfway down?
14 A. Uh-huh.
15 Q. It says, The statements were classified
16 as strong recommendations, which were indicated by
17 "we recommend," for those interventions/
18 therapies/strategies where the evidence is of high
19 quality. Do you see that?
20 A. I see that.
21 Q. Do you think that the evidence
22 supporting Statement 7.1 through 7.14 is all of
23 high quality?
24 A. That is kind of a hard question to

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1 answer without context. And, one, I want to go
2 back to the S250 in terms of the statements were
3 classified as strong recommendations because it
4 does not end at the evidence is high quality. It
5 also includes, Estimate of effective and
6 intervention therapy or strategy, as in there's a
7 high degree of certainty that effects will be
8 achieved in practice.
9 Also, there are a few downsides of the
10 therapy, intervention, and strategy, and there's a
11 high degree of acceptance among providers and
12 patients for whom the recommendation applies. If
13 we look at Statement 7.1 on page S69, it reads, We
14 recommend health care professionals working with
15 gender-diverse children receive training and have
16 expertise in gender development, in gender
17 diversity in children and possess a general
18 knowledge of gender diversity across the lifespan.
19 To develop so-called high-quality
20 evidence for that statement, in terms of comparing
21 individuals who do not have any expertise or
22 experience working with transgender youth to those
23 who do have expertise or experience in working with
24 transgender youth, would be to set up a study that

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1 has so many problems and ethical issues as to
2 render it meaningless. And I think that there is
3 broad clinical consensus that having expertise in a
4 subject is important if you are going to treat
5 individuals with that condition.
6 We could imagine, for example, there's
7 no high-quality evidence to suggest that health
8 care professionals working with children with
9 cancer have training and expertise in cancer and in
10 cancer treatments and understand the impacts of
11 cancer across the lifespan. There's similarly no
12 evidence to suggest that that has a high quality of
13 evidence in supporting it, but it's self-evident
14 because of the requirements involved in training
15 and the broad clinical consensus.
16 That is why it's a little bit tricky to
17 talk about it in a binary way of high-quality
18 evidence or not. The presence of very rigorous and
19 very clear consensus among an expert body is an
20 element of high-quality evidence, and that is the
21 evidence that we are leaning on in supporting this
22 recommendation.
23 Q. Okay. So on S250, where it says that
24 all the "we recommend" statements were made where

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1 the evidence of high quality -- excuse me -- the
2 evidence is of high quality; is that accurate?
3 A. I'm not -- I was not involved in that
4 process as -- in your language, I lost visibility,
5 so whether these are ors or ands that follow these
6 bullets, that is not something that I'm going to
7 know.
8 Q. Okay.
9 A. From my experience as an author and
10 somebody who works in the field, a lot of the
11 evidence that we are working with requires broad
12 clinical consensus. Whether you call that high
13 quality or not, I think, is up for debate in the
14 field.
15 Q. Sticking with Exhibit 3, going to S251,
16 right column, under 3.17. It says, The final
17 document was presented to the WPATH board of
18 directors for approval and it was approved on the
19 20th of June 2022. Do you see that?
20 A. I see that.
21 Q. And is that true?
22 A. I do not know. I was not a part of the
23 process of presenting this to the board.
24 Q. Do you know if changes were made to the

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1 SOC 8 after June 2022?
2 A. From my -- from what I can recall, there
3 were no changes made to the Children chapter or the
4 Mental Health chapter that I was involved in.
5 Q. Were you aware of changes to any other
6 chapters to the SOC 8 after June 2022?
7 A. I'm not. I don't know one way or the
8 other. I don't have a timeline in my head on when
9 things were finalized from the other chapters. I
10 just know the experience of my -- my own.
11 Q. And when you say "the experience of your
12 own," what do you mean?
13 A. Meaning that from my recollection, there
14 were no changes made to the Children chapter or the
15 Mental Health chapter after we submitted.
16 Q. And throughout the drafting of SOC 8,
17 you would not have been involved with any drafting
18 of the adolescent chapter; is that right?
19 A. That is correct. I was not involved in
20 the drafting of the adolescent chapter.
21 Q. Were you ever involved with discussions
22 surrounding edits to the adolescent chapter?
23 A. I don't recall certainly anything
24 formally within my role. I knew people who are on

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1 the adolescent chapter. Whether we had a
2 discussion about our shared experiences of writing
3 the SOC 8, I don't recall any specifics, but it
4 would not surprise me if I had conversations with
5 colleagues at some point.
6 Q. When you say it would not surprise you
7 if you had conversations, you mean informal
8 conversations?
9 A. Correct.
10 Q. But you had no involvement in a more
11 formal capacity with edits to the Adolescent
12 chapter; is that correct?
13 A. That's correct.
14 Q. Okay. Switching gears. Do you agree
15 that not all people who identify as transgender
16 experience gender dysphoria?
17 A. Yes, I would agree with that.
18 Q. Do you agree that not all people who
19 experience gender dysphoria identify as
20 transgender?
21 A. Yes, I would agree with that as well.
22 Q. Is gender a social construct?
23 A. Social constructs influence the
24 experience and understanding of gender in

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1 culturally bound ways.
2 Q. What do you mean by that?
3 A. Well, gender is a bit of a messy
4 construct. The way that I define gender, at least
5 the way that I most often tend to teach about it,
6 is that we have identity aspects of gender, we have
7 culturally bound social roles that influence
8 gender, and we have relationship to the body, which
9 influences gender. All three of those things are
10 components of what we call gender.
11 Q. If somebody defined transgender youth as
12 those whose gender identity does not conform to
13 culturally-defined expectations for their
14 designated sex at birth, would you agree with that
15 definition?
16 A. I would have to see the context in which
17 that was written to tell you.
18 MR. RAMER: I ask the court reporter to mark
19 this document.
20 (WHEREUPON, a certain document was
21 marked Janssen Deposition Exhibit
22 No. 4, for identification.)
23 MR. RAY: Counsel, do you have a copy for us
24 too?

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1 MR. RAMER: Sure.
2 BY MR. RAMER:
3 Q. So the court reporter has handed you
4 what has been marked as Janssen Exhibit 4. Do you
5 recognize this article?
6 A. I do.
7 Q. Are you an author on this article?
8 A. I am.
9 Q. And the first sentence says, Transgender
10 and gender-diverse (TGD) youth are those whose
11 gender identity or expression does not conform to
12 culturally-defined expectations for their
13 designated sex at birth. Do you see that?
14 A. I do.
15 Q. And is that statement accurate?
16 A. With the inclusion of the word
17 "gender-diverse," yes, it is.
18 Q. What difference does that make to what I
19 previously asked you?
20 A. Most people define transgender as an
21 incongruence between sex assigned at birth and
22 current identity, that there's a specific identity
23 question at play. Whereas, gender diversity is
24 more inclusive of social constructs of gender and

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1 gender expression, gendered expectations,
2 et cetera.
3 Q. But here you say that transgender and
4 gender-diverse youth are those whose gender
5 identity or expression does not conform to
6 culturally-defined expectations, right?
7 A. That is what is written, yes.
8 Q. Why do you say that is what is written?
9 Do you disagree with the meaning of the sentence?
10 A. No, I don't disagree with the meaning of
11 the sentence. I can tell you what I mean by the
12 sentence.
13 Q. Please.
14 A. Which is that transgender includes those
15 who have diversity of gender identity that is in
16 some way incongruent with their sex assigned at
17 birth, and those who are gender diverse sometimes
18 are transgender but oftentimes just transgress
19 expected social behaviors and engagements or
20 expressions that are culturally known.
21 Q. Where it says the identity does not
22 conform to culturally-defined expectations, what
23 does that mean?
24 A. Typically, what that is meaning is that

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1 there's an incongruence between the sex assigned at
2 birth and the affirmed identity of the individual.
3 Q. So are you saying the sex assigned at
4 birth is the culturally-defined expectation in that
5 context?
6 A. I would say in almost all contexts, the
7 cultural expectation of somebody assigned male at
8 birth is to develop a male identity.
9 Q. You use the DSM-5 to diagnose patients
10 with gender dysphoria, correct?
11 A. Correct.
12 Q. Would you ever recommend puberty
13 blockers for a patient who does not satisfy the
14 diagnostic criteria of the DSM-5?
15 A. Specifically for gender dysphoria?
16 Q. Yes.
17 A. No. Gender dysphoria is a required
18 diagnosis to make the recommendation of
19 puberty-blocking agents specifically for gender
20 dysphoria.
21 Q. And the same is true for cross-sex
22 hormones as a treatment for gender dysphoria,
23 correct?
24 A. The diagnosis of gender dysphoria is a

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1 required element of that process?
2 Q. And the same is true for surgery,
3 correct?
4 A. Correct.
5 Q. Do you think it would be inappropriate
6 for a mental health provider to recommend these
7 interventions for a patient who does not satisfy
8 the diagnostic criteria of the DSM-5?
9 A. I would really need to know the
10 specifics and the specific context for that
11 recommendation before making any judgments.
12 Q. In what situation would it be
13 appropriate to do that?
14 A. It's hard for me to say because it feels
15 very hypothetical. I have worked with some
16 therapists who don't like the diagnosis of gender
17 dysphoria, so maybe the patient has met all of the
18 diagnostic criteria for gender dysphoria, but the
19 individual working with that patient does not like
20 using that diagnosis. There might be a context for
21 that.
22 Q. My question was about satisfying the
23 diagnostic criteria, not so much labelling the
24 diagnosis. So the question is, would it be

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1 inappropriate for a mental health provider to
2 recommend puberty blockers as a treatment for
3 gender dysphoria if the patient does not satisfy
4 the diagnostic criteria of the DSM-5?
5 A. The current standards of care recommend
6 that a diagnosis of gender dysphoria be met prior
7 to the initiation of puberty blockers.
8 Q. Do you think it should require that?
9 A. I do personally, yes.
10 Q. Why?
11 A. A diagnosis of gender dysphoria or
12 gender dysphoria not otherwise specified is the
13 framework by which most of the studies that have
14 been done in this population hangs on, so the best
15 evidence that we have is that these treatments are
16 effective for youth with that diagnosis.
17 Q. Why don't you use the ICD-11?
18 A. I do use the ICD-11.
19 Q. Would you ever recommend puberty
20 blockers as a treatment for gender dysphoria in a
21 patient who satisfied the diagnosis for gender
22 incongruence under the ICD-11 but did not satisfy
23 the diagnostic criteria for gender dysphoria under
24 the DSM-5?

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1 A. I use the ICD in the context of billing
2 and not in the context of clinical care. In the
3 process of clinical care, we are using the
4 diagnosis of gender dysphoria to make
5 recommendations.
6 Q. Is there any substantive difference
7 between the definition of gender dysphoria under
8 the DSM-5 and gender incongruence under the ICD-11?
9 A. I'm more familiar with the DSM-5
10 criteria for gender dysphoria than the specific
11 criteria listed under the ICD for gender
12 incongruence. One substantive difference is that
13 gender dysphoria is listed in the DSM as a
14 psychiatric condition and gender incongruence is
15 not.
16 Q. Do you recall, does gender incongruence
17 require the presence of distress associated with
18 the incongruence?
19 A. I would be happy to review the ICD-11
20 criteria, if you have it.
21 Q. But as you sit here, you don't know the
22 answer to that?
23 A. Yeah, as I don't use the ICD in everyday
24 clinical practice, so it's not something that I can

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1 recall.
2 Q. Do you agree that the DSM-5 requires the
3 presence of distress to make the diagnosis?
4 A. Yes.
5 (WHEREUPON, a certain document was
6 marked Janssen Deposition Exhibit
7 No. 5, for identification.)
8 BY MR. RAMER:
9 Q. And the court reporter is handing you
10 Janssen Exhibit 5, and does this appear to be the
11 definition of gender incongruence from the ICD-11?
12 A. I would assume so, yes.
13 Q. And so do you agree that this definition
14 does not require the presence of distress?
15 A. If you give me a moment, I'll read it.
16 The word "distress" is not used.
17 Q. So an individual can be diagnosed with
18 gender incongruence under the ICD-11 even though
19 the individual is not experiencing distress,
20 correct?
21 A. Distress is a term that -- it's a term
22 of art, and if we look at the gender incongruence
23 in childhood definition as an example, it includes
24 a strong desire to be of a different gender than

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1 the assigned sex, a strong dislike on the child's
2 part of his or her sexual anatomy or anticipated
3 secondary sex characteristics and/or a strong
4 desire for the primary and/or anticipated secondary
5 sex characteristics that match the experience
6 gender.
7 Strong dislike does not sound like
8 distress in the context of this definition. The
9 way that this looks clinically is highly
10 distressing for most of the patients that have --
11 that meet all of these characteristics, but the
12 distress is often inherent into that dislike and
13 that incongruence, so it's often implied, even if
14 it is not a specific term that is used in this
15 definition.
16 Q. Does the gender incongruence for
17 adolescents require the strong dislike that you
18 just discussed?
19 A. Again, there's a difference between the
20 pragmatic approach to this work and what is
21 specifically documented. It does not specifically
22 say, Distress is a required element, the way that
23 it does in the DSM-5.
24 Q. Do you diagnose gender dysphoria in

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1 children?
2 A. Yes.
3 (WHEREUPON, a certain document was
4 marked Janssen Deposition Exhibit
5 No. 6, for identification.)
6 BY MR. RAMER:
7 Q. The court reporter has handed you what
8 has been marked as Janssen Exhibit 6, and it says,
9 Diagnostic and Statistical Manual of Mental
10 Disorders on the first page; is that right?
11 A. That is correct.
12 Q. And then I'll just represent to you,
13 this is an excerpt from that. It's not the entire
14 DSM that has been produced as an exhibit.
15 On the second page of this exhibit, do
16 you see the diagnostic criteria for gender
17 dysphoria in children?
18 A. Yes.
19 Q. And in Part A, it refers to a marked
20 incongruence between one's experience/expressed
21 gender and assigned gender; is that right?
22 A. Yes.
23 Q. How does one determine whether an
24 incongruence is marked or not?

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1 A. Again, it's a term of art. Is it
2 consistent, what is the degree of distress, and is
3 it supported by additional criteria that are listed
4 between -- that are labelled 1 through 8.
5 Q. And why does the DSM require six months'
6 duration of this marked incongruence?
7 A. It requires a consistency of identity
8 incongruence and distress in order to approve
9 specificity of the diagnosis.
10 Q. Why -- sorry. Why does the length of
11 time matter?
12 A. There's a difference between transient
13 questioning of one's identity and a consistent
14 incongruence over time.
15 Q. And six months is how you determine
16 whether it's transient or consistent?
17 A. That is the amount that is required for
18 the diagnosis. In practice, we typically see much
19 longer time periods of consistent incongruence.
20 Q. Do you ever see the transient
21 incongruence that you referenced?
22 A. Yes.
23 Q. What does that look like in clinical
24 practice?

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1 A. In clinical practice, you have
2 individuals who are wondering and questioning their
3 gender identity in a way that is misaligned with
4 their sex assigned at birth, but after further
5 explanation or exploration, don't consistently
6 continue to have that incongruence experienced.
7 Q. In Criterion 6 here, what are typically
8 masculine toys?
9 A. That is culturally bound, so it's going
10 to depend upon the cultural context in which that
11 child is raised.
12 Q. So in the culture here, what is a
13 typically masculine toy?
14 A. It's a -- as an example, I'm dating
15 myself, but GI Joe, sports, wrestling. These are
16 kind of things that are stereotypically associated
17 with boys more so than girls.
18 Q. And rough and tumble play, would that be
19 like the wrestling you just mentioned?
20 A. Sure.
21 Q. Why is that part of the criterion for
22 gender dysphoria in boys?
23 A. How much time do you have?
24 Q. I would say five and a half hours, but

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1 I'm not inviting you to --
2 A. For me to answer this question
3 accurately would probably take about an hour to
4 kind of go through the developmental processes of
5 gender, so I will try to tailor it and narrow it
6 down to just a minute or two, which is to say that
7 development is a nonlinear process, and the
8 multiple aspects of gender identity development
9 happen over time in different ways for different
10 people. So some youth who in adulthood are clearly
11 transgender, stably transgender, have been
12 transgender --
13 THE REPORTER: Sorry.
14 BY THE WITNESS:
15 A. Oh, slower. I have to fit it into a
16 minute.
17 Some youth who as adults have been
18 transgender forever, can point to experiences in
19 childhood in which they were not 100 percent clear
20 around identity, and yet had some digressions or
21 transgressions of expected gender norms in
22 childhood that predated the conscious awareness
23 that their identity was incongruent with their sex
24 assigned at birth. I don't know that I'm trans. I

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1 just know that I like being around boys. I like
2 doing all of the things that boys are doing, and
3 that is -- that is what feels good to me.
4 So in childhood prior to development of
5 the metacognitive processes that are required to
6 investigate one's identity, label one's identity,
7 we have stand-ins that are gender role based
8 behaviors that point us in a direction that maybe
9 there's something happening here when it comes to
10 gender.
11 It is one criteria but not all criteria.
12 And you did not ask this question, but I'm going to
13 answer this question, which is to say that one of
14 the changes between DSM-IV and DSM-5 requires a 1,
15 which is the strong desire to be the other gender
16 or an insistence that one is of the other gender.
17 So a core sense of difference or incongruence
18 between one's expressed identity and one's assigned
19 identity is integral to the diagnosis of gender
20 dysphoria in childhood.
21 Q. So then going to the next page where it
22 lists the diagnostic criteria for gender dysphoria
23 in adolescents and adults. Do you see that?
24 A. I do.

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1 Q. Down in Criterion 6, it refers to a
2 strong conviction that one has the typical feelings
3 and reactions of the other gender or some
4 alternative gender different from one's assigned
5 gender. Do you see that?
6 A. I do.
7 Q. And what are the typical feelings of the
8 female gender?
9 A. I do not ascribe to be able to
10 articulate what are typical feelings of the entire
11 female gender across all cultures and contexts.
12 What I'm going to be asking in my clinical
13 assessments is, What is this like for your family
14 in your culture, in your context? What are your
15 archetypes for female reactions, behaviors,
16 expectations, and what have been your experiences
17 in that realm. What feels the same? What feels
18 different?
19 It's much more nuanced and
20 context-driven discussion than it appears to be
21 just by reading the text alone.
22 Q. And so you ask the patient, What do you
23 think the typical feelings of the female gender
24 are? And then ask, Do you feel those feelings? Or

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1 how does it work?
2 A. It's hopefully slightly less clumsy than
3 that. Typically, the patient has self-identified
4 experiences. They are telling their story. Tell
5 me about your experience. Tell me what you are
6 looking for. Tell me about what childhood was like
7 for you. Tell me about your family. Tell me about
8 the women in your family. Tell me about the men in
9 your family.
10 Typically, when we are working with
11 older adolescents and adults, open-ended questions
12 elicit more content than close-ended questions.
13 And so part of the job of us as mental
14 professionals and in our training is to be able to
15 adapt our interview processes to be able to elicit
16 the most information in order to make these
17 diagnoses. If it were just about the check boxes,
18 we could send people forms and give good care based
19 upon the responses to those forms.
20 But good mental health care requires
21 looking at nuance, looking at responses, body
22 reactions, context, cultural phenomenon, et cetera.
23 Q. It seems though that if you do it that
24 way, through asking them to tell you about these

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1 various things, that then it does fall to you to
2 decide, is this a typical feeling of the other
3 gender or not?
4 A. In some ways it falls to the diagnosing
5 provider to assign whether or not a diagnostic
6 criteria has been met or not. My point is that
7 the -- there's not one way of meeting this
8 criteria, that that is going to be culturally and
9 family bound based upon the expectations of that
10 patient.
11 Q. The expectations about what the typical
12 feelings are for the other gender?
13 A. Correct. It's going to be different
14 here than it is in Afghanistan, than it is in
15 New York City, than it is in Toronto.
16 Q. And so when you are diagnosing children
17 here, you are taking into account the typical
18 feelings of genders here in Chicago?
19 A. No, because that is not a requirement
20 for the diagnosis of gender dysphoria in children.
21 For adolescents and adults, this is one of the
22 diagnostic criteria, and we are asking about more
23 microsystems. It's not what is different in
24 Chicago, but it's more what is your understanding

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1 of what this means and what it means in your family
2 and what it means in your community.
3 Q. So then it does sound like it's -- the
4 patient says, This is how I think females act --
5 let me restart. The patient says, This is how --
6 these are the typical feelings of this particular
7 gender, and I have those feelings too, therefore I
8 satisfy this criterion?
9 A. That is closer. Yes, it is. This is
10 how the women in my life respond in these
11 situations, and I find myself responding and
12 reacting in that kind of way as well. Again, it's
13 one part of a whole.
14 On its own, it's not a particularly
15 meaningful construct, but when wrapped into the
16 rest of the diagnostic criteria, particularly the
17 incongruence, it's one data point among many that
18 we are gathering.
19 Q. Do you think the DSM-5 improperly
20 pathologizes gender nonconformity?
21 A. I don't. I don't.
22 MR. RAMER: We have been going for about an
23 hour, so let's go off the record.
24 (WHEREUPON, a recess was had.)

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1 BY MR. RAMER:
2 Q. Dr. Janssen, do you think that
3 transgender identity has a biological basis?
4 A. I do.
5 Q. And what do you mean by that?
6 A. It's complicated. There's multiple
7 factors that are involved in transgender identity.
8 Probably -- I would point to the lived experience
9 of transgender people over eons and the fact that
10 transgender people have always existed despite many
11 attempts to change identities over time, and none
12 have proved successful.
13 Q. When you say "multiple factors
14 involved," what do you mean by that?
15 A. I mean, there's certainly implications
16 that there's biological components that predict
17 identity, that there are components that have to do
18 with hormonal milieu, particularly in utero. There
19 are components of social experience and family
20 systems that influence how you express or
21 experience gender identity.
22 It's a complex multifactorial process,
23 which is why in psychiatry in particular, we tend
24 to approach our patients with a biopsychosocial

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1 formulation, meaning that -- really to capture the
2 essence of an individual's experience, we have to
3 understand the biological, psychological, and
4 social factors that influence the experience of
5 whatever distress is leading the patient to seek
6 care.
7 Q. When you say that there are biological
8 components that predict identity, are you saying
9 that we are able to predict identity by examining
10 some sort of biological component?
11 A. No. There's no evidence to suggest that
12 we have a universal predictive machine that can
13 predict identity. It's much more complex than
14 that. But there are studies that have looked at
15 some of the biological constructs that are shared
16 among transgender individuals.
17 Q. And what were they looking at, like
18 brain scans?
19 A. Brain scans, brain imaging mostly.
20 Q. Anything else?
21 A. Twin studies.
22 Q. And when did you reach the conclusion
23 that transgender identity has a biological basis?
24 A. I don't think that I could tell you a

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1 specific date on that, but as I have been doing my
2 research, it has certainly been consistent with
3 what I have seen published and what I have
4 experienced in working with the patients that I
5 have had the privilege of being able to work with.
6 Q. And was the basis for the conclusion the
7 studies that we just mentioned about brain scans
8 and twin studies and anything else?
9 A. I think there's more to it than just
10 that. I think from a kind of literature review,
11 part of it is recognizing the amount of conversion
12 type interventions that many trans folks have been
13 exposed to in childhood that were unsuccessful.
14 The life histories and the reported life histories
15 of transgender adults in discussing their early
16 childhood experiences. The personal experiences
17 that I have had with patients who describe their
18 feelings and their experiences with identity in a
19 much more deterministic way, despite multiple
20 factors that might influence it one way or the
21 other, but the identity persists nevertheless. All
22 of these things come together for me to make that
23 conclusion.
24 Q. Do you think that there's enough

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1 literature to provide a clear understanding of the
2 biological components of gender identity?
3 A. I don't think biological components of
4 gender identity are sufficient in addressing the
5 complex needs and opportunities of our transgender
6 and gender-diverse patients. Just having a
7 biological underpinning of identity alone is not
8 going to be sufficient to recognize the whole
9 person that is in your office with you, and those
10 whole person's needs, wants, desires, hopes, fears,
11 challenges.
12 Q. Is gender identity determined at birth?
13 A. Gender identity is also a bit of a
14 complicated term that many people think about in
15 different ways. My expert testimony from my
16 recall, recollection from the statement --
17 Q. And just for the record, is that your
18 expert report in front of you?
19 A. Yes, it is.
20 -- is that there's an innate piece to
21 gender identity. There are factors that influence
22 the experience and expression of that gender
23 identity over time, but there is an innate
24 component of gender identity that is relatively

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1 fixed. Saying whether or not it exists at birth or
2 not, I think, is not aligned with developmental
3 processes that we understand developmental
4 processes to engage with. That an understanding of
5 one's identity can change over time but that does
6 not mean that it was not innate or fixed in some
7 way.
8 Q. So the understanding of one's identity
9 is distinct from the gender identity itself; is
10 that right?
11 A. That is correct.
12 Q. And the gender identity itself is
13 innate; is that right?
14 A. Correct.
15 Q. And you think that that is fixed, right?
16 A. Correct.
17 Q. Do you think that gender identity is
18 informed by cultural -- excuse me.
19 Do you think that gender identity is
20 informed by culturally-defined expectations?
21 A. I think that is a component of how
22 people understand and experience and express their
23 gender identity.
24 Q. Again, you are drawing a distinction

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1 between the identity itself and their understanding
2 and expression of that identity; is that right?
3 A. Yes.
4 Q. And so the identity itself is not
5 informed by culturally-defined expectations; is
6 that right?
7 A. I would say that it's not wholly
8 defined, that there is an element of gender
9 identity that is innate, yes, but it is primarily
10 the experience and expression of that gender
11 identity that is informed by cultural factors.
12 Q. Is gender identity partly informed by
13 culturally-defined expectations?
14 A. Sure. Because what it means to be of a
15 particular gender is different from one culture to
16 the next.
17 Q. And if that is true, how can identity
18 also be biological?
19 A. Let me see if I can figure out an
20 analogy or a metaphor that might make sense. And I
21 do and have taught on sexual orientation
22 development as well, so that is kind of where my
23 brain is going.
24 In the world of sexual orientation

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1 development, sexual orientation or your sense of
2 attractiveness is something that we know is fixed.
3 That is something that is inherent. What you do
4 with those attractions is very different and how
5 you label those attractions is very different. In
6 an environment where it is unsafe to identify as a
7 gay person, as an example, you are going to have
8 people who have same sex sexual attractions who
9 nevertheless do not identify as gay or affirm
10 themselves as gay or behave in such a manner that
11 would label themselves as gay. Does it mean that
12 there are less gay people? No. It means that he
13 cultural milieu is such that it influences how one
14 is able to express the identity.
15 So with gender identity, there's a fixed
16 gender identity. There are factors that make
17 expression of that identity more and less safe,
18 more and less valid with more and less
19 consequences, and those factors influence that
20 expression of the gender identity. It does not
21 express or change the innate incongruence that is
22 present for transgender individuals.
23 Q. So the gender identity itself, as
24 distinct from gender expression or understanding,

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1 is not shaped by culture, right?
2 A. Yeah. I would say that there's an
3 element of gender identity that is independent of
4 culture.
5 Q. When you say "an element of gender
6 identity," what do you mean?
7 A. Well, let me just talk about my clinical
8 experience. When I'm working with patients and we
9 are doing an assessment, it does not parse in such
10 a neat way. I don't have patients who describe,
11 Here is my gender identity, this is the element of
12 my gender identity that is influenced, this is how
13 I experience it in this kind of particular format.
14 When we are putting it in these parsed
15 kind of scientific terms, it's less relevant to the
16 patient's experience who talk about, This is how it
17 has felt to me, these are the cultural factors that
18 have informed how I feel and how I experience it.
19 These are the cultural factors and family factors
20 that influence how I express it, what feels
21 meaningful and important and valuable to me. It's
22 just a bit of a dichotomy that does not exist in
23 clinical practice.
24 Q. I guess where I'm just getting a little

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1 confused is, we are distinguishing between gender
2 identity, gender expression, gender understanding,
3 but then you are also referring to elements of
4 gender identity. And when you are doing that, are
5 you referring to only that first category, or are
6 you describing gender expression and gender
7 understanding as an element of gender identity?
8 A. There's no way to put gender identity in
9 a vacuum. If there were, there would be a fixed
10 state of gender identity. But all of these factors
11 exist, and they are always co-occurring with this
12 core sense of development.
13 So I guess what I'm trying to say is
14 that there's a fixed element of gender identity.
15 How that gets expressed is culturally bound.
16 Q. Okay. So can a person's gender identity
17 change?
18 A. I don't think so, no.
19 Q. And so gender identity is static?
20 A. Yes.
21 Q. And gender identity is not a choice?
22 A. Gender identity is not a choice.
23 Q. Is gender expression a choice?
24 A. Yes.

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1 Q. And is the type of secondary sex
2 characteristics that a person desires a form of
3 gender expression?
4 A. It can be for some people, yes.
5 Q. Can it ever not be?
6 A. There are certainly some individuals who
7 are less distressed by secondary sex
8 characteristics than others.
9 Q. And how did you reach the conclusion
10 that a person's gender identity cannot change?
11 A. That has been through my clinical
12 experience and a review of the literature.
13 Q. Can you elaborate on what you have seen
14 in the literature and you have seen in your
15 clinical experience that led you to the conclusion
16 that a person's gender identity cannot change?
17 A. Sure. We have unfortunately decades of
18 experience of clinicians who have tried to change
19 both sexual orientation and gender identity without
20 success, and with reports of individuals who have
21 gone through those types of treatments with an
22 attempt to change gender identity, have experienced
23 those treatments as quite harmful and at times
24 destructive.

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1 So I think that provides support for my
2 conclusions that there's a fixed and unchangeable
3 element of gender identity. Personally and in
4 clinical experience, I have worked with countless
5 adolescents, adults who wish to God they were not
6 transgender and have made every attempt possible to
7 not be, and yet the identity persists. So that
8 supports it to me.
9 Q. The first thing you were talking about,
10 is that colloquially known as conversion therapy?
11 A. Correct, yes.
12 Q. Do you see a distinction between someone
13 using conversion therapy to try to change someone's
14 gender identity and another individual's gender
15 identity organically changing?
16 A. Well, the premise of the question sounds
17 like people's gender identity changes. I think
18 people's understanding of gender identity and their
19 expression of that gender identity changes over
20 time. I don't think it's a -- that fixed element
21 of gender identity is not something that changes
22 with psychotherapeutic intervention or with
23 conversion efforts.
24 Q. What about just naturally as the person

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1 grows?
2 A. No. Understanding evolution of -- how
3 you understand it and how you express it certainly
4 changes over time.
5 Q. And so this is a hypothetical. If you
6 have a natal female adolescent who identifies as a
7 male, is diagnosed with gender dysphoria, and two
8 years later the same individual says she now
9 identifies as a female and does not have gender
10 dysphoria, that person's gender identity has not
11 changed; is that right?
12 A. Correct.
13 Q. Only the individual's gender expression
14 has changed, right?
15 A. And their understanding of their gender,
16 yes.
17 Q. Okay. And how do you know that?
18 A. How do I know it? "Knowing" is a term
19 that I don't like because it's not something that I
20 use in my day-to-day practice. This is the
21 conclusion that I have come to from the review of
22 the literature and my experience working with these
23 patients. I think to know something means that
24 there's a period at the end of that sentence as

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1 opposed to continuously wanting to understand what
2 patients' experiences are. And, in general, that
3 is my philosophy of care is, I work with the
4 patients that I'm working with, and I want them to
5 tell me about their experiences and what it means
6 to them. So it's not a question that I feel like I
7 have a clear sense of knowing how to answer.
8 Q. What in the literature or your clinical
9 practice lends support to this dichotomy between
10 gender identity and gender expression?
11 A. I would go back to the same things that
12 I have discussed before, that there have been
13 countless efforts to change core gender identity
14 that have been unsuccessful.
15 Q. Why can't those efforts be seen as
16 efforts to change gender expression?
17 A. Because oftentimes the gender expression
18 does change and yet the core incongruence between
19 assigned gender and experienced gender are not
20 resolved.
21 Q. When you say the gender expression
22 changes in response to conversion therapy, I mean,
23 that is effectively a compelled change, right?
24 A. Not always, no. I have had patients,

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1 and it is not uncommon for patients to seek out
2 conversion efforts voluntarily. Many people are
3 highly distressed by the concept of having a trans
4 identity and seek out efforts to change it.
5 Q. So in the hypothetical of the natal
6 female adolescent who identifies as male and then
7 subsequently identifies as female, what is the
8 individual's gender identity?
9 A. I could not tell you.
10 Q. Why not?
11 A. One, the individual patient is going to
12 have to tell me, but, two, they are now my patient
13 and there's a lot more than just two data points
14 that go into understanding an assessment of gender
15 identity. It's a much more complicated evaluation
16 that we are doing with an actual patient.
17 Q. If I said it's not possible to predict
18 with certainty a child's ultimate gender identity,
19 given what you have said about gender identity
20 today, is that statement even comprehensible?
21 A. I would wholeheartedly agree with that
22 statement. I'm not in the position of being a
23 psychic who can predict the future. That is not
24 the job that I have as somebody who makes an

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1 assessment of these children.
2 My job is to assess the history and make
3 a diagnosis of gender dysphoria and understand the
4 individual's identity in the context of
5 biopsychosocial factors.
6 Q. Why is it predicting the future, if you
7 are trying to determine the child's ultimate gender
8 identity as opposed to figuring out what the
9 biologic, static gender identity is presently?
10 A. Because children don't live in vacuums.
11 They live in families and cultures that influence
12 how they understand and experience and whether they
13 are able to or whether they want to make changes in
14 how they express that over time.
15 Q. Does gender identity evolve?
16 A. One's understanding of it can evolve
17 over time. The change in how one expresses it can
18 evolve over time.
19 Q. But gender identity cannot evolve over
20 time?
21 A. Yes.
22 Q. Are you familiar with the term
23 "detransition"?
24 A. Yes.

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1 Q. And what is your understanding of that
2 term?
3 A. The term "detransition" means different
4 things to different people, and it's one of the
5 biggest challenges in talking about detransition
6 because nobody is working from the same definition.
7 Q. What is your definition?
8 A. I don't have a specific definition
9 because what I'm going to ask is, patients who have
10 gone through a process, to name and describe what
11 that process is rather than ascribe a term to it
12 that may or may not apply to them.
13 In general, most people are referring to
14 detransitioned as a person who has made steps
15 towards typically medical transition that have
16 opted to stop medical transition. Some people
17 refer to just those who have had surgical
18 transition. Some people refer to it, those who
19 have had social transition. Some people refer to
20 it who have made no steps towards transition at
21 all. Some people include people who have a
22 tremendous amount of distress and some people do
23 not.
24 So there's probably ten plus cohorts of

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1 individuals that are classified colloquially as
2 detransitioners that probably don't belong
3 together.
4 Q. But in all of those cases, what is
5 really happening is just the individual's gender
6 expression or gender understanding is changing,
7 right?
8 A. Not necessarily, no.
9 Q. What else could be going on?
10 A. Oftentimes what we see are people
11 stopping treatment because they lack access to it.
12 They lose access to it. Their insurance changes.
13 Their family is unsupportive. They are in a work
14 environment that does not allow gender transition
15 safely. They have other things going on in their
16 life that are pressing.
17 There's a lot of other reasons that
18 individuals stop transitioning other than my
19 experience and my culturally bound experience of my
20 expression of gender has changed.
21 Q. But nobody has ever detransitioned
22 because their gender identity has changed, right?
23 A. Well, what I have testified to is that
24 there's an innate piece of gender identity that is

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1 not changeable.
2 Q. So it seemed like the answer then has to
3 be yes?
4 A. I think that is correct.
5 Q. Do you agree that gender is a spectrum?
6 A. Yeah, I do.
7 Q. Can you just explain what that means?
8 A. Sure. So there's a range of intensity
9 and valence of gender identity across the spectrum
10 between masculinity and femininity, between male
11 and female, and even within our bodies, there's a
12 range of hormonal expression, there's a range of
13 how our genitals look.
14 Q. And do you agree that an adolescent can
15 be diagnosed with gender dysphoria even if the
16 adolescent does not identify as the other gender?
17 A. Yes. There are alternative gender
18 categories that many adolescents may use to
19 describe their sense of incongruence.
20 Q. So, for example, an individual who
21 identifies as nonbinary can still be diagnosed with
22 gender dysphoria, correct?
23 A. That is correct.
24 Q. And if medically indicated, it would

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1 still be appropriate to recommend puberty blockers
2 for cross-sex hormones for that individual,
3 correct?
4 A. If after an assessment that is done with
5 the expected elements of that assessment, by the
6 people who are appropriate for doing that
7 assessment, and it's indicated to be medically
8 necessary, yes, it is indicated in those
9 situations.
10 Q. And what do the secondary sex
11 characteristics of a nonbinary person look like?
12 A. Secondary sex characteristics are
13 determined by the hormonal milieu, not by the
14 identity.
15 Q. How is that responsive -- what do you
16 mean by that?
17 A. It depends upon -- for a person with a
18 nonbinary identity, unless I know how much
19 testosterone or estrogen that they have in their
20 system, I have no way of predicting what their
21 secondary sex characteristics would be.
22 Q. If you have -- this is a hypothetical.
23 If you have a natal male adolescent who is
24 suffering from severe psychological distress

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1 because he desires more masculine secondary sex
2 characteristics, would you recommend testosterone
3 for that patient?
4 MR. RAY: Object to form.
5 BY THE WITNESS:
6 A. As somebody who is working with kids
7 with gender dysphoria and gender-diverse identities
8 in your hypothetical, somebody who is assigned male
9 at birth who has an identity of male does not have
10 an incongruence between assigned sex at birth and
11 gender identity and, thus, would not meet criteria
12 for A1 of gender dysphoria and would not --
13 necessarily would not be eligible for treatments
14 for gender dysphoria if the diagnosis of gender
15 dysphoria is not present.
16 BY MR. RAMER:
17 Q. How would you treat that patient for
18 their severe distress?
19 A. It's a hypothetical patient that I have
20 never encountered in all of my clinical practice.
21 Q. Given your experience, if this
22 hypothetical patient was presented to you, how
23 would you go about it?
24 MR. RAY: Object to the form.

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1 BY THE WITNESS:
2 A. It has never occurred to me. If a
3 patient comes in and experiences distress, I'm
4 going to do an assessment and understand where that
5 distress comes from. I can't really speak to
6 specifics unless I have an actual patient in front
7 of me with whom I have done a biopsychosocial
8 formulation in order to make a diagnosis and a
9 treatment plan that is effective for the specific
10 needs of that individual patient.
11 Q. Why can a natal male be diagnosed with
12 gender dysphoria only if the incongruence leads to
13 desire for more feminine secondary sex
14 characteristics?
15 A. The diagnosis of gender dysphoria is
16 inherently based on in the incongruence between sex
17 assigned at birth and identity.
18 Q. Do you think that the distinction
19 between male assigned at birth and nonbinary is an
20 incongruence?
21 A. I do.
22 Q. How is that different from what I'm
23 describing?
24 A. Because it's a different

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1 characterization. Patients describe it as
2 incredibly different.
3 Q. What do you mean by that?
4 A. There's an incongruence, that it's not a
5 matter of degree as in your hypothetical. I'm a
6 man, but I wish I were more masculine is different
7 than, I'm not a man and everybody thinks that I'm a
8 man. That is a separate experience and a separate
9 category that is aligned with a diagnosis of gender
10 dysphoria. Whereas, your hypothetical likely would
11 not be.
12 Q. But if gender is a spectrum as opposed
13 to binary, I don't see how that conclusion can
14 hold.
15 A. I guess I'm confused by the question.
16 Q. So is there anything in between
17 nonbinary and identifying as a male?
18 A. It depends upon who you are asking.
19 Many people have different terms to describe
20 different experiences. Practically speaking, when
21 I'm working with adolescents in particular, I'm
22 asking for them to describe their own terms, and
23 what is important about the DSM-5 diagnostic
24 criteria for gender dysphoria is a lot of things.

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1 Among them, that there is an incongruence between
2 the assigned sex at birth and the identity.
3 There's not alignment but that there's
4 incongruence, and that there is distress and
5 impairment, that that is an integral part of the
6 diagnosis. There's lots of people with distress
7 that don't have the incongruence. There's fewer
8 people who have incongruence without the distress,
9 but that also can happen, as we talked about at the
10 beginning.
11 Q. So taking into account the gender
12 spectrum that you described earlier and you have a
13 male assigned at birth, gender dysphoria can only
14 run one way, which is toward the feminine end of
15 the spectrum; is that right?
16 A. So there's multiple categories that go
17 into gender. There's gender identity, which is the
18 piece that you are assessing in terms of the
19 incongruence. You are assigned this sex at birth,
20 you are assigned male at birth, some incongruence
21 with that is required.
22 That is different from gender role or
23 gender-based expression. These are the culturally
24 bound elements of gender that define what

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1 masculinity and femininity are in the United States
2 versus anywhere else in any other culture. The
3 concept of masculinity is culturally bound as a
4 phenomenon. What is masculine is different in one
5 culture compared to the next. That is separate
6 from the concept of gender identity, which is, by
7 the definition of gender dysphoria, incongruent
8 with the sex assigned at birth.
9 You can have people who have a gender
10 identity as more feminine who, nevertheless, have a
11 more masculine appearance that their gender
12 role-based behaviors are separate from their gender
13 identity. But to make a diagnosis of gender
14 dysphoria, there's an incongruence between the sex
15 assigned at birth and that core gender identity.
16 Q. And for a natal male, the incongruence
17 you are discussing has to go in the feminine
18 direction on the spectrum; isn't that right?
19 A. Or towards a nonbinary or a gender
20 direction. It has to go away from male.
21 Q. Do you agree research has not been
22 conclusive about what percentage of youth will
23 eventually experience a desire to detransition?
24 A. I think there's very little that is

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1 conclusive, so, yes, I would agree with that
2 statement.
3 Q. Do you think that we have good evidence
4 about what percentage of youth will eventually
5 experience a desire to detransition?
6 A. The best evidence that we have from
7 longitudinal studies as well as from large
8 population-based studies show that the rates of
9 people who regret their transition or stop their
10 transition are incredibly low.
11 Q. Do you see a distinction between
12 describing the best evidence that we have and
13 describing evidence sufficient to make a confident
14 decision about an outcome?
15 A. Well, I can't make any decisions other
16 than with the best evidence that we have, so that
17 statement will always be true, whether that is
18 today, whether that is 40 years from now. I'm
19 always going to be making a decision based upon the
20 best evidence that we have.
21 Q. Could there ever be a situation where
22 there's some evidence but you don't think it is
23 enough to warrant recommending a particular
24 intervention?

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1 A. Sure.
2 Q. What is an example?
3 A. Off the top of my head, use of ketamine
4 for adolescents with bipolar disorder, there's some
5 evidence but probably not enough right now for me
6 to make a recommendation for it in my practice.
7 Q. And why not?
8 A. In part because there has not been a
9 long track record of published data in the field,
10 only a year or two of actual study.
11 Q. And the risk could be extreme or
12 something, or what is on the other side?
13 A. Yeah, potentially. Yeah, that the risks
14 are less well-known.
15 Q. And what would it take for you to feel
16 confident prescribing ketamine as that treatment?
17 A. Probably nothing because that is not the
18 population of patients that I typically would work
19 with. I feel lucky to be in an academic
20 environment, so in these contexts, it's about
21 finding people who have actual clinical experience
22 working in this population who are doing some of
23 the research and can start building some of the
24 evidence base to support this.

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1 Q. Do you agree that adolescence plays a
2 role in the crystallization of one's gender
3 identity?
4 A. For some people, yes.
5 Q. And what do you mean by that?
6 A. There's no one correct trajectory to
7 come to a transgender identity. Some people come
8 to it as early as 2 to 3, have real clear
9 recognition and expression of gender identity.
10 Other people don't come to recognize their
11 transgender or gender-diverse identity until late
12 into adulthood, so there's no one right way of
13 going through this process. That is what I mean by
14 it.
15 Q. And have you ever heard the phrase
16 "gender identity development"?
17 A. Sure.
18 Q. And what is your understanding of that
19 phrase?
20 A. My understanding of that phrase is that
21 is a complex biosocial process that involves
22 multiple developmental tasks over multiple areas
23 over multiple time points.
24 Q. I'm sorry. I missed you toward the end.

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1 Could you repeat that?
2 A. Multiple areas, multiple time points via
3 psychosocial developments.
4 Q. Do you agree that the etiologic process
5 of gender identity development is unclear?
6 A. I think it's not fully explicated.
7 There are elements that are clear.
8 (WHEREUPON, a certain document was
9 marked Janssen Deposition Exhibit
10 No. 7, for identification.)
11 BY MR. RAMER:
12 Q. All right. And the court reporter has
13 handed you what has been marked as Exhibit 7, and
14 it says, Expert Report of Aron Janssen on the
15 front; is that right?
16 A. It does say that, yes.
17 Q. And is this the expert report that you
18 submitted in this case?
19 A. It looks like it, yes.
20 Q. And on page 10, you refer to something
21 you discussed briefly today, where you talk about
22 conducting an assessment for each patient, correct?
23 A. Uh-huh, correct.
24 Q. And is this assessment required by the

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1 SOC 8?
2 A. It depends upon the context.
3 Q. How so?
4 A. A mental health assessment is required
5 if one is considering one of the medical
6 interventions for adolescents.
7 Q. And so a provider has to conduct this
8 assessment before recommending puberty blockers as
9 a treatment for gender dysphoria, correct?
10 A. That is correct.
11 Q. And same for cross-sex hormones for
12 adolescents, correct?
13 A. Correct.
14 Q. And same for surgery for adolescents,
15 correct?
16 A. Correct.
17 Q. And is the assessment for adults the
18 same as the assessment for adolescents?
19 A. It depends upon the context. In some
20 clinics the assessment for adults is the same, and
21 in our clinic, as an example, we see young adults
22 and our assessment process is the same.
23 Q. And just as a general matter, what is
24 the purpose of this assessment?

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1 A. As a general matter, the purpose of the
2 assessment is to, one, evaluate the mental health
3 of the individual who is seeking care, assess
4 whether or not a diagnosis of gender dysphoria is
5 present, assess the impact of the diagnosis of
6 gender dysphoria on the individual's functioning,
7 assess whether any co-occurring mental health
8 disorders or mental illnesses are present and what
9 role, if any, they have on the experience and
10 understanding of that individual's gender identity,
11 that you are understanding the family and social
12 context in which this patient lives, that you are
13 understanding what the patient is hoping for in
14 seeking out care, and eventually to the point where
15 one is understanding the expectations of whether or
16 not a patient can and does understand the risks,
17 benefits, and alternatives of that intervention as
18 well as in the case of children and adolescents,
19 whether the decision maker, most of the time being
20 a parent, is aligned with the child's -- or child's
21 preferences and wishes and is able to provide an
22 informed consent to whatever intervention that you
23 are recommending after discussion of those risks,
24 benefits, and alternatives.

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1 Q. And do you think the assessment requires
2 a discussion of all of those things that you just
3 listed?
4 A. I do, yes.
5 Q. And in your clinic, are the mental
6 health professionals responsibile for performing
7 the initial assessment?
8 A. It depends upon which route the
9 individuals are entering the clinic. The majority
10 of the patients who enter our clinic do so in a
11 multidisciplinary assessment, where there are
12 medical and mental health providers together in the
13 assessment.
14 Q. Would there ever be an assessment where
15 there is not a mental health provider involved?
16 A. There's any kind of assessment one could
17 imagine, but in terms of what is recommended as a
18 part of the standard of care, if you were
19 considering a medical intervention as an
20 adolescent, a mental health evaluation is a
21 requirement of that process. Where it fits in the
22 process, there's a fair amount of variability.
23 Q. I guess my question is, who conducts
24 that assessment that you were just describing?

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1 A. For children and adolescents, primarily
2 that is mental health providers.
3 Q. But not exclusively?
4 A. I can't speak to how practice happens
5 throughout the entirety of the world but that has
6 been the experience in all the of the clinics that
7 I have talked to and all of the clinicians that I
8 have worked with over the years.
9 Q. When you say "that has been the
10 experience," you mean that the mental health
11 provider is the one conducting this assessment that
12 we are discussing in your report?
13 A. Correct.
14 Q. Under the SOC 8, does it have to be a
15 mental health professional who conducts this
16 assessment?
17 A. I would have to review the specific
18 assessment chapter and the adolescent chapter to
19 make a fierce determination that I was certain of.
20 It requires a qualified mental health professional
21 for assessment of the mental health needs in
22 children, yes.
23 Q. And for adolescents, do you think that
24 the assessor should be a mental health

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1 professional?
2 A. I do, yes, but part of what we recognize
3 is that this is a global context in which we work,
4 and so there are going to be other countries that
5 don't have access to mental health professionals.
6 In the United States, do I think that a mental
7 health professional should be a part of the
8 assessment? Yes, I do.
9 Q. And how long does an adequate assessment
10 take?
11 A. It depends upon the complexity of the
12 child and the system in which they live.
13 Q. What is the shortest assessment that you
14 have ever conducted?
15 A. The shortest assessment that I have ever
16 conducted in what context?
17 Q. The context that we are talking about.
18 What do you mean? The context of assessing an
19 adolescent for pubertal suppression.
20 A. I mean, that helps, right, because that
21 is a specific context. I have patients consult
22 with me and are not interested in treatments other
23 than information, and that is going to be a shorter
24 assessment or valuation time than somebody who is

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1 seeking out a medical intervention.
2 The shortest assessment that I have done
3 for puberty blockers probably is, if I were to
4 guess, on the order of four to six hours over
5 several sessions.
6 Q. Do you think that it would be possible
7 to adequately assess all of the items that you
8 described that are part of the assessment in
9 60 minutes?
10 A. Sometimes, yes.
11 Q. But that has never happened for you?
12 A. It has not happened for me, in part
13 because of how my clinic is structured. The times
14 in which it would happen would be individuals that
15 have had ongoing mental health treatment by a
16 provider over an extended period of time in which
17 those of us who are doing the final assessment are
18 in a consultative role with those individuals.
19 Q. So what you are describing is a
20 situation where an individual has been working with
21 a mental health provider outside of the clinic,
22 then the individual comes to the multidisciplinary
23 clinic and you don't -- basically, you don't have
24 to start from ground zero, is that the point?

1 A. Correct. It's about -- there's not any
2 magic about the time spent. It's about the content
3 of the assessment, and there's a lot in there. And
4 some people are more efficient than others, some
5 have outside providers that can gather a lot of
6 information ahead of time. Others do not, and so
7 length of time is going to be incredibly variable
8 from one clinic practice to another.
9 The important part is that the
10 components of the assessment that are required to
11 make a recommendation are made, and whatever time
12 that takes is the time that it should take.
13 Q. At your clinic, do you ever receive
14 letters of -- "recommendation" may not be the right
15 word, but letters from mental health professionals
16 outside of the clinic recommending a patient for
17 pubertal suppression, for example?
18 A. Yes.
19 Q. And do you take those letters at face
20 value, or do you inspect the basis for the
21 conclusions in them?
22 A. Our process at our clinic is that we
23 liaise with the community therapists that are
24 writing that letter to have a discussion about the

1 content of the letter and to vet the practice and
2 the assessment processes that these patients have
3 undergone.
4 Q. Do you think that that's a best
5 practice?
6 A. I think it's a best practice. It's not
7 a required element, but it's what we have come to
8 as believing is in the best of interest of the
9 patient.
10 Q. Have you ever recommended puberty
11 blockers as a treatment for gender dysphoria after
12 just one meeting with a patient?
13 A. I cannot recall all of my patient
14 encounters.
15 Q. But that is not outside of the realm of
16 possibility?
17 MR. RAY: Object to form.
18 BY THE WITNESS:
19 A. I think in the context of a patient who
20 had already been under care with a qualified gender
21 health provider, who had already made a decision
22 and was looking for a second opinion, it is
23 conceivable in that hypothetical that I might
24 recommend it after one session.

1 BY MR. RAMER:
2 Q. What about outside of that context?
3 A. That would be atypical for me.
4 Q. But you can't say it has never happened?
5 A. I would have to go through hundreds and
6 hundreds of charts to say with certainty, so I
7 don't know, is the honest answer.
8 Q. And you may have mentioned this earlier,
9 but besides the patient as part of this assessment
10 process, who else are you talking to?
11 A. Relevant informants, whomever they may
12 be. Our process is to speak to as many people as
13 we can, so certainly primary caregivers, whomever
14 that may be.
15 Whenever possible in child mental
16 health, kids live in systems, so how they are
17 responding when they are at home is different than
18 how they are responding when they are at school,
19 which is different than how they are responding on
20 sports teams and religious contexts. So we want to
21 gather as much information about the different
22 systems that a child is engaged with.
23 At a minimum, we require parent
24 involvement, but at a maximum, often we are

1 incorporating information from school, community
2 leaders, et cetera.
3 Q. Other care providers, outside of the
4 clinic?
5 A. Yeah, and other therapists, other
6 physicians. Anybody who has context to provide, we
7 welcome.
8 Q. Do you ever talk to teachers?
9 A. Yes.
10 Q. Siblings?
11 A. Yes.
12 Q. And do you typically receive the
13 patient's medical records from the other providers?
14 A. These days typically the medical records
15 are accessible via the electronic medical record,
16 so when they have provided us consent for us to
17 review outside records, we will review those.
18 Q. Do you require that as part of your
19 treatment of a patient?
20 A. That outside medical records are
21 reviewed?
22 Q. That you are able to access and review
23 their medical records.
24 A. It's not a required element and is not

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1 often relevant, but when it's relevant, we will do
2 everything that we can to obtain consent. I have
3 never had an issue with anybody not providing
4 consent to looking at old records.
5 Q. Switching gears a little bit. As a
6 theoretical matter, are you familiar with the
7 distinction between an informed consent model of
8 care and an assessment model of care?
9 A. That is -- it's a false dichotomy. To
10 me, as I hear that question, it implies that
11 informed consent does not have an assessment, and
12 informed consent is discussing a treatment option
13 where you are reviewing the risks, benefits,
14 alternatives, expected impact, expected downsides
15 and capacity to consent, all of which requires an
16 assessment.
17 Q. What about a distinction -- are you
18 familiar with the distinction between an informed
19 consent model of care and a gatekeeping model of
20 care?
21 A. All of these are kind of colloquial
22 terms to describe different models of health care
23 delivery more specifically within the adult care
24 space.

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1 Q. Why more specifically within the adult
2 care space?
3 A. The recommendations are such that for a
4 child and adolescent who is seeking out medical
5 interventions, that a mental health assessment by a
6 qualified mental health provider is a required
7 element of this care. For adults seeking medical
8 interventions, sometimes an informed consent
9 process in which there is no mental health
10 professional doing the assessment is a standard
11 work flow.
12 Q. In your view, is one model better than
13 the other?
14 A. I think it's context dependent. I think
15 some models work better for some people and some
16 models work better for others.
17 Q. For treating gender dysphoria, is one
18 model better than the other?
19 A. It's person dependent, not diagnosis
20 dependent.
21 Q. Is it person dependent for treating
22 gender dysphoria in adolescents as well?
23 A. In adolescents, the recommendations from
24 the standards of care is that a mental health

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1 professional do an assessment of the patient prior
2 to initiation of care, and that is my practice as
3 well.
4 Q. And do you think that -- I mean, I guess
5 have you ever used the term "gatekeeping" to
6 describe a model of care?
7 A. I have not.
8 Q. Do you think that the SOC 8
9 represents -- well, I guess would it be a false
10 dichotomy to even ask the question of whether the
11 SOC 8 represents an informed consent model or an
12 assessment model?
13 A. It would be a false dichotomy. The
14 SOC 8 recommends assessment occur prior to
15 initiation of any medical care regardless of age
16 and requires a mental health assessment by a
17 qualified mental health assessor to be done prior
18 to initiation of any medical care for an
19 adolescent.
20 Q. Do you think that the SOC 8 places
21 mental health providers in the role of gatekeeper?
22 A. I reject the term, so no.
23
24

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1 (WHEREUPON, a certain document was
2 marked Janssen Deposition Exhibit
3 No. 8, for identification.)
4 BY MR. RAMER:
5 Q. And the court reporter has handed you
6 what has been marked as Exhibit 8; is that right?
7 A. Yes.
8 Q. And Exhibit 8 is an article entitled
9 Readiness Assessments for Gender-Affirming Surgical
10 Treatments, A Systematic Scoping Review of
11 Historical Practices and Changing Ethical
12 Considerations; is that right?
13 A. That is right.
14 Q. And did you help author this?
15 A. I did.
16 Q. And at the bottom of page 1, I'm just
17 going to read this last sentence that carries over
18 onto the next page, and I'll first ask if I read it
19 correctly.
20 It says, We identified a trend across
21 successive iterations of the guidelines in both
22 reducing stigma against TGD individuals and shift
23 in ethical considerations from do no harm to the
24 core principle of patient autonomy. Did I read

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1 that correctly?
2 A. I'm not seeing where that is.
3 Q. So on page 1 of the --
4 A. Got it. It went over to the next page.
5 Q. Yeah. Sorry.
6 A. Got it. Yes.
7 Q. And can you explain what you meant by a
8 shift in ethical considerations from do no harm to
9 the core principle of patient autonomy?
10 A. Sure. So this is more specific to adult
11 care than it is to the care of children and
12 adolescents and is in reference to the changing
13 recommendations of standards of care prior to being
14 able to access medical or surgical interventions.
15 As an example, in previous iterations of
16 the standards of care developed by WPATH, so moving
17 from WPATH 6 or standards of care 6 to 7, one of
18 the things that changed was prior to any initiation
19 of care there was what was called a "real life
20 test," meaning that individuals had to live for two
21 years in their preferred gender role prior to
22 consideration of many of the interventions.
23 There was no evidence to support the
24 need for living in one's desired gender role for

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1 that specific period of time and also required
2 therapeutic interventions that were not often
3 indicated. In that context, providing a sense of
4 do no harm, ensuring that patients could jump
5 through as many hoops as possible over an extremely
6 long period of time, was in contradiction with many
7 of the patients' experience who during that
8 two-year period were very clear and likely would
9 have benefited from interventions within that
10 process.
11 That was recognized and a reflection of
12 both patient experience in the extant literature
13 that was reviewed in the transition from SOC 6 to
14 SOC 7 to remove a lot of those standards and focus
15 on the recognition that most patients, when
16 provided with accurate information about decisions,
17 can make informed decisions about their care.
18 Q. And so what is the ethical consideration
19 of do no harm? I understand that you described
20 what prior requirements were and that, in your
21 view, those were unnecessary and even harmful; is
22 that right?
23 A. I would say so, yes.
24 Q. But in this sentence, you are talking

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1 about the ethical consideration of do no harm, and
2 you are contrasting it with the core principle of
3 patient autonomy. So it seems like this sentence
4 is less in the concrete and more in the theory of
5 ethics. Do you think that I'm misunderstanding
6 that?
7 A. No. I think that you are correct, that
8 it's more situated within the theory of ethics.
9 Q. Okay. So on page 2, the next sentence,
10 it says, This has helped reduce barriers to care
11 and connect more people who desire it to
12 gender-affirming care, GAC, but in these authors'
13 opinions does not go far enough in reducing
14 barriers. Did I read that correctly?
15 A. You read that correctly.
16 Q. Do you think that there needs to be a
17 further shift in ethical considerations from do no
18 harm towards the core principle of patient
19 autonomy?
20 A. What I mean in this sentence is that
21 there should not be unnecessary barriers to
22 accessing evidence-based effective and safe care.
23 Q. But is an unnecessary barrier
24 necessarily serving the ethical consideration of do

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1 no harm?
2 A. There are many barriers that have no
3 relationship whatsoever to the ethical principle of
4 do no harm.
5 Q. And here you are talking about the
6 ethical principle, and you are saying that there
7 needs to be a shift from the ethical principle of
8 do no harm toward the core principle of patient
9 autonomy, right?
10 A. My read -- and I wrote this a long time
11 ago, and I was not the primary author. My read of
12 this is that what does not go far enough is the
13 reduction of barriers.
14 Q. And this is written in October -- sorry.
15 This was published in October of 2022, correct?
16 A. Correct.
17 Q. And when you say that you were not the
18 primary author, what is the point of that
19 statement?
20 A. In the typical processes of scientific
21 peer-reviewed literature, the primary author is the
22 person who does the majority of the actual drafting
23 of the text.
24 Q. But did you approve of the submitted

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1 version?
2 A. I did, yeah.
3 Q. And now sticking with this Exhibit 8, I
4 would like to go to page 12. And the right column
5 below Discussion and below Changing Standards, it's
6 about three-quarters of the way down. There is a
7 sentence that begins with, Requiring TGD people to
8 have. Just let me know when you --
9 A. I see it.
10 Q. Okay. And it says, Requiring TGD people
11 to have a diagnosis at all to obtain care, no
12 matter the terminology used is pathologizing. The
13 practice of requiring a diagnosis continues to put
14 mental health and other medical providers in the
15 position of gatekeeping. Continuing the vestigial
16 historical focus on confirming a person's gender
17 identity rather than trusting that TGD people
18 understand their identities better than providers
19 do. Did I read that correctly?
20 A. You did.
21 Q. Do you think it is wrong to require a
22 diagnosis before transgender individuals receive
23 medical interventions?
24 A. I do not.

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1 Q. I'm sorry?
2 A. I do not.
3 Q. Do you think the practice of requiring a
4 diagnosis puts mental health providers in the
5 position of gatekeeping?
6 A. Not inherently, no.
7 Q. What do you mean "not inherently"?
8 A. When it's done appropriately and with
9 reduced barriers, having a mental health assessment
10 particularly for children and adolescents, which is
11 a requirement, opens more doors than it closes.
12 Q. What do you mean "opens more doors than
13 it closes"?
14 A. Meaning an affirming assessment can help
15 to identify strengths, weaknesses of any
16 individual, address any co-occurring issues that
17 may be present that may impact the success of care.
18 As a psychiatrist and somebody who is a mental
19 health professional, I don't believe that inherent
20 in having a mental health professional be involved
21 in your life is stigmatizing. That is what I mean.
22 Q. Do you think that applying the criteria
23 of the DSM-5 continues the vestigial historical
24 focus on confirming a person's gender identity?

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1 A. I think it's complicated, and I think
2 that many people have different opinions, including
3 the authors of this paper in terms of how firmly
4 they would agree or disagree with that statement.
5 I think in adulthood in particular, that there had
6 historically been a significant number of barriers
7 that had been placed in the way of accessing care
8 that was safe and effective that has led to
9 significant harms.
10 Q. So you would not advocate for the
11 removal of a diagnosis under the DSM-5 as a
12 requirement for medical interventions for gender
13 dysphoria, correct?
14 A. I would not. I think there's -- it's
15 not an easy discussion, and I think it's a very
16 complex one. I have had patients who say having
17 this diagnosis is stigmatizing, that it's not for
18 you to decide who I am and how I'm feeling, and I
19 have had patients say, It's incredibly affirming
20 for me to have a diagnosis that describes how I'm
21 feeling and the distress that I have.
22 And so I think it's an evolving process
23 that we will understand with lived experience being
24 our guide in terms of how best to talk about and

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1 situate this diagnosis in an individual's
2 experience.
3 Q. Sticking with Exhibit 8, I would like to
4 go to page 13, and right column, first full
5 paragraph, first sentence says, As understanding
6 around the experiences of TGD individuals has
7 evolved over time, the emphasis has shifted from
8 the reliance on a nonmaleficence towards elevating
9 patient autonomy as the guiding principle of care.
10 Did I read that correctly?
11 A. I don't see where that is, but you read
12 it well.
13 Q. I appreciate that. So page 13, right
14 column.
15 A. Okay.
16 Q. First full paragraph, first sentence.
17 A. Yes, you read that correctly.
18 Q. And do you think that patient autonomy
19 should be the guiding principle of care for
20 adolescents with gender dysphoria?
21 A. Inherent in the care of children and
22 adolescents is a complex dynamic between patient
23 autonomy and caregiver rights, and in the world of
24 child and adolescent care, this is a much muddier

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1 context than it is for adults. And so autonomy and
2 care delivery, when we are talking about children
3 and adolescents, including the autonomy of the
4 parent and the caregiver, who ultimately has the
5 decisional capacity for these interventions in
6 addition to respecting the autonomy of the
7 individual patient regardless of age.
8 Q. And so I understand that in the context
9 of treating adolescents with gender dysphoria, you
10 are taking into account the autonomy of both the
11 caregiver and the adolescent. Is that what you are
12 saying?
13 A. Correct.
14 Q. And my question though is, is patient
15 autonomy the guiding principle of that care?
16 A. I think it's more complicated than that.
17 Q. How so?
18 A. Because we are working with
19 development -- the ethical principles not just of
20 autonomy but of beneficence, nonmaleficence.
21 Justice often gets left out in discussions of
22 medical ethics, but it's an important piece. But
23 what we are doing in individual care is assessing
24 the specific intrafamilial dynamics and making

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1 recommendations based upon our comprehensive
2 psychosocial assessment.
3 Depending upon who is in the room with
4 us and what the dynamics are is going to guide how
5 we are going to approach it. We are always going
6 to keep all of our medical ethical principles in
7 mind as we are making decisions, but we want to
8 understand what a child is thinking, feeling, and
9 experiencing. And having that as a guiding
10 principle is incredibly valuable, but it's not
11 ultimately going to be the only thing that is
12 considered when deciding on a care plan.
13 Q. So you are saying that it's -- you are
14 saying that patient autonomy in the context of
15 treating adolescents with gender dysphoria is a
16 guiding principle of care but not the guiding
17 principle of care; is that right?
18 A. Yeah, this specific article is about
19 adult care primarily.
20 Q. Okay.
21 A. As an example, in a very concrete
22 clinical way, I have had patients with a diagnosis
23 of gender dysphoria for whom a medical intervention
24 would likely have been beneficial, and the

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1 adolescent is very clear about wanting to make a
2 decision and the parents say no. Respecting the
3 autonomy of a patient without taking into
4 consideration the parents' wishes as well as legal
5 responsibility for the child, is not something that
6 happens. We don't prescribe a course of treatment
7 without somebody legally capable of providing
8 consent.
9 MR. RAY: Counsel, we have been going for
10 about an hour, and lunch is here.
11 MR. RAMER: Perfect. We'll go off the record.
12 MR. RAY: Okay.
13 (WHEREUPON, a recess was had.)
14 BY MR. RAMER:
15 Q. Dr. Janssen, we left off touching on the
16 concept of informed consent a little bit. I just
17 want to ask some more questions about that.
18 As a mental health professional, is it
19 your job to ensure that the patient can provide
20 informed consent for a particular intervention?
21 A. That really depends upon the context.
22 Q. So in the context of an adolescent
23 diagnosed with gender dysphoria and you are
24 considering pubertal suppression, as the mental

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1 health professional, is it your role to ensure that
2 the patient can provide informed consent for that
3 intervention?
4 A. Ultimately, the informed consent for the
5 medical intervention is done by the medical
6 provider who is prescribing the specific indication
7 in question. That said, as a part of the mental
8 health assessment, we are also independently
9 assessing for capacity to provide informed consent,
10 which is the caregivers, but the adolescents are
11 providing assent so understanding the risks,
12 benefits, alternatives, and expected outcomes of
13 the intervention.
14 Q. And for informed assent, is what you
15 just said -- how would you characterize what
16 constitutes informed assent, the understanding of
17 those enumerated items?
18 A. That is correct.
19 Q. And as a general matter, how do you
20 determine whether a patient is able to provide
21 informed assent in this context?
22 A. In this context, part of that goes back
23 to the training that I have had as a mental health
24 provider in terms of gauging accuracy of responses,

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1 being able to ensure that the patient can restate
2 what the risks, benefits, and alternatives are,
3 that they are providing thoughtfulness, nuance, and
4 consideration that the expectations of the
5 intervention are realistic and that there's a sense
6 of capacity to challenge thoughts and beliefs.
7 Q. So returning to Exhibit 1, which is the
8 Children chapter of the SOC 8. I would like to go
9 to page S75 and the right column, and there's a
10 list of bullets there about items that can be
11 discussed with gender-diverse children and their
12 families and caregivers. Do you see that?
13 A. I do.
14 Q. And do you discuss these items with your
15 patients?
16 A. It depends upon which patients and what
17 the context is for these discussions.
18 Q. How could the context be different, that
19 you would not discuss these things?
20 A. Not all patients I'm assessing for
21 particular interventions or for gender dysphoria in
22 particular.
23 Q. So when you do have a child patient who
24 has been diagnosed with gender dysphoria and you

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1 are assessing them for pubertal suppression, would
2 you discuss these topics?
3 A. Yes, I would discuss these topics.
4 Q. And let's take one as an example. The
5 third bullet down says, The impact of medical
6 interventions on later sexual functioning and
7 infertility. Do you see that?
8 A. I do.
9 Q. And do you discuss that with your child
10 patients who have been diagnosed with gender
11 dysphoria for whom pubertal suppression may be
12 medically indicated?
13 A. Yes.
14 Q. And what do you say to them about that?
15 A. Probably we don't have time here today
16 to go into the full depth of these discussions, and
17 the efficacy of these discussions are improved when
18 they are brought into the context of the way that
19 patients can best understand.
20 But, in essence, the discussions are
21 about what is known about the potential risks of
22 fertility loss with the medications that postdate
23 use of puberty-blocking agents and a discussion
24 about fertility wishes in the future, how stable

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1 those wishes are, how realistic those thoughts are,
2 the possibility for change of those wishes over
3 time, discussions about the potential risks of the
4 intervention.
5 Q. For someone who is not a child
6 psychologist, can you explain, how do you actually
7 communicate information like that, which seems very
8 complicated, to a prepubescent child?
9 A. Well, typically we are not having these
10 discussions with prepubescent children because
11 prepubescent children are not eligible for the
12 intervention of puberty blockers, but we do speak
13 about fertility issues with some prepubertal
14 children, depending upon the context. A lot of it
15 is about eliciting understanding of the children
16 themselves, about how their bodies work, what parts
17 of their bodies do what, how they understand it,
18 how babies are made, and what their thoughts are
19 about their family.
20 When we are talking about the
21 adolescents who have entered at least Tanner
22 Stage 2 of puberty and are considering this
23 intervention, typically the discussions are more
24 detailed.

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1 Q. And just to confirm, this statement,
2 7.11, this is in regards to prepubertal children,
3 correct?
4 A. Correct. This entire chapter was about
5 prepubertal children.
6 Q. And so you would discuss the impact of
7 medical interventions on later sexual functioning
8 and fertility with prepubertal children to comply
9 with Statement 7.11, right?
10 A. As the child approaches gender, the
11 statement recommends that we, as health care
12 providers, provide information about potential
13 gender-affirming medical interventions and the
14 effects of these interventions, yes.
15 Q. I think you may have said, As the child
16 approaches gender. Did you mean, As the child
17 approaches puberty?
18 A. Yes, as the child approaches puberty.
19 Thank you.
20 Q. And still on S75, right column, and the
21 bullets, the fifth bullet down, so two bullets
22 below the one that we were previously discussing.
23 Do you discuss the current lack of
24 clinical data in certain areas related to the

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1 impacts of puberty suppression?
2 A. Yes.
3 Q. And what are the areas related to the
4 impact of puberty suppression for which we
5 currently lack clinical data?
6 A. The primary areas in which we are
7 talking about this are around fertility. That is
8 the primary area.
9 Q. Anything else?
10 A. In a typical discussion, when we are
11 talking with the parent and their family around
12 puberty suppression in particular, we talk about a
13 number of known and unknown risks, including on
14 fertility, including on cognition, cognitive
15 development.
16 (WHEREUPON, a certain document was
17 marked Janssen Deposition Exhibit
18 No. 9, for identification.)
19 BY MR. RAMER:
20 Q. Dr. Janssen, our court reporter has
21 handed you what has been marked as Exhibit 9, and
22 it says, Chapter 6, Adolescents, at the top. Do
23 you see that?
24 A. I do.

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1 Q. And does this appear to be the
2 Adolescents chapter of the SOC 8?
3 A. Yes, it does.
4 Q. I would like to go to page S61
5 and on this page, do you see that's there's
6 Statement 6.12C?
7 A. Yes.
8 Q. Do you know what this statement is
9 generally discussing?
10 A. Capacity to provide assent for care.
11 Q. And do you use this statement and the
12 supporting text to guide you in obtaining an
13 assessment of the capacity for informed consent or
14 assent?
15 A. I'll have to read the supporting text to
16 tell you that.
17 Q. So you might depart from the text that
18 is in Statement 6.12.C?
19 A. I could not tell you unless I read the
20 full supporting text, which I'm happy to do.
21 Q. I guess my question is more simpler,
22 which is just, as you sit here, you can't say, Yes,
23 I follow all the supporting text of Statement
24 6.12.C; is that correct?

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1 A. I would have to read it, what all of the
2 supporting text asks.
3 Q. Left column, same page, and the second
4 paragraph in Statement 6.12.C. I'll just read the
5 first sentence. It says, A necessary step in the
6 informed consent/assent process is for considering
7 gender-affirming medical care -- sorry. I'm going
8 to restart.
9 A necessary step in the informed
10 consent/assent process for considering
11 gender-affirming medical care is a careful
12 discussion with qualified HCPs trained to assess
13 the emotional and cognitive maturity of
14 adolescents. Did I ultimately read that correctly?
15 A. You did.
16 Q. And do you agree that you must assess
17 the emotional and cognitive maturity of adolescents
18 for purposes of informed assent for these
19 treatments?
20 A. Yes.
21 Q. How do you do that?
22 A. That is, the decades of training that is
23 required to become a health care professional, in
24 part, trains you to make these kinds of

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1 assessments.
2 Q. Have you ever had a patient whom you
3 deem lacks the cognitive maturity to provide
4 informed assent for one of these interventions?
5 A. Yes.
6 Q. Why?
7 A. There have been a number of reasons,
8 including patients with developmental and
9 intellectual disabilities who lack the capacity to
10 grasp potential effectuating outcomes of these
11 medications or patients who had a treatable mental
12 health condition that temporarily impaired capacity
13 to consent.
14 Q. If a patient tells you, I'm going to
15 kill myself if I don't receive puberty blockers, is
16 that patient capable of providing informed assent?
17 A. It depends on the context.
18 Q. What would you explore to determine
19 that?
20 A. We want to understand in an as
21 evidence-based way as possible what the
22 individual's actual suicide risk is, so you would
23 want to get a sense of safety and about whether
24 there were any processes that impaired this

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1 individual's capacity to provide consent and
2 understanding of the specific interventions. Was
3 it a statement that is -- is made as an exaggerated
4 attempt. Is it communicating suicide attempt, or
5 is it communicating distress? These are all
6 important things that we would evaluate as a part
7 of our assessment.
8 Q. And just as a general matter of
9 assessing suicide risk, how do you do that?
10 A. Well, there are a number of things that
11 you can do to assess suicide risk. My preference,
12 although everybody has a different process for
13 doing assessment of suicide risk, is that there are
14 evidence based tools that can screen for suicide
15 risk and can assess for suicide risk and put
16 patients in a stratification of low, medium, or
17 high risk for following through.
18 This is at a clinical interview most
19 often that is done by qualified professionals, and
20 they can be mental health professionals but also
21 may be other medical professionals of other types.
22 These evaluations include co-occurring mental
23 health disorders, assessment of impulsivity,
24 assessment of access to means, assessment of the

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1 type of statements that are made, assessment of the
2 statements over time, assessment of risk factors,
3 resilience factors, protective factors, all of
4 which are predictive in one way or another.
5 Q. And can you explain what a resilience
6 factor and a protective factor is?
7 A. Yeah. So if you have a family that
8 loves and supports you, that is a protective factor
9 for suicide. If you have a family that does not,
10 that increases suicide risk.
11 Q. And what about a resilience factor?
12 A. Resilience factor that you have belief
13 in yourself, that you have good qualities, that you
14 have capacity to access care and help when
15 necessary.
16 Q. Before you recommend cross-sex hormones
17 as a treatment for gender dysphoria in adolescent
18 patients, do you confirm that the patient has
19 experienced several years of persistent gender
20 diversity or incongruence?
21 A. The diagnosis of gender dysphoria
22 requires six months in order to make that
23 diagnosis. In practice, the vast majority of the
24 adolescent patients that I have worked with have

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1 experienced many, many years of persistent
2 symptoms. So it's kind of asking a question that
3 does not really have a clear clinical correlate in
4 the real world.
5 Q. I guess not so much as the diagnosis, my
6 question is about the actual intervention of
7 cross-sex hormones itself, and maybe the answer is
8 the same.
9 But what I was asking is, before you
10 recommend that intervention, assuming they have
11 already been diagnosed with gender dysphoria, do
12 you confirm that they have experienced several
13 years of persistent gender diversity or
14 incongruence?
15 A. It's a bit of a muddy statement, and I
16 recognize where it comes from, but operationalizing
17 that is challenging.
18 In the assessment process prior to
19 initiating gender-affirming hormones for an
20 adolescent, we are evaluating for a diagnosis of
21 gender dysphoria, but we are also gathering a
22 gender history almost universally. The patients
23 that I'm seeing that are interested in pursuing and
24 are appropriate for pursuing medical interventions

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1 have a history of gender diversity that predates
2 the six-month required time period for the
3 diagnosis of gender dysphoria.
4 Q. And so your point is, it just does not
5 come up in practice, is what you are saying?
6 A. Essentially, yes.
7 Q. Do you think that it should be required
8 as a matter of theory?
9 A. I do not because several years is
10 completely an operational criteria. I don't know
11 what that means.
12 Q. You don't know what "several years"
13 means?
14 A. It's nonspecific in a way that is not
15 helpful and, in my opinion, not particularly tied
16 to published literature.
17 Q. So sticking with Exhibit 9 and the same
18 page that we are on, S61, right column, about a
19 third of the way down there is a sentence that
20 begins with, Gender-diverse youth. Do you see
21 that?
22 A. Yes.
23 Q. Gender-diverse youth should fully
24 understand the reversible, partially reversible,

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1 and irreversible aspects of a treatment as well as
2 the limits of what is known about certain
3 treatments, e.g., the impact of pubertal
4 suppression on brain development, and then there's
5 a citation. Did I read that correctly?
6 A. You read that correctly.
7 Q. And do you ensure that your patients
8 fully understand these enumerated items?
9 A. To the best of our ability, yes.
10 Q. Who is the "our," in "the best of our
11 ability" there?
12 A. Myself and the folks -- my colleagues.
13 Q. When you are assessing the ability of an
14 adolescent to provide informed assent for puberty
15 blockers, do you also discuss the risks and
16 benefits associated with cross-sex hormones?
17 A. It depends upon the context. Sometimes
18 yes, sometimes no.
19 Q. How do you determine when you do and
20 when you don't?
21 A. It's clinically dependent, based upon
22 the presenting symptoms and the family dynamics at
23 the time. Because we know that many individuals
24 who pursued puberty suppression go on to pursue

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1 gender-affirming hormones, I will typically include
2 almost universally discussions around fertility
3 treatment and potential impact on fertility of
4 gender-affirming hormones, not just the puberty
5 suppressions prior to initiation of that care.
6 Q. And when wouldn't you do that?
7 A. Specific to fertility, I do that for
8 everybody, but there are patients for whom there is
9 no clear indication that they are going to start
10 gender-affirming hormones and that discussion may
11 be a little bit premature. Functionally, most of
12 the time people who are considering puberty
13 suppression have information and are curious about
14 potential options post puberty suppression, so,
15 again, functionally and actually the clinical work
16 that I do, it is most common that we are having
17 these discussions all at once.
18 Q. So are there times when an adolescent is
19 about to begin pubertal suppression where you think
20 there is already a clear indication that the
21 adolescent will proceed to cross-sex hormones?
22 A. There are hypotheses about that, yes.
23 Q. What do you mean by that?
24 A. Meaning, if we look at the Steensma

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1 article in terms of factors that protect
2 persistence, if we are working with kids prior to
3 puberty and they check every one of those criteria,
4 I'm not going to make an assumption that that kid
5 is going to follow in any one specific trajectory.
6 I'm working with the child individually, but
7 certainly they are likelier to be in a category
8 that -- a patient that persists through
9 adolescence, and the patients who persist through
10 adolescence are likelier to persist into adulthood.
11 So we have our history and clinical
12 experience that helps guide us in terms of making
13 predictions about who is likely to want to pursue
14 medication, but most of the time it's the patients
15 themselves that say, I want to think about this and
16 are bringing that to the floor.
17 Q. When you are assessing -- when you are
18 assessing the capacity of an adolescent to provide
19 informed assent for puberty blockers, do you also
20 discuss the risks and benefits associated with
21 surgery?
22 A. Not typically.
23 Q. And do you ever?
24 A. When assessing for surgery?

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1 Q. No. I'm sorry. You said not typically
2 when you are assessing for puberty blockers, and I
3 guess the "typically" to me left open the
4 possibility that sometimes you do. When assessing
5 for puberty blockers, you do discuss risks and
6 benefits of surgery; is that correct?
7 A. Yes.
8 Q. In what situation would you do that?
9 A. As an example, for folks assigned male
10 at birth, you go on puberty blockers quite early.
11 Some of the surgical techniques for vaginoplasty
12 may be impacted by the lack of growth of penile
13 tissue that is often used in that process.
14 Recognizing that, for some individuals
15 who are blocked early in puberty, they may require
16 a different process or procedure if they opt to go
17 through that surgery. Those are some times in
18 which we may consider a discussion, and that
19 discussion is most important to have with the
20 patient's parents at that point in terms of
21 potential impact on the care plan over time.
22 Q. From your clinical experience, do you
23 think that most adolescents and parents view
24 pubertal suppression as the first in multiple steps

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1 in transitioning?
2 A. It really is context dependent. Some
3 yes, some no.
4 Q. And going back to Exhibit 9 and the same
5 page, S61, and the same sentence we read about a
6 third of the way down, where it's discussing the
7 impact of pubertal suppression on brain
8 development. Do you see that?
9 A. Yes, I do.
10 Q. What do you tell patients about the
11 impact of pubertal suppression on brain
12 development?
13 A. Again, we have less time here than the
14 time that I would spend with my patients and their
15 parents in discussing all of the comprehensive
16 risks and benefits. Typically, what I point to is
17 that we have some limited data that is mostly in
18 sheep about potential impacts of puberty
19 suppression agents on some aspects of cognitive
20 development and that there are going to be aspects
21 of cognitive development that we are not going to
22 know whether they are impacted by this intervention
23 or not.
24 Q. And what do those sheep studies say?

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1 A. I would have to go through the specific
2 sheep studies, but, generally, a potential impact
3 on executive functioning is -- from what I recall,
4 has been demonstrated.
5 Q. And how do you explain that to an
6 adolescent?
7 A. To an adolescent, it depends upon the
8 adolescent. There's not a blanket. It's part
9 of -- the reason that this is an individualized
10 process is because you are going to need to use the
11 level of description that is based and aligned with
12 how the adolescent can retain and understand
13 information.
14 Q. As a clinician, does it concern you that
15 we lack evidence regarding the effect of pubertal
16 suppression on an individual's brain development?
17 A. Can you define what you mean by
18 "concern"? I wish we had more information.
19 Q. You don't think that the lack of data on
20 the effect of pubertal suppression on an
21 individual's brain development is a reason to not
22 recommend pubertal suppression for adolescents?
23 A. I got lost in the semantics there.
24 Q. The triple negatives?

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1 A. Yes.
2 Q. I guess, you don't understand what it
3 means to be concerned about a lack of evidence
4 before recommending an intervention?
5 A. It's just not aligned with how practice
6 works. When we are considering puberty-blocking
7 medications, the option is not nothing happens on
8 the other side of not doing it. The option is
9 puberty continues and you develop irreversible
10 changes in your body that are unaligned with one's
11 identity that cause tremendous amounts of distress,
12 and we have evidence that that kind of chronic
13 stress and exposure to stress also impacts
14 cognitive development in some known and some
15 unknown ways.
16 So we have a decision about puberty
17 blockers that have some study versus impact of
18 stress and distress that have some study. So it's
19 a question of what is known and unknown about this
20 particular intervention on cognitive development
21 versus what is known and unknown about this
22 intervention of cognitive development.
23 And so it's a nuanced process, so I have
24 concern in terms of wishing that we had more

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1 complete information about impacts of
2 puberty-blocking medications on cognitive
3 development, and I wish we had more information and
4 I'm concerned about the information that we have
5 about impact of toxic stress on inflammation in the
6 brain and how that impacts cognitive development.
7 Q. And given these two, you know,
8 considerations that you are weighing here, you
9 ultimately conclude that the better decision is to
10 pursue pubertal suppression, correct?
11 A. I don't conclude anything. My job is to
12 provide the families with the information required
13 to make a decision. I'm happy to provide a
14 recommendation, but, ultimately, the decision is
15 theirs. And based upon their understanding the
16 risks, benefits, and alternatives, they are making
17 a choice about how best to proceed.
18 Q. But with respect to the competing
19 considerations that we were discussing, you are
20 willing to make a recommendation for pubertal
21 suppression, correct?
22 A. Correct. In the studies that we have of
23 individuals with gender dysphoria who receive
24 puberty blockers, their self-reported outcomes are

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1 better than those who wished to have blockers and
2 did not have access to them.
3 Q. Do you think it would be unreasonable
4 for somebody else to look at the same evidence and
5 say, I don't think that I'm -- I would not
6 recommend pubertal suppression, given these
7 competing considerations?
8 A. I'm not sure what is meant by
9 "unreasonable." Certainly, there are people who
10 come to different conclusions reading the same
11 literature that I have read. I don't think that it
12 makes sense. I would not see that as a reasonable
13 conclusion from the literature that exists in the
14 field.
15 Q. Do you agree that it's unknown -- let me
16 start again, since we don't like the word "known"
17 and "unknown."
18 Do you agree that we do not have good
19 evidence about how long one can safely medically
20 suppress puberty during a time when an adolescent
21 is physiologically supposed to be going through
22 puberty?
23 A. We have reams and reams of data of
24 patients who have been suppressed for periods of

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1 time. Is there a study that has looked at the
2 upper limit of how many years would be safe? No,
3 there has not been that kind of study.
4 But that is not the process of clinical
5 care delivery or within the recommended standards
6 of care. Most -- in practice, patients are not on
7 these medications indefinitely, and there are
8 recommendations made by my medical colleagues about
9 the amount of time that patients should be in
10 puberty suppression without some additional
11 hormone. But that is not my field and not my area
12 of expertise that I would testify to.
13 Q. Because you are not an endocrinologist?
14 A. I'm not an endocrinologist.
15 Q. Do you agree that puberty blockers could
16 disrupt an adolescent's gender exploration?
17 A. No.
18 Q. Do you agree that it's currently unknown
19 how puberty blockers affect the long-term metabolic
20 process?
21 A. Metabolic process is not specific.
22 There's many, many, many things that fall under
23 metabolic processes. Some are known, some are less
24 known.

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1 Q. Do you agree that there's a lack of data
2 examining the long-term outcomes of using puberty
3 blockers with adolescents as a treatment for gender
4 dysphoria?
5 A. I would not agree. I think we have
6 longitudinal data, particularly from the Dutch
7 cohort, of impacts of puberty suppression over the
8 long-term.
9 Q. Is there anything outside of the data
10 from the Dutch clinic that would provide evidence
11 of long-term outcomes?
12 A. The use of puberty suppression agents
13 was initially used in the treatment of central
14 precocious puberty, so there's data from those
15 patients in the long-term.
16 Q. Apart from the data from the Dutch
17 clinic, is there any other data providing evidence
18 of long-term outcomes for using puberty suppression
19 as a treatment for gender dysphoria?
20 A. There is increasing data that is being
21 published on that question every year.
22 Q. Are you aware of any study examining the
23 potential negative psychosocial implications of not
24 initiating puberty with one's peers?

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1 A. I'm going to have to restate that in my
2 head a few times to make sure I'm getting this
3 right.
4 Q. I can explain it in plain terms, which
5 is you have an adolescent who is diagnosed with
6 gender dysphoria, and there's discussion of
7 using -- pursuing pubertal suppression.
8 And the question is, does the -- has any
9 study examined whether there's any potential
10 negative psychosocial implication for this
11 individual to not be progressing through puberty at
12 the same time the individual's peers are
13 progressing through puberty?
14 MR. RAY: Object to the form.
15 BY THE WITNESS:
16 A. Got it. So the way that I would think
17 about designing a study to get at that question
18 would be to look at outcomes of transgender adults
19 who did and did not have access to puberty
20 suppression agents and compare outcomes between
21 those two groups of people, those who wanted it and
22 did not have access versus those that wanted it and
23 did have access.
24 And those studies have been done, and

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1 what it has demonstrated is that those that wanted
2 it and had access to it, did better than those that
3 did not.
4 BY MR. RAMER:
5 Q. What studies are you referring to, like
6 Dr. Turban's?
7 A. Correct.
8 Q. Do you know where the data for that came
9 from?
10 A. That came from a national representative
11 sample of trans-identified adults in the United
12 States.
13 Q. What do you tell your patients about the
14 expected benefits of cross-sex hormones as a
15 treatment for gender dysphoria?
16 A. It's mostly a discussion, and as with
17 most things in working with adolescents, I like to
18 elicit their understanding of the potential
19 benefits as a first step and then refine the
20 discussion from there.
21 Most adolescents who are pursuing this
22 care have done a fair amount of research and often
23 are very clear about the potential benefits, but
24 the primary benefits of gender-affirming hormones

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1 is development of secondary sex characteristics
2 that are aligned with one's gender identity.
3 Q. And do you tell them that is going to
4 improve their mental health?
5 A. This is a point of frustration with me
6 in some of the studies because mental health is
7 used almost like a shibboleth of the entirety of
8 health and wellness as opposed to defining what is
9 specifically meant by which components of mental
10 health. Gender dysphoria treatments treat gender
11 dysphoria.
12 We see occasional benefits on other
13 mental health symptoms, particularly mental health
14 symptoms that derive from the distress related to
15 the gender dysphoria, but many people have
16 independent mental health symptoms. So when we
17 talk about mental health, we want to be specific
18 about which aspects of mental health we anticipate
19 will improve and which will not.
20 It is a part of my practice in the
21 informed consent process, in speaking with
22 adolescents and their parents, that if there are
23 other medical or mental health conditions that are
24 present, that my anticipation is not that the

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1 hormones will treat their underlying anxiety or
2 depression or suicidality or OCD or autism or ADHD,
3 that we have to have a wholistic look at a child
4 and understand what is the treatment plan for every
5 diagnosis that they have.
6 Q. And can someone with psychosis provide
7 informed consent or informed assent for puberty
8 blockers as a treatment for gender dysphoria?
9 A. Rates of psychosis among prepubertal and
10 Tanner Stage 2 youth are incredibly rare.
11 Significantly less than 0.1 percent of the
12 population experience psychosis at that age. So
13 it's a bit of a theoretical question that does not
14 have a genuine correlate.
15 That said, there's many different
16 reasons. Psychosis is a nonspecific symptom that
17 can be caused by many different etiologies. The
18 majority of the etiologies of psychosis,
19 particularly in childhood, are time limited, often
20 substance induced, trauma related.
21 And even when there's a chronic
22 psychotic disorder, such as something like
23 schizophrenia or schizoaffective disorder or
24 bipolar disorder with psychotic features, the

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1 psychosis is typically limited to an episode of
2 illness and resolves completely when the illness is
3 complete.
4 When we are doing an assessment of an
5 individual with gender dysphoria who has severe
6 co-occurring mental health issues, part of the
7 assessment is recognizing how does the patient's
8 gender dysphoria and how have the symptoms of
9 gender dysphoria changed or not changed between
10 illness states and over time. And the idea that a
11 patient who has once been psychotic cannot consent
12 is not accurate.
13 In fact, there's data from a number of
14 studies that have looked at our most severely ill
15 patient populations, including those that are in
16 state psychiatric institutions with chronic
17 psychotic disorders and even in a majority of those
18 cases, our most ill patients, most of them retain
19 capacity to consent for many of the procedures and
20 medications that they are prescribed.
21 Q. So you would not treat psychosis as some
22 sort of bright line rule that would foreclose the
23 patient from receiving cross-sex hormones as a
24 treatment for gender dysphoria, correct?

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1 A. In practice, psychosis in an adolescent
2 patient is something that we have to prioritize in
3 the treatment plan. There have been times in which
4 the presence of psychosis has been a bright line
5 and has disallowed patients from being able to
6 safely access gender-affirming care, and there are
7 times where the psychosis is chronic, the patient
8 retains capacity to consent, the gender dysphoria
9 is present across both euthymic mood states and
10 bipolar mood states, psychotic processes and
11 nonpsychotic processes, and in those cases it's not
12 an absolute contraindication to proceed with
13 gender-affirming care as medical --
14 gender-affirming medical care.
15 Q. And what data is there regarding the
16 potential impact of hormone treatment on psychotic
17 symptoms?
18 A. There have been some reviews that have
19 looked at impact. We have not seen -- there's not
20 a ton that is out there. Most of it is in the
21 context of -- as an example, in the Klinefelter's
22 population, people who have low testosterone
23 syndromes, when given testosterone, actually
24 improve in psychotic symptoms, but there's not a

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1 ton of data that is out there.
2 (WHEREUPON, a certain document was
3 marked Janssen Deposition Exhibit
4 No. 10, for identification.)
5 BY MR. RAMER:
6 Q. Dr. Janssen, the court reporter has
7 handed you what has been marked as Janssen
8 Exhibit 10, and it says, Chapter 8, Gender
9 Dysphoria and Autism Spectrum Disorders at the top;
10 is that right?
11 A. That's correct.
12 Q. Is this a chapter from a book that you
13 wrote?
14 A. Yes, it is.
15 Q. And you wrote this chapter, correct?
16 A. I did, yeah.
17 Q. In this chapter, you discuss a case
18 study of a patient who you labelled JM; is that
19 right?
20 A. That's correct.
21 Q. And was this a real patient?
22 A. It is a conglomeration of a few real
23 patients.
24 Q. What do you mean by that?

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1 A. There are elements from one real
2 patient, elements from another real patient in
3 this.
4 Q. How does that work?
5 A. It's pretty typical for these kinds of
6 case discussions in terms of exculpating the point.
7 The majority of things are a real patient, yes.
8 Q. And if we assume -- I guess for this
9 case study or case discussion to be relevant, we
10 could treat this as a hypothetical patient,
11 correct?
12 A. Sure. I would be happy to treat this
13 patient as a hypothetical patient.
14 Q. And based on the first sentence here,
15 the first time you saw this hypothetical patient
16 was when the patient was 13 years old; is that
17 right?
18 A. Correct.
19 Q. And the patient had been diagnosed with
20 intellectual disability, correct?
21 A. Yes.
22 Q. And specifically had been determined to
23 have an IQ of 55; is that right?
24 A. That's correct.

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1 Q. And the patient was also diagnosed with
2 autism, correct?
3 A. Yes.
4 Q. And had been diagnosed with bipolar
5 disorder, correct?
6 A. Correct.
7 Q. And the patient was also in foster care
8 for a period of time, correct?
9 A. Yes.
10 Q. And on page 124, you say, The patient
11 was living in a residential treatment facility for
12 the past two years to manage his increasingly
13 unsafe behaviors at home, and that is on page 124,
14 second paragraph, third sentence?
15 A. Uh-huh.
16 Q. And what does that mean?
17 A. Typically, that means aggression and/or
18 self-harm.
19 Q. And what is a residential treatment
20 facility?
21 A. A residential treatment facility is a
22 facility that provides psychiatric care in a
23 residential setting.
24

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1 (WHEREUPON, a certain document was
2 marked Janssen Deposition Exhibit
3 No. 11, for identification.)
4 BY MR. RAMER:
5 Q. And the court reporter has handed you
6 what has been marked as Janssen Exhibit 11, and
7 that is entitled The Complexities of Treatment
8 Planning For Transgender Youth with Co-Occurring
9 Severe Mental Illness: A Literature Review and
10 Case Study, correct?
11 A. Correct.
12 Q. And you helped author this, correct?
13 A. That is correct.
14 Q. And in here this must be a function of
15 bringing together multiple patients, but the
16 patient you discuss in this article is labelled JB;
17 is that right?
18 A. Uh-huh.
19 Q. But JB is different from JM; is that
20 right?
21 A. Yeah. Many of the elements are the
22 same, but, yes, it's a different case study.
23 Q. And in Exhibit 11, going to page 2004,
24 which is the second page of the article.

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1 A. Uh-huh.
2 Q. Left column, first paragraph, about
3 halfway through, it says, He had periods of
4 aggression and fixation on enacting violence
5 towards his mother. He was described as having a
6 degree of paranoia about his mother and -- excuse
7 me -- that was thought to be psychotic; is that
8 right?
9 A. That's correct.
10 Q. And same page, second paragraph, just
11 under halfway through, you note that the patient
12 had frequent pronoun reversals and used male or
13 female pronouns; is that right?
14 A. Correct.
15 Q. I would like to go back to Exhibit 10,
16 which is Chapter 8 of your book.
17 A. Uh-huh.
18 Q. I would like to go to page 125, and
19 first full paragraph, second sentence, you say, The
20 patient "could not understand why she could not
21 wear a ball gown in every context." Is that right?
22 A. Uh-huh.
23 Q. But in your view, you think this patient
24 could fully understand the effects of pubertal

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1 suppression?
2 A. If I may, I can kind of talk about --
3 even though these are composite cases, let me talk
4 about what typically happens with this degree of
5 complexity, which is that the assessment of
6 interventions for puberty suppression for these
7 kinds of patients typically occurs over the period
8 of months to years, that get condensed in a case
9 study to look like it was no time at all.
10 But the development and the elucidation
11 of the capacity to understand the potential
12 interventions took place over a much longer period
13 of time.
14 Q. But, ultimately, you reached the
15 conclusion that this patient could fully understand
16 the effects of pubertal suppression, correct?
17 A. Yes.
18 Q. And you also reached the conclusion that
19 the patient could fully understand the effects of
20 cross-sex hormones?
21 A. Yes, eventually.
22 Q. And did you eventually reach the
23 conclusion that this patient could fully understand
24 the unknowns regarding the effects of pubertal

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1 suppression on brain development?
2 A. To the degree that this individual could
3 understand that, yes. The parent and the
4 caregiver, who was providing consent, recognized
5 and understood those risks as the person providing
6 the informed consent to this intervention.
7 Q. But as part of informed assent, wouldn't
8 the patient also need to understand the unknowns
9 regarding the effect of pubertal suppression on
10 brain development?
11 A. To their developmentally appropriate
12 level, the patient understood that there would be
13 potential impact, but that was about -- that was
14 clear, from my recollection.
15 Q. Sorry. At the end there you trailed.
16 A. From my recollection, that was clear.
17 Q. Would there ever be a situation where an
18 adolescent patient with gender dysphoria can
19 provide informed consent for hormones but you still
20 would not recommend them?
21 A. Yes.
22 Q. In what kind of situation?
23 A. There's a number of different kinds of
24 situations. If an individual does not have a

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1 diagnosis of gender dysphoria, that would be one
2 set. If there are co-occurring diagnoses that
3 interfere with the capacity to make a diagnosis of
4 gender dysphoria, that would be another reason. If
5 there are medical contraindications to the
6 intervention, that could be a different reason.
7 Q. And has that ever happened in your
8 practice?
9 A. Yes, it has.
10 Q. Would there ever be a situation where an
11 adolescent patient with gender dysphoria cannot
12 provide informed assent for hormones but you would
13 still recommend them?
14 A. No, not that I can think of.
15 Q. Is the same true for puberty blockers?
16 A. Capacity to understand the risks,
17 benefits, and alternatives is a required element of
18 the assessment.
19 Q. So if the patient is unable to provide
20 informed assent, does that mean that the
21 interventions are not medically necessary?
22 A. It means that they are not indicated.
23 It does not make a statement about necessity.
24 There are many things that are necessary that,

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1 nevertheless, people do not have access to.
2 Q. Like what else?
3 A. Well, I mean, my thought goes to a
4 patient of mine that I had that did not have gender
5 dysphoria that had leukemia and had a requirement,
6 a necessity to have a chemotherapeutic drug that he
7 did not respond well to and was allergic to. It
8 was a necessary intervention that, nevertheless, he
9 did not have access to.
10 Q. Can you provide any examples where the
11 impediment to access is a lack of capacity to
12 provide informed assent as opposed to an allergy?
13 A. Sure. I mean, patients who have
14 substance abuse disorders who are chronically
15 impaired are not going to be able to provide
16 consent in most situations while they are impaired
17 on substances.
18 Q. But does that mean that they are not
19 able to access necessary medical care because they
20 are impaired?
21 A. Yes.
22 Q. So you wrote this chapter back in 2018,
23 correct?
24 A. Which chapter?

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1 Q. Sorry. Exhibit 10, Chapter 8.
2 A. I mean, it was published in 2018. That
3 was a long labor, so I could have written it any
4 time between 2014 and 2018.
5 Q. And do you know where this patient is
6 today?
7 A. I moved from New York, so he's no
8 longer -- this kid is no longer under my care, or
9 the amalgamation of kids that formed these case
10 studies are no longer under my care.
11 Q. So sticking with Exhibit 10, going to
12 page 126.
13 A. Uh-huh.
14 Q. The carryover paragraph, it's a little
15 over halfway down. It says, The reality is that
16 there is a different developmental process for
17 gender identity than for a child's normal
18 imaginative process of trying on different personas
19 and interests. Did I read that correctly?
20 A. You did.
21 Q. And could you explain what you are
22 saying there?
23 A. Yeah, that there's a difference between
24 exploring identity and playing with expectations of

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1 gender than that core sense of gender identity,
2 that not all children who wear dresses are
3 transgender. Some just like to wear dresses.
4 Q. And how did you reach that conclusion
5 that somebody who likes to wear a dress is not
6 transgender?
7 A. With time.
8 Q. I'm sorry?
9 A. With time.
10 Q. What do you mean by that?
11 A. Meaning in prepubertal youth, you
12 observe but you are not intervening medically. And
13 you continue to observe over time, and particularly
14 when kids hit Tanner Stage 2, whether or not
15 there's distress or not.
16 And there's also been kids that I have
17 seen that parents have asked questions. Should I
18 be concerned that my boy is wearing a dress? And
19 the kid themselves has no questions about gender.
20 Like, no, I'm a boy, I just like wearing dresses,
21 it's fun to play. That is a different process,
22 right, and those kids are not assessed to have a
23 diagnosis of gender dysphoria. They are not
24 assumed to be transgender. But, again, with those

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1 kids, I'm not assuming what your lifetime course is
2 going to be, but, certainly, there's no indication
3 to intervene with a diagnosis that does not exist.
4 Q. So is it fair to say in this sentence,
5 you are also saying that there's a different
6 developmental process for gender identity than for
7 gender nonconforming interests?
8 A. That is fair.
9 Q. And how do you know that there's a
10 different developmental process?
11 A. That's been studied over decades and
12 decades and decades.
13 Q. Maybe it's lost on me because I don't
14 understand the term "developmental process," but
15 what does that mean here?
16 A. So gender role based behaviors present
17 early on, and there's a number of factors that
18 influence gender role based behavior, so that whole
19 category of diagnostic criteria with the DSM that
20 allude towards rough and tumble play, playmate
21 preference, et cetera, those gender role based
22 behaviors emerge very early in childhood, prior to
23 most kids having a sense of differentness around
24 their identity.

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1 There are these differential
2 developmental trajectories around gender, around
3 gender identity, around gender expression, around
4 playmate preference that all are on different
5 timelines. That is the difference, and that is
6 partially at least what I believe I was getting to.
7 Sometime between 2014 -- ten and eight years ago.
8 Q. I'm at a good stopping point, if you
9 want to take a break.
10 MR. RAY: Sure.
11 MR. RAMER: Go off the record.
12 (WHEREUPON, a recess was had and a
13 certain document was marked Janssen
14 Deposition Exhibit No. 12, for
15 identification.)
16 BY MR. RAMER:
17 Q. Dr. Janssen, you have been handed what
18 has been marked as Janssen Exhibit 12 and at the
19 top, it says, Chapter 3, Transgender Adolescents
20 and Gender-Affirming Interventions: Pubertal
21 Suppression, Hormones, Surgery, and Other
22 Pharmacological Interventions, correct?
23 A. Yes.
24 Q. And you helped write this, correct?

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1 A. I did.
2 Q. And I would like to go to page 56, and
3 middle of the page, there's a new section entitled
4 Reversible Androgen Blocking and Menstrual
5 Suppression. Do you see that?
6 A. I see that, yes.
7 Q. And am I correct in reading this part to
8 just generally be discussing the use of
9 interventions other than GnRHa to suppress the
10 effects of hormones released during puberty?
11 A. To at least mitigate the impacts of the
12 distress caused by it, yes.
13 Q. And in the first paragraph of the
14 section, the last sentence of that paragraph, I'll
15 just read it first. It says, They may be
16 beneficial to use with adolescents who cannot
17 access GnRHa for either lack of insurance coverage
18 or parental consent reasons. Did I read that
19 correctly?
20 A. Correct.
21 Q. What are you referring to when you say
22 "parental consent reasons"?
23 A. Simply if you have a parent who does not
24 consent to use of GnRH analogues.

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1 Q. So why would you recommend these
2 alternatives in a circumstance where a parent
3 refuses to consent to the use of GnRH analogues?
4 A. To alleviate distress and improve
5 functioning.
6 Q. Is the point that you do not need
7 parental consent to use these other interventions?
8 A. No. You need parental consent for those
9 other interventions for this purpose. Effectively,
10 for this diagnosis, you still require parental
11 consent, but there are differential treatment plans
12 that parents can or can't consent to. And it's not
13 uncommon for a parent who is not providing consent
14 to a GnRH agonist to provide consent for an oral
15 contraceptive pill that suppresses or reduces the
16 impact of menstruation.
17 Q. Why would that -- in your experience,
18 where would that be the case?
19 A. Sometimes it's just a matter of
20 familiarity. Most adults are familiar with the
21 concept of oral contraceptive pills.
22 Q. And so -- I'm sorry. Go ahead.
23 A. Go ahead.
24 Q. So in this section, you are saying --

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1 you are saying use these alternatives -- I guess
2 I'm just trying to understand, parental consent
3 reasons, and the answer is that by parental consent
4 reasons here, you are referring to parents who
5 would not consent to GnRHa analogues but would
6 consent to these other pharmacological
7 interventions; is that correct?
8 A. Yes, that is correct.
9 Q. And then the next paragraph, final
10 sentence, it says, Their effectiveness and safety
11 have not been studied in adolescents with gender
12 dysphoria. However, anecdotally they have been
13 used clinically to help adolescents feel their
14 gender dysphoria is being addressed medically. Did
15 I read that correctly?
16 A. You read that correctly.
17 Q. Are you describing a placebo effect
18 here?
19 A. I am not.
20 Q. And are you recommending the use of
21 these interventions even though you admit their
22 effectiveness and safety have not been studied?
23 A. Recommendations of specific treatment
24 plans are only made to specific patients, so they

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1 are context dependent. The use of oral
2 contraceptive pills for the sake of menstrual
3 suppression, there exists wide data on the evidence
4 and safety of that as an intervention.
5 Q. Then what do you mean when you say,
6 Their effectiveness and safety have not been
7 studied in adolescents with gender dysphoria?
8 A. At the time of the writing of this
9 chapter, which was probably closer to 2014, there
10 was not a ton of data on the use of menstrual
11 suppression for gender dysphoria specifically, but
12 there had been decades and decades of data on the
13 use of menstrual suppression using oral
14 contraceptive pills in natal females.
15 Q. And given -- or I should say, despite
16 the lack of study of the effectiveness and safety
17 of these interventions in adolescents with gender
18 dysphoria, you were comfortable writing in this
19 textbook chapter that these pharmacological
20 interventions can be used for treating gender
21 dysphoria, correct?
22 A. The question is what is being treated
23 and what the goals of treatment are. In these
24 particular cases, when you have a patient with

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1 gender dysphoria who has severe distress from
2 menstruation, what we have is robust literature
3 supporting the use of oral contraceptive pills to
4 reduce the intensity, frequency, and duration of
5 menstruation.
6 The evidence for the robustness of that
7 effect is quite clear. The evidence of safety and
8 efficacy of menstruation and suppression is quite
9 clear. Whether it had been specifically studied in
10 this population, it still allows as a possible
11 option. That said, I'm a psychologist. I'm not an
12 endocrinologist or adolescent medicine physician,
13 so I'm not prescribing these medications.
14 Q. But you would be in the position of
15 recommending them as a treatment for gender
16 dysphoria, correct?
17 A. I would be in the position of
18 recommending that they speak with a medical
19 provider about their options.
20 Q. But you would not further list what
21 options they should be speaking with their medical
22 provider about?
23 A. I would be happy to provide what
24 potential options are out there to discuss.

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1 Q. And would you include these
2 pharmacological interventions on the list of
3 possible options to discuss?
4 A. On menstrual suppression, yes.
5 Spironolactone is not something that I typically
6 recommend.
7 Q. Did you ever typically recommend that?
8 A. It's not a typical recommendation in the
9 context in which I practice.
10 Q. Why is that?
11 A. In part, because most individuals who
12 are seeking out care are doing so with the consent
13 of their parents, and often if are considering
14 puberty-blocking agents or have distress from the
15 impacts of testosterone, are typically opting to
16 proceed with gender -- or puberty suppression as
17 opposed to use of an adjunctive agent.
18 Q. Do you agree that an older adolescent is
19 likely to have more developed executive functioning
20 skills to weigh the pros and cons of an
21 intervention, compared to a younger adolescent?
22 A. There's not necessarily a whole robust
23 literature that says executive functioning is the
24 primary component of capacity to consent.

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1 Q. I was just -- I was asking whether an
2 older adolescent is likely to have more developed
3 executive functioning skills to weigh the pros and
4 cons of an intervention compared to a younger
5 adolescent?
6 A. I'm separating the two. Do older
7 adolescents have more executive functioning skills?
8 Sometimes, but not always. It depends upon the
9 individual adolescent. There certainly have been
10 12-year-old adolescents who have highly -- highly
11 developed executive functioning skills, so that is
12 part one of your question.
13 Part two of your question implied that
14 the presence or absence of executive functioning is
15 what determines capacity to consent. That is not
16 true.
17 Q. If you have a patient who is an
18 adolescent, who is 16 years old, has been diagnosed
19 with gender dysphoria and desires a phalloplasty,
20 what would you do?
21 A. I mean, this is a very complicated
22 question in terms of what the actual process looks
23 like, but a 16-year-old is not eligible for a
24 phalloplasty. So we would talk about what their

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1 hopes are, what their embodiment goals are, what
2 the distress is, what they aim to achieve with the
3 phalloplasty, what they understand about a
4 phalloplasty, and what it's there and what it's
5 for. What kinds of information that they are
6 gathering about a phalloplasty, so that if in five,
7 ten years, when it's available to them, that they
8 have information that is accurate and sourced from
9 appropriate areas.
10 Q. If the individual is suffering distress
11 due to not being able to access a procedure for a
12 phalloplasty, how would you treat that distress?
13 A. Empathy goes a long way. So does
14 listening and a recognition that when the time is
15 right, if the patient meets qualifications for that
16 particular intervention, that they'll be able to
17 access that particular intervention.
18 Q. And earlier we were discussing
19 something, it was real life, and I think the third
20 word was a T. But, basically, living in role, for
21 lack of a better term. What was the phrase that
22 you used earlier today?
23 A. Real life test.
24 Q. Do you require a prolonged period of

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1 living in role or a real life test before
2 recommending a medical intervention as a treatment
3 for gender dysphoria?
4 A. No, I do not.
5 Q. And why not?
6 A. It's not practical for all people, and
7 even the terminology that was used in terms of a
8 real life test implies that the onus is on the
9 transgender individual to prove that their identity
10 is valid, which does not create a treatment
11 alliance that is effective in providing the support
12 that is necessary.
13 By and large, most people who do pursue
14 medical interventions do so in tandem or after
15 social transitions, but it's not possible for all
16 people to do that safely.
17 Q. Why not?
18 A. People live in hostile environments in
19 which they are targeted for their identities.
20 Q. And do you have a particular -- I guess,
21 is it fair to say that you have a particular
22 specialty in assessing individuals with
23 co-occurring mental health conditions?
24 A. Yes.

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1 Q. And what percentage of your patients who
2 have been diagnosed with gender dysphoria have
3 co-occurring mental health conditions?
4 A. Context is important. In my clinical
5 work now, those are the only patients that I'm
6 seeing. I'm only referred patients who have
7 co-occurring mental health disorders, so
8 100 percent of the patients.
9 Q. Got it. And that would suffer from
10 selection bias, you might say, in terms of
11 comparing to the other population?
12 A. Correct.
13 Q. And do you agree that research efforts
14 developing best practice guidelines for examining
15 the mental health needs of transgender youth remain
16 lacking?
17 A. I'm not sure I know what you mean.
18 There's always room for improvement, but I would
19 not say that they are lacking.
20 Q. And I would like to go back to
21 Exhibit 9, which is the Adolescence chapter of
22 SOC 8.
23 A. Okay.
24 Q. And I would like to go to S62, and the

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1 right column, Statement 6.12.D, and this statement
2 relates to assessing co-occurring mental health
3 conditions, correct?
4 A. Yes, it does.
5 Q. And the statement directs providers to
6 ensure that any co-occurring mental health
7 conditions do not "interfere with diagnostic
8 clarity"; is that right?
9 A. I don't see where you are reading that,
10 but that sentiment is correct.
11 Q. Just for the record, it's in the bold
12 below Statement 6.12.D. It says, The adolescent's
13 mental health concerns, if any, that may interfere
14 with diagnostic clarity, capacity to consent,
15 and/or gender-affirming medical treatments have
16 been addressed.
17 A. That is correct.
18 Q. And how could a co-occurring mental
19 health condition interfere with diagnostic clarity?
20 A. A co-occurring mental health condition
21 could interfere with diagnostic clarity in a number
22 of ways. If it's okay, I'll give a patient
23 example.
24 One young person I treated who had

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1 bipolar disorder during acute manic episodes would
2 describe an identity of a woman in those periods,
3 and with resolution of the manic episode, that
4 identity resolved completely. If one was only
5 looking at a moment in time and not looking at the
6 entire context, this person may have met criteria
7 for gender dysphoria. It's part of the reason that
8 we have both the six-month duration criteria as
9 well as a caveat that it's not better explained by
10 another co-occurring mental health diagnosis.
11 Q. Can family conflict potentially
12 influence an adolescent's assertion of gender
13 incongruence?
14 A. How the gender incongruence is
15 expressed, experienced, and intervened on can
16 absolutely be influenced by family stress and
17 family conflict.
18 Q. Can an individual's temperament and --
19 can an individual's temperament potentially
20 interfere with diagnostic clarity?
21 A. I mean, temperament has a very specific
22 meaning in the world of child and adolescent mental
23 health. In my definition of temperaments, no, it
24 would not interfere with diagnostic clarity.

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1 Q. What is your definition of temperament?
2 A. There's four types of temperament that
3 are really defined by early childhood attachment.
4 But in the more colloquial sense of temperament,
5 part of the job of a mental health professional is
6 to learn how to build rapport across multiple
7 temperamental types. So I don't see how
8 temperament could interfere with diagnostic
9 clarity, at least in my experience.
10 Q. Can an adolescent's cognitive ability
11 lead them to conflate gender identity, gender
12 expression, and sexual orientation?
13 A. It may in some cases.
14 Q. And if that happens, can it interfere
15 with diagnostic clarity?
16 A. Not if you know what you are doing.
17 Q. And suppose you have a patient with
18 psychotic spectrum symptoms, can gender dysphoria
19 ever stem from the psychosis?
20 A. By definition, no.
21 Q. What do you mean "by definition, no"?
22 A. If you have symptoms of gender dysphoria
23 that are better explained by co-occurring mental
24 health issues, it's not gender dysphoria. You

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1 would not meet diagnostic criteria.
2 Q. Well, why wouldn't you, if you have all
3 of the symptoms associated with it? You would
4 still meet the diagnostic criteria, wouldn't you?
5 A. No. And let me just go back. Since we
6 have in the exhibits, the DSM, I think you might
7 have cut off the piece that is relevant.
8 Q. That is Exhibit 6.
9 A. Let me just double-check here. My
10 recollection was from the DSM-IV, which had a
11 specific callout that it's not better explained by
12 another co-occurring mental health diagnosis, but
13 it is a part of the assessment process to ensure
14 that if the symptoms are solely related to a
15 co-occurring mental health disorder, such as a
16 psychotic spectrum illness or a bipolar spectrum
17 illness, such as my example, that would not qualify
18 as a diagnosis of gender dysphoria.
19 Q. And so how do you make that
20 determination of whether there is a better
21 explanation?
22 A. Well, practically speaking, most of the
23 things that would present with gender dysphoria
24 symptoms outside of gender dysphoria that are

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1 caused by a co-occurring mental health disorder
2 tend to be time limited and not exceed that
3 six-month period.
4 But our responsibilities, if we identify
5 co-occurring mental health issues, that we are not
6 ignoring them and that we are treating them. And
7 when you treat those that lead to diagnostic
8 imprecision or a lack of clarity around the
9 diagnosis of gender dysphoria and the psychosis
10 resolves, if there's still gender dysphoria
11 present, it's not likely that it was related to the
12 underlying mental health condition.
13 And the opposite is true. If the
14 psychosis resolves, you treat the co-occurring
15 mental health condition that was leading to a lack
16 of diagnostic specificity, and the symptoms of
17 gender dysphoria resolved and you know it was
18 secondary to that other co-occurring illness as
19 opposed to an independent entity.
20 Q. But isn't part of the assessment that
21 you have to make that determination beforehand?
22 A. No.
23 Q. If psychosis might be the explanation,
24 it seems like the only way to confirm that would be

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1 to treat the psychosis first, right?
2 A. It depends. History is our friend in
3 evaluations, and if you have a clear history from
4 multiple informants about a pattern of behavior and
5 a pattern of identity that is consistent and
6 predictable over time, that has a relationship to
7 the psychotic symptoms, you often have a lot of
8 that content and information prior to the
9 evaluation.
10 The important pieces, as a person who is
11 assessing for -- if we are talking about
12 recommendations for medical or surgical
13 interventions, you have to make a diagnosis of
14 gender dysphoria and understand how and if any
15 co-occurring mental health conditions are
16 interfering with that person's capacity to consent
17 to care or with the clarity around the diagnosis.
18 If you can get that in a brief
19 assessment, you can get that in a brief assessment.
20 If that requires multiple months of treatment and
21 care, it will take multiple months of treatment or
22 care. Again, it's not about a specific time. It's
23 about resolution of symptoms or resolution of the
24 lack of clarity.

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1 Q. And, I guess, what is -- how do you
2 determine once you have resolved the lack of
3 clarity? Like how do you measure that?
4 A. In part, by meeting the diagnostic
5 criteria.
6 Q. Of gender dysphoria?
7 A. If that is the question. If the -- the
8 lack of diagnostic clarity is whether or not gender
9 dysphoria exists as a diagnosis, and then, yes, you
10 have to meet the criteria for gender dysphoria in
11 order to clarify that diagnosis.
12 If there is a developmental process or
13 developmental history that is complicated by
14 co-occurring mental health disorders, you gather a
15 very comprehensive history of those developmental
16 impacts, the mental illness, on the patient's
17 experience and expression of identity over time.
18 So it's not a very straightforward process in terms
19 of explaining it. It takes time. It takes careful
20 consideration.
21 Q. And how do you know if you got it right?
22 A. How do we know if we got it right?
23 Q. Yeah.
24 A. The same way we know if we got it right

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1 for most of medicine. You never make an
2 assumption, that you test the intervention and you
3 follow up to see is it working, is it not working,
4 which parts are working, which parts aren't.
5 Q. But is it possible that the intervention
6 used to treat gender dysphoria could be more
7 intrusive than the intervention that would be used
8 to treat this other co-occurring mental health
9 condition that is interfering with diagnostic
10 clarity?
11 A. It depends upon the condition. Many, as
12 an example, of the psychotic spectrum illnesses
13 require treatment with antipsychotics that can
14 cause incredibly significant life altering symptoms
15 in that some cases never go away.
16 Q. Sorry. Say that part again. I did not
17 catch what you were saying at the end there.
18 A. There are risks to the treatments of
19 these co-occurring mental health conditions that
20 can cause lifetime impairments.
21 (WHEREUPON, a certain document was
22 marked Janssen Deposition Exhibit
23 No. 13, for identification.)
24

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1 BY MR. RAMER:
2 Q. Dr. Janssen, you have been handed what
3 has been marked as Exhibit 13, and it's Chapter 12,
4 Gender Dysphoria and Psychotic Spectrum Disorders;
5 is that correct?
6 A. That's correct.
7 Q. And did you help write this chapter?
8 A. I did.
9 Q. In this chapter you provide a case study
10 about a patient named Amy, correct?
11 A. Yes.
12 Q. Was this a real patient?
13 A. An amalgamation of several patients,
14 mostly Dr. Ito's patients.
15 Q. And is the information that you wrote in
16 this chapter truthful?
17 A. Well, in a case report of this type,
18 this is not one specific patient, so truthful but
19 not completely accurate.
20 Q. Do you know how many patients made up
21 Amy?
22 A. No, I don't recall.
23 Q. I would like to go to page 188, and a
24 few sentences down in this last paragraph, there's

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1 a sentence starting with, We know. And I'll just
2 read the sentence first, it says, We know that
3 accessing gender-affirming care improves quality of
4 life and diminishes GD, and without evidence to the
5 contrary, we can assume that it will also benefit
6 those with psychotic symptoms. Did I read that
7 correctly?
8 A. You did.
9 Q. When you wrote this, what was the basis
10 for asserting that we know that accessing
11 gender-affirming care improves quality of life and
12 diminishes GD?
13 A. The long-term studies of gender
14 dysphoria.
15 Q. Out of the Dutch clinic?
16 A. Not just with children but in adults,
17 particularly out of Belgium.
18 Q. And what does it mean to say, We know an
19 intervention improves quality of life?
20 A. There are measures of quality of life
21 that are looked at pre and post intervention, and
22 that post intervention quality of life improves.
23 Q. Is saying that "we know this care
24 improves quality of life" the same as saying that

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1 this care causes improved quality of life?
2 A. In the context of a clinical case book,
3 language is going to be different than what it
4 would be in a peer-reviewed journal article. This
5 is probably not language that I would use in a
6 peer-reviewed journal article because we would want
7 to make sure that we are supporting the evidence
8 with the citations, as appropriate.
9 But, colloquially, it's very clear that
10 interventions for gender dysphoria improve quality
11 of life when patients have access to it.
12 Q. At this -- when you wrote this, if you
13 had been writing a peer-reviewed article, would
14 there have been sufficient evidence to say that
15 this care causes improved quality of life?
16 A. We would say that studies demonstrate
17 that accessed evidence-based interventions for
18 gender dysphoria improve quality of life and
19 functional outcomes, including reduction of gender
20 dysphoria symptoms as measured by the Utrecht
21 Gender Dysphoria Scale and other symptom
22 inventories of gender dysphoria.
23 Q. And so you think that at this time the
24 evidence was sufficient to make that statement that

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1 you just said?
2 A. Yes.
3 Q. So sticking with that sentence, the
4 second half of it, you say, Without evidence to the
5 contrary, we can assume that it will also benefit
6 those with psychotic symptoms. And do you
7 typically assume an intervention is safe as long as
8 there's no evidence to the contrary?
9 A. I might dispute the premise. I don't
10 think that I was talking about the safety but about
11 the efficacy.
12 Q. Do you typically assume an intervention
13 is effective as long as there's no evidence to the
14 contrary?
15 A. That is not a typical assumption outside
16 of the context of, if we know that an intervention
17 is effective for a large group of a population and
18 the clinical experience and the extant literature
19 to date do not demonstrate a significant
20 contraindication or reason why this evidence-based
21 intervention would not also be effective in this
22 specific population, yes.
23 To bring back your previous example,
24 menstrual suppression, we know, is efficacious at

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1 expressing menstruation. We have no reason to
2 believe that it won't also be efficacious for
3 transgender individuals assigned female at birth in
4 expressing their menstruation as well.
5 Q. And here you see no problem with
6 changing a variable as significance -- or as
7 significant as the presence of psychotic symptoms
8 in simply assuming the outcome will be the same?
9 A. I don't assume the outcome would be the
10 same for these individuals. It's an individualized
11 intervention and an individualized assessment for
12 the sake of a case book. The recommendations are
13 to open up a discussion with patients who have
14 these symptoms, in addition to symptoms of gender
15 dysphoria, and not foreclose the possibility of
16 access to gender-affirming medical care for all
17 patients who have psychotic symptoms.
18 Q. But in this sentence, you say, It will
19 also benefit those with psychotic symptoms. You
20 don't say, It will benefit some individuals with
21 psychotic symptoms, correct?
22 A. I mean, as I read it, the implication of
23 that statement is that -- if you read the rest of
24 the case book, the only people who are going to

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1 have access to these interventions are people who
2 have had an assessment and that their informed
3 consent process has been complete, that they have
4 the capacity to understand the risks, benefits, and
5 alternatives of the intervention, and that they are
6 likely to benefit from it, that it's medically
7 indicated.
8 If folks are not meeting that criteria
9 because of the psychotic symptoms, they are not
10 appropriate for care.
11 Q. But isn't the question here not
12 necessarily about satisfying the criteria or
13 diagnostic clarity but, rather, whether these
14 particular interventions will benefit this
15 different patient population?
16 A. I can't tell you with certainty what I
17 was thinking when I was writing this, but my
18 recollection in this chapter was that at the time
19 of practice, that many individuals with
20 co-occurring mental health disorders and gender
21 dysphoria were barred access to care without a full
22 investigation of their capacity to provide consent,
23 in part, because there were recommendations about
24 co-occurring mental health conditions that were

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1 somewhat vague in the prevailing standards of care
2 at the time.
3 Q. What was vague?
4 A. In the Standards of Care 7, there was a
5 statement about if co-occurring mental health
6 conditions are present, they must be reasonably
7 well-controlled, and there was always a lot of
8 debate about what that means.
9 Q. And now it says, Addressed?
10 A. The change now is more towards whether
11 or not a co-occurring mental health condition
12 impairs with either diagnostic clarity or the
13 capacity to provide consent to treatment.
14 Q. Did your practice change at all from the
15 SOC 7 to the SOC 8?
16 A. It has changed. My practice changes
17 continuously, as I continue to update what we know
18 from the literature.
19 Q. Did your practice of treating
20 co-occurring mental health conditions change at all
21 from when the SOC 7 was the reigning guideline to
22 when the SOC 8 was published?
23 A. I mean, I would say that I have always
24 assertively treated co-occurring mental health

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1 conditions and tried to create a treatment plan
2 that was aligned with evidence-based guidelines for
3 every diagnosis that I made for every patient that
4 I saw.
5 Q. What did you think addressed meant --
6 I'm sorry. What did you think that reasonably
7 well-controlled meant?
8 A. To me, reasonably well-controlled meant
9 that the diagnosis was not impairing or the --
10 excuse me. Let me back up.
11 To me reasonably well controlled meant
12 that the co-occurring mental health disorders did
13 not interfere with diagnostic clarity nor did it
14 interfere with the capacity of the patient to
15 understand the treatment that was provided and the
16 risks, benefits, and alternatives of that
17 treatment. So much more aligned with what the
18 current recommendation explicated.
19 Q. And so you basically read that language
20 from SOC 7 to mean what it currently says in SOC 8;
21 is that fair?
22 A. Correct.
23 Q. Going back to Exhibit 13, same page, and
24 the sentence after the one that we were previously

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1 discussing. It says, As for nonmaleficence or the
2 concept of doing no harm, we must build a more
3 robust evidence base. There's no compelling
4 evidence that estrogen or testosterone at usual
5 treatment doses is any more dangerous to those with
6 severe mental illness. However, there is also no
7 compelling evidence that it is safe. There's
8 simply no evidence either way. Did I read that
9 correctly?
10 A. You read that correctly.
11 Q. You have recommended hormone treatment
12 for individuals with severe mental illness who have
13 gender dysphoria, correct?
14 A. Yes.
15 Q. Are you familiar with the term
16 "borderline personality disorder"?
17 A. I am.
18 Q. Is that sometimes referred to as BPD, as
19 a shorthand?
20 A. Yes.
21 Q. Have you ever diagnosed or treated BPD?
22 A. Yes.
23 Q. What is the treatment for BPD?
24 A. The majority of the treatment for BPD or

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1 at least the evidence-based treatments for BPD,
2 there's a number. The one that I would most
3 typically refer my patients to is something called
4 dialectical behavioral therapy.
5 Q. And what is that?
6 A. It's difficult to explain. It is a type
7 of intervention originally created by Marsha
8 Linehan that incorporates risk assessment, risk
9 reduction, mindfulness, group work, and
10 skills-based interventions to improve functioning
11 and mitigate risk.
12 Q. And so what form do those interventions
13 take, for you as the mental health provider? Like,
14 what do you do?
15 A. I don't typically work with folks in DBT
16 presently. At my last institution, I had patients,
17 as the psychiatrist, so I was not doing the
18 individual therapy or the group therapy for these
19 patients but doing the medication management for
20 these patients. And not everybody in DBT has
21 borderline personality disorder and not all people
22 with borderline personality disorder benefit from
23 DBT.
24 Q. Is DBT used for other mental health

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1 conditions apart from BPD?
2 A. Yes.
3 Q. Does the treatment for BPD involve any
4 form of medical intervention?
5 A. On occasion, yes.
6 Q. And what type of medical intervention?
7 A. Generally, psychiatric medication.
8 Q. Have you ever had a patient who was
9 diagnosed with both BPD and gender dysphoria?
10 A. I think so. I don't recall with
11 100 percent certainty. None of the patients under
12 my current care have both diagnoses.
13 Q. If a patient had a diagnosis for both
14 BPD and gender dysphoria, would you deem that
15 patient ineligible for medical intervention for
16 treatment of the gender dysphoria?
17 A. Well, first, it's important to note that
18 personality disorders, of which borderline
19 personality disorder is one, are not typically
20 diagnosed until adulthood, and as I'm mostly seeing
21 children and adolescents, there's not much of an
22 opportunity there.
23 Again, the goal with care is to
24 recognize if there's a co-occurring mental health

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1 disorder present, regardless of what that diagnosis
2 is, is it interfering with diagnostic clarity and
3 capacity to consent? For some patients with
4 borderline personality disorder, that answer is
5 yes. It interferes with diagnostic clarity or
6 capacity to consent, and for others it's no.
7 Q. And you said typically minors are not
8 diagnosed with BPD; is that correct?
9 A. That's correct.
10 Q. Why not?
11 A. Because adolescence is a time of
12 consolidation of many different types of
13 identities, and personality disorders imply a
14 nearly static response to stressful events that are
15 maladaptive and dysfunctional.
16 Q. Can you explain that last part in a
17 little more laymen's terms?
18 A. Sure. Many adolescents are --
19 classically think the world is ending and that only
20 they can understand their own problems and that
21 everything that happens to them is a disaster.
22 That is a pretty normal part of adolescent
23 development.
24 As an adult, that is not a typical

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1 response to life stressors, and if you are stuck in
2 that box where that is the only way that you can
3 respond to all situations, that is what defines a
4 personality disorder. And in adolescence, part of
5 what would look like a borderline personality is
6 just a normal part of adolescence.
7 Q. And does the diagnostic criteria for BPD
8 include a markedly and persistently unstable
9 self-image or sense of self?
10 A. From my recollection, yes.
11 Q. Does it also include recurrent suicidal
12 behavior?
13 A. That is a criteria. Not everybody has
14 that.
15 Q. Have you ever considered the possibility
16 that an individual's identity disturbance for BPD
17 could be experienced as a disturbance in gender
18 identity?
19 A. Yes.
20 Q. Is BPD more common in natal females?
21 A. I would have to go back and look at the
22 prevalence. I'm not a BPD expert, but from my
23 recollection, yes.
24 Q. Do you agree that a task of a mental

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1 health provider, when assessing a patient for
2 gender dysphoria, is to determine the relationship
3 between the patient's gender dysphoria and any
4 co-occurring mental health conditions?
5 A. That is a task, not the only task.
6 Q. And individuals with autism spectrum
7 disorders are more likely to have gender dysphoria,
8 correct?
9 A. That is what the research has
10 demonstrated, yes.
11 Q. And individuals with gender dysphoria
12 are more likely to have an ASD, correct?
13 A. That is correct.
14 Q. There is no agreed-upon etiology for
15 ASDs, correct?
16 A. That is correct.
17 Q. And there's no agreed-upon etiology for
18 gender dysphoria, correct?
19 A. There is not one factor that people can
20 point to and say, This is it.
21 Q. What is the nuance that you are drawing
22 there?
23 A. I don't think there is a particular
24 nuance that I'm drawing. Autism is a very

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1 complicated set of disorders under one umbrella.
2 Q. And individuals with ASDs have
3 difficulties with what is called theory of mind,
4 correct?
5 A. Many do, yes.
6 Q. And does theory of mind have
7 implications for the development of gender
8 identity?
9 A. Not that we know of. It likely has
10 implications in the expression and understanding of
11 gender identity, but with no clarity around --
12 there's no evidence to support that it impacts core
13 gender identity.
14 Q. What would be the implications for
15 understanding and awareness and expression of
16 gender?
17 A. I mean, I can give some concrete
18 clinical examples, including, I think, one
19 amalgamation of a case that I presented, where an
20 individual socially transitioned in their mind but
21 did not change anything about their appearance and
22 could not understand why people did not recognize
23 and acknowledge that they had transitioned.
24 This individual lacked the capacity to

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1 recognize that making a momentous life change
2 without changing anything exterior would not be
3 automatically understood by the people in their
4 life.
5 Q. Do you think it can be challenging to
6 distinguish between gender dysphoria and autism
7 spectral disorders?
8 A. No, not for me.
9 Q. That was my question. So are you good
10 at it, was my next question?
11 A. Yeah, I think so. Yeah.
12 Q. And how do you know that you are good at
13 that?
14 A. I don't actually think that you have to
15 be very good at it to be able to differentiate it.
16 They are very different diagnostic entities.
17 The question and the overlap that most
18 people point to when they talk about a potential
19 struggle and diagnostic clarification is there is a
20 symptom of autism around restricted and repetitive
21 interests or behaviors. Theoretically, one of
22 those interests could be around expressing feminine
23 gender roles, if you were assigned male at birth,
24 as most individuals with autism are.

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1 There's a very clear phenomenology of
2 how those kind of restricted interests look, but
3 it's very different than what you see for
4 transgender individuals who experience an
5 incongruence in their identity.
6 Q. Can you unpack the word "phenomenology"
7 for me?
8 A. Sure. With many kids with autism, a
9 restricted interest is not just, I like trains and
10 I really like Thomas the Tank. It is, I can tell
11 you every subway stop for the entire MTA, and I can
12 tell you what year the trains turn over, and I can
13 tell you how many cars in each train. And if you
14 let me, I will talk about this for hours and hours
15 and hours, and even when I'm giving you a cue that
16 I am not interested anymore, I'm going to continue
17 to talk about it for hours and hours and hours such
18 that I drive away friends, people get exasperated
19 by me. That is different, and that is not the
20 characterization of how trans people talk about
21 their experience of identity. It's just a very
22 different phenomenology.
23 Q. But could it ever center on gender, I
24 mean, that -- I'm sorry. What is the phrase of

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1 the -- when we talk about something over and over?
2 A. The restricted interests.
3 Q. Could that ever center on gender?
4 A. I think theoretically, it could, yes.
5 Q. And when that happens, how do you
6 distinguish between that and gender dysphoria?
7 A. Typically, when that happens and it's
8 just a restricted interest, you are not meeting
9 criteria for the other symptoms of gender
10 dysphoria.
11 Q. Because -- or can you give me an example
12 of what you mean, like how you would not? I guess,
13 to me, just hearing you describe it, if the
14 restricted interest was being the opposite gender,
15 it seems like you would come pretty close to
16 hitting all of the criteria as long as distress was
17 present?
18 A. It's just not something that I have
19 heard reported or I have seen. I have seen, I like
20 wearing dresses, I'm obsessed with Disney
21 princesses. I have not seen that there's a
22 restricted interest that, I'm a girl. That is not
23 something that I have seen.
24 Q. Do you agree that the distress from

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1 gender dysphoria can take on different forms, such
2 as anxiety and depression?
3 A. I agree that gender dysphoria can lead
4 to anxiety and depressive symptoms, which is
5 different than a diagnosis of an anxiety disorder
6 or a depressive disorder.
7 Q. That is fair. And I guess my question
8 is, I'm talking specifically about the distress
9 from the gender dysphoria, that takes on the form
10 of anxiety or depression. Is that something that
11 can happen?
12 A. Yes.
13 Q. Do you agree that clinicians can adapt
14 evidence-based cognitive behavioral interventions
15 to address depression and anxiety in transgender
16 youth?
17 A. We have been trying, yes.
18 Q. Are you aware of any study researching
19 the effect of puberty blockers on neurodevelopment
20 in adolescents with neurodiverse characteristics?
21 A. I guess it depends on what you mean by
22 "neuro development."
23 Q. What would be your -- I'm sorry. Go
24 ahead.

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1 A. I mean, folks have looked at
2 neuropsychiatric functioning or IQ or general
3 cognitive development as a part of these
4 treatments. The Dutch cohort had several patients
5 with autism or many patients with autism in it, and
6 they were followed longitudinally, but I am not
7 sure if that is exactly what you mean.
8 Q. Do you know how many were -- you said
9 they had ASDs in the Dutch study?
10 A. They did.
11 Q. And do you know --
12 A. I don't know how many off the top of my
13 head.
14 Q. Have you ever diagnosed a patient with
15 an eating disorder?
16 A. Yes.
17 Q. Have you ever treated a patient with an
18 eating disorder?
19 A. Yes.
20 Q. What was the treatment?
21 A. In the context of my role on the team,
22 mostly on providing the psychiatric medication
23 management of a patient with an eating disorder.
24 Q. Would that patient also receive

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1 psychotherapy?
2 A. It depends on the kid.
3 Q. What does it depend upon?
4 A. Their willingness to participate and
5 their likeliness to respond.
6 Q. What is -- you said that your role in
7 treating a patient with an eating disorder was
8 helping with medication; is that right?
9 A. That's correct.
10 Q. And what was the purpose of the
11 medication that you were providing?
12 A. I don't see very many kids with eating
13 disorders, so the ones that I do see typically have
14 had co-occurring psychiatric disorders that would
15 be appropriate for treatment.
16 Q. And so the medication that you were
17 providing was not to treat the eating disorder, it
18 was to treat the co-occurring psychiatric disorder;
19 is that correct?
20 A. That is correct.
21 Q. So then what treatment would the
22 individual have been receiving for the eating
23 disorder?
24 A. There are some medications that are

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1 indicated for the use of eating disorders. That is
2 not my role and has not been my role on the
3 treatment team. Most of the interventions are
4 therapeutic.
5 Q. Have you ever had a patient diagnosed
6 with both gender dysphoria and an eating disorder?
7 A. Yes.
8 Q. And how do you go about treating that
9 patient?
10 A. You treat -- it depends. It's highly
11 individualized. You are doing your full
12 assessment, and you are recognizing and trying to
13 parse the relationship between the eating disorder
14 and the gender dysphoria and you are treating both.
15 You get a sense of what are the
16 evidence-based interventions for eating disorders,
17 what are the evidence-based interventions for
18 gender dysphoria, and coming together with your
19 patient and family to prioritize a treatment plan
20 and order the interventions in a way that makes
21 sense for the family and for the patient.
22 Q. Does having a patient with both of those
23 diagnoses make treatment more complex because part
24 of the treatment for the eating disorder is to help

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1 the patient become comfortable with their body,
2 whereas, that goal could somehow conflict with the
3 treatment for gender dysphoria?
4 A. I would not -- not necessarily. It's
5 highly individualized.
6 Q. For an adolescent with gender dysphoria,
7 would it be inappropriate to use psychotherapy with
8 the goal of helping the adolescent see that
9 medicalized transition may not be necessary?
10 A. We have to provide significant context
11 to that question. We have to do an assessment and
12 recognize what diagnoses are present, and what is
13 the treatment plan for those diagnoses. When
14 there's a lack of clarity around a particular
15 diagnosis, sometimes the treatment plan is,
16 Continue to explore until there's clarity around a
17 diagnosis and a more concrete treatment plan can be
18 enacted.
19 Q. Do you see a distinction between
20 conversion therapy and psychotherapy that is
21 conducted for the purpose of trying to help the
22 adolescent determine that medicalized transition
23 may not be necessary?
24 A. The way that I understand conversion

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1 therapy as being significantly different from
2 supportive psychotherapy for children who are
3 exploring gender identity is that conversion
4 therapy predisposes one outcome as preferable over
5 the other. Namely, that a cis gender identity at
6 the end of treatment is the goal of treatment.
7 In gender-affirming care and in my
8 practice, I'm not privileging one outcome for the
9 other. The outcome that I'm privileging is that
10 the individual that I'm working with develops a
11 nuanced and coherent sense of self, that their
12 co-occurring mental health disorders are treated,
13 that their functioning and quality of life
14 improves, regardless of the ultimate outcome of the
15 identity.
16 Based upon that assessment, we are going
17 to make evidence-based interventions based upon the
18 best available evidence that we have. If after
19 that assessment, the best evidence suggests that a
20 medical intervention that is desired for and
21 requested by the patient is medically indicated, it
22 would not be appropriate for me to make a
23 recommendation for an intervention of psychotherapy
24 for which there is no evidence to support it.

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1 Q. I guess going back to the hypothetical
2 16-year-old adolescent who wants a phalloplasty but
3 is ineligible for it, so the treatment that you
4 would provide that individual is just to basically
5 buy time up until they age into the ability to
6 receive the phalloplasty; is that right?
7 A. Yeah. Hopefully you can help that
8 individual build resilience and skills for
9 tolerating distress.
10 Q. How would you do that?
11 A. Well, typically, given the patients that
12 I'm working with and my role on the team, I'll
13 refer to a really good therapist who does that, but
14 a lot of it is about building capacity and skills,
15 providing opportunities for an adolescent to feel
16 competent in domains, and part of that is when that
17 distress is related to gender dysphoria, in this
18 hypothetical 16-year-old who wants a phalloplasty,
19 typically that is not in isolation and there are
20 other aspects of therapeutic and medical care that
21 we can engage in at that age.
22 Q. Shifting gears a little bit. How do you
23 stay informed about developments in research?
24 A. Me personally?

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1 Q. Yes.
2 A. Partially, it's by reviewing articles,
3 and as the former associate editor of Transgender
4 Health, I get a lot of things that would come my
5 way. But I have Google alerts set up for Google
6 Scholar, so when a paper with key words or authors
7 comes up, it pings into my inbox. But I also work
8 with a multidisciplinary team that is constantly
9 updating their knowledge and reviewing the
10 literature, so we have a cohort of folks that we
11 work with to stay on top of things.
12 Q. And it sounds like you get a lot of
13 alerts or opportunities to read articles?
14 A. I do.
15 Q. How do you determine which articles you
16 actually are going to read?
17 A. It's quite variable. It's quite
18 variable. It really depends. I can't say I have a
19 rubric. Typically, if it's from a reputable
20 journal, I will prioritize it, but it really
21 depends. If it seems interesting, if it seems
22 relevant, if I'm preparing a lecture or talk about
23 a specific aspect of the care, I'll go back and see
24 the relevant literature to that topic. Otherwise,

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1 it just depends.
2 Q. And how do you determine whether an
3 article is reliable?
4 A. You have to read it.
5 Q. And when you are reading it, what are
6 you thinking about to determine the reliability of
7 the study?
8 A. What is included, how is the study
9 designed, how did the authors talk about their
10 limitations, do the conclusions match the data as
11 presented, is there anything that is missing.
12 There's a lot of ways of doing that.
13 Q. And this is a hypothetical. If you have
14 a longitudinal study where adolescents with gender
15 dysphoria received cross-sex hormones and
16 psychotherapy and the adolescents showed improved
17 quality of life, do you think that study provides
18 evidence that cross-sex hormones improve quality of
19 life in adolescents with gender dysphoria?
20 A. It would depend upon how the study was
21 designed and reviewing -- because in the world of
22 practice, we don't gauge treatment decisions based
23 upon one study. We look at the entirety of the
24 literature and draw conclusions from that

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1 experience and the experience that we have of
2 working with our patients to make the best possible
3 decisions that we can with and for our patients and
4 their families.
5 Q. So let's suppose that you have 20
6 longitudinal studies where adolescents with gender
7 dysphoria receive cross-sex hormones and
8 psychotherapy and the adolescents showed improved
9 quality of life. Do you think that those studies
10 provide evidence that cross-sex hormones improved
11 quality of life in adolescents with gender
12 dysphoria?
13 A. It provides some evidence, but not
14 conclusive evidence. One would hope that there
15 would be additional studies that could look at
16 impacts of lack of access to psychotherapy or lack
17 of access to hormones on quality of life outcomes
18 for those individuals. Again, we have survey data
19 of adults that look at that, so these studies are
20 not done in isolation.
21 But in order to know whether or not a
22 particular study can draw conclusive evidence about
23 the impact of one intervention versus another, you
24 need multiple different types of studies in order

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1 to say that conclusively.
2 Q. Do you think that we have conclusive
3 evidence about the efficacy of hormone therapy for
4 treating gender dysphoria in adolescents?
5 A. The evidence that we have from the
6 studies that have done this rigorously has
7 consistently demonstrated improvements in gender
8 dysphoria and quality of life when given access to
9 care.
10 Q. Would you describe it as conclusive
11 evidence?
12 A. I would. But, you know, in a world of
13 academic medicine, what I think of as conclusive is
14 probably different from what it's meant
15 colloquially. I think there's enough evidence for
16 me to make a strong recommendation, but I continue
17 to review the literature and keep an open mind.
18 Q. Are you aware of any studies
19 demonstrating that medical interventions alone are
20 effective in the treatment of gender dysphoria?
21 A. I would have to look back at the
22 specific studies, particularly the recent studies
23 that have come out of the ForesiGHt NIH trial and
24 from Seattle Children's to see for sure. I think

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1 certainly some of the patients in those cohorts did
2 not have psychotherapy and demonstrated benefit
3 from medical interventions.
4 Q. Are you able to name any systematic
5 reviews relating to the treatment of gender
6 dysphoria that you have read?
7 A. Can I name them, like the authors and
8 the --
9 Q. Can you describe them? Have you ever
10 read them?
11 A. Yeah, I have read multiple systematic
12 reviews.
13 Q. Like what? Could you give some
14 examples?
15 A. I wrote a systematic review.
16 Q. On the treatment of gender dysphoria?
17 A. Yeah.
18 Q. And what was the title of that?
19 A. I can't remember. I would have to go
20 through my CV and look.
21 Q. And what did you --
22 A. This was on surgery, so it was in
23 adulthood.
24 Q. And what about systematic reviews

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1 relating to the treatment of gender dysphoria in
2 adolescents?
3 A. I have read several. There have been
4 several that have been recently published.
5 Q. Like what?
6 A. I could not tell you the authors off the
7 top of my head.
8 Q. Not the authors. But is it coming from
9 a health authority? Is it coming from researchers
10 somewhere or just --
11 A. There have been a lot of systematic
12 reviews. So I would be happy to do a Google
13 Scholar search and give you the ones that have been
14 published, but giving you the names of articles off
15 the top of my head, I am not able to do right now.
16 Q. Do you recall what any of the analysis
17 was that came from those systematic reviews?
18 A. I would be happy to comment on the
19 specific analyses of a specific systematic review.
20 Q. Did you testify before the Florida Board
21 of Medicine in 2022?
22 A. Yes.
23 Q. And are you aware that the State of
24 Florida took steps to restrict the use of puberty

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1 blockers and cross-sex hormones as a treatment for
2 gender dysphoria in minors?
3 A. Yes, I'm aware.
4 Q. Did you ever investigate the evidentiary
5 basis for the board's decision?
6 A. I believe so, yes.
7 Q. And what did you think?
8 A. I thought they drew the wrong
9 conclusions from the literature that exists.
10 (WHEREUPON, a certain document was
11 marked Janssen Deposition Exhibit
12 No. 14, for identification.)
13 BY MR. RAMER:
14 Q. Dr. Janssen, you were just handed what
15 has been marked as Exhibit 14, Janssen Exhibit 14,
16 and the title is Effects of Gender-Affirming
17 Therapies in People With Gender Dysphoria:
18 Evaluation of the Best Available Evidence; is that
19 right?
20 A. That is what it says.
21 Q. Have you seen this document before?
22 A. I could not tell you. I don't see any
23 citation for where this might have been published.
24 Q. Have you ever heard of Romina

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1 Brignardello-Petersen?
2 A. Not really, no.
3 Q. If you see on the first page, the first
4 sentence, it says, We prepared this report to
5 fulfill a request from the Florida Agency for
6 Health Care Administration. Do you see that?
7 A. No, I'm not seeing where that is. I
8 believe you, but I don't see where it is.
9 Q. The first page under the introduction,
10 first sentence.
11 A. Got it. Yeah.
12 Q. Does that refresh your recollection of
13 whether you have ever seen this before?
14 A. No, it does not. I don't recall.
15 Q. And so do you -- sorry.
16 A. I do not recall if I have read this
17 specific document.
18 Q. Okay. I would like to just go to
19 page 5. I'm going to ask you --
20 A. I apologize. Can I ask a question about
21 this?
22 Q. Please.
23 A. Because my read of this, just from the
24 introduction of this, this was not a peer-reviewed

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1 document; is that correct?
2 Q. You tell me. Is it a peer-reviewed
3 document?
4 A. It appears not to be a peer-reviewed
5 document, based upon how they are describing it.
6 Q. And why is that significant?
7 A. Because peer-review is an integral part
8 of the scientific process, particularly when folks
9 might not have experience or expertise in the field
10 about which they are describing. I mean, I'm
11 having a hard time getting past the first two
12 sentences of Dr. Brignardello-Petersen's
13 qualifications, which demonstrate that she is a
14 dentist and an epidemiologist.
15 Q. And were the SOC 8 peer-reviewed?
16 A. They went through the Delphi process and
17 were published in a peer-reviewed journal, so yes.
18 Q. You think -- sorry. What do you mean by
19 that, when you say peer-reviewed? How does the
20 typical peer-review process go?
21 A. Articles are submitted to a journal.
22 They are sent to typically an associate editor, who
23 does the initial run-through to decide whether it's
24 appropriate enough to send out to for editing, and

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1 then it's sent to reviewers who are experts in the
2 field who make comments and suggestions. That is
3 typically how that process works.
4 Q. And the idea there is that somebody who
5 was not involved with drafting the article is doing
6 the reviewing, correct?
7 A. Yes, somebody with expertise in the
8 field who can comment on strengths and deficiencies
9 of a particular article.
10 Q. Do you think that it's significant that
11 it's somebody who was not involved with drafting
12 the article?
13 A. I think that is the best case scenario,
14 yes. You can't have a typical peer-review process,
15 if you are reviewing your own work.
16 Q. Did the SOC 8 go through a typical
17 peer-review process, as you just described it?
18 A. I'm not on the editorial board for the
19 International Journal of Transgender Health, where
20 that was published, but typically things that I
21 have submitted to that journal or that I know that
22 people have submitted to that journal have gone
23 through a typical peer-review process. But I'm not
24 a part of the editorial board, so I can't tell you

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1 what the process was.
2 Q. So you don't know whether SOC 8 was
3 peer-reviewed; is that correct?
4 A. My assumption, given the fact that we
5 had a Delphi process with multiple peers reviewing
6 the other chapters and the chapters' statements,
7 that there were certainly elements of peer review
8 as a part of it. My assumption would be that peer
9 review happened as a part of the publication, but I
10 don't know for sure.
11 Q. And just going to page 5 on this, just
12 the conclusion, I'm just going to ask you one
13 question about it.
14 Toward the bottom, under 6, Conclusions,
15 it says, Due to the important limitations in the
16 body of evidence, there's great uncertainty about
17 the effects of puberty blockers, cross-sex
18 hormones, and surgeries in young people with gender
19 dysphoria. This evidence alone is not sufficient
20 to support whether using or not using these
21 treatments. Did I read that correctly?
22 A. You did.
23 Q. And do you disagree with that
24 conclusion?

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1 A. I do.
2 Q. And on what basis do you disagree?
3 A. The extant literature and my clinical
4 experience.
5 MR. RAY: Counsel, I think we have -- I'm
6 sorry. I just observed that we have been going for
7 about 70 minutes?
8 MR. RAMER: No, that is a good stopping point,
9 so go off the record.
10 (WHEREUPON, a recess was had.)
11 BY MR. RAMER:
12 Q. Dr. Janssen, are you aware that health
13 authorities in the United Kingdom have taken steps
14 to restrict the use of puberty blockers and
15 cross-sex hormones for adolescents with gender
16 dysphoria?
17 A. Yes, I'm aware.
18 Q. And do you agree that the
19 recommendations of those health authorities depart
20 from the recommendations of the SOC 8?
21 A. Yes.
22 Q. Did you ever attempt to review the
23 evidentiary basis for those decisions?
24 A. Most of the evidence that was reviewed

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1 in those decisions had been published already and
2 was subject to review by those of us who are on the
3 SOC 8 revision committee.
4 Q. When you say "subject to review," what
5 do you mean by that?
6 A. Most of the literature that has been
7 published in this field has been reviewed by those
8 of us on the committees that revise the standards
9 of care.
10 Q. So did you read any of the systematic
11 reviews that were published by the UK's National
12 Institute for Health and Care Excellence?
13 A. I think there were several. Yes, I have
14 read some of them. I would have -- I would have to
15 see the ones to be sure which ones I have read and
16 which ones I have not.
17 (WHEREUPON, a certain document was
18 marked Janssen Deposition Exhibit
19 No. 15, for identification.)
20 BY MR. RAMER:
21 Q. Dr. Janssen, you have been given what
22 has been marked as Janssen Exhibit 15, that says,
23 Evidence Review, and then a title after Evidence
24 Review; is that correct?

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1 A. Yes.
2 Q. And do you recognize this document?
3 A. I do.
4 Q. And do you understand this to be a
5 systematic review?
6 A. I recognize it as an evidence review. I
7 would have to go into the details to see if this
8 was a systematic review.
9 Q. What would you be looking for to
10 determine whether it's a systematic review?
11 A. Description of the methodology of the
12 systematic review.
13 Q. What is the methodology of a systematic
14 review?
15 A. A systematic review typically is done by
16 somebody with expertise in the field who ahead of
17 time provides search terms and expectations for
18 inclusion and exclusion criteria for particular
19 research studies that are around a particular
20 question or outcome. That is what I'm typically
21 looking for.
22 Q. And then does a systematic review
23 typically assess individual studies for risk of
24 bias?

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1 A. Typically, it's often a part of a
2 systematic review.
3 Q. And is this -- I think you said this,
4 but just to confirm, is this document something
5 that you have read before?
6 A. It is, but I believe this is the one
7 that was prepared in 2020, so it's been quite some
8 time since I read it.
9 Q. And in what level of detail did you read
10 it, when you read it?
11 A. Oh, I don't recall the level of detail
12 in which I read it.
13 Q. Do you recall having a reaction to it?
14 A. I do not.
15 Q. Do you recall whether the review reaches
16 conclusions that you disagree with?
17 A. I would have to read it to be sure.
18 Q. And did you ever, when you first read
19 it, actually ever attempt to analyze the review's
20 methodology?
21 A. It was 2020, so I can't recall. There
22 was a lot going on in 2020.
23 Q. Fair. So I would like to go to page 45,
24 and halfway down the page, there's a conclusion,

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1 and then I'm going to read the first sentence under
2 the conclusion. The results of the studies that
3 reported impact on the critical outcomes of gender
4 dysphoria and mental health, depression, anger, and
5 anxiety, and the important outcomes of body image
6 and psychosocial impact, global and psychosocial
7 functioning in children and adolescents with gender
8 dysphoria are at very low certainty using modified
9 grade. Did I read that correctly?
10 A. You read that correctly.
11 Q. Do you agree that the evidence quality
12 for the use of puberty blockers to treat gender
13 dysphoria is very low on the grade scale?
14 A. I'm not testifying as an expert on the
15 grade scale or on research methodology. I would
16 have to see the grade scale in order to apply its
17 methodology to the current extant literature.
18 Q. Did you ever apply the grade scale to
19 any of the studies that you cite in your expert
20 reports?
21 A. Not me personally, no.
22 (WHEREUPON, a certain document was
23 marked Janssen Deposition Exhibit
24 No. 16, for identification.)

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1 BY MR. RAMER:
2 Q. Dr. Janssen, you have been handed what
3 has been marked as Exhibit 16, which is also an
4 evidence review similar to the one that we just
5 looked at, but this one is for gender-affirming
6 hormones, correct?
7 A. That is correct.
8 Q. And have you read this one before?
9 A. I have read this one. I have not read
10 it since 2020. I don't recall if I had any
11 reactions to it, and I do not recall how closely I
12 read it.
13 Q. Do you have any reason to doubt whether
14 the analysis in this document is reliable?
15 A. Which part of the analysis? I have
16 reason to doubt some of the analysis.
17 Q. And why?
18 A. Well, in part, from just skimming
19 through the recent document that you showed me on
20 puberty suppression, there were logical leaps and
21 misappropriation of effects that were somewhat
22 concerning to me.
23 Q. Can you elaborate? And feel free to
24 reference the document, if you would like. But

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1 what logical leaps are you referring to?
2 A. Sure. In the section that you have
3 pointed out, the conclusion on page 31 of the
4 evidence review of gonadotropin-releasing hormones.
5 Q. That is Exhibit 15, for the record.
6 A. I guess it was not 31, but I will
7 paraphrase because I'm not going to be able to find
8 it quickly.
9 But reported a lack of evidence for the
10 impact of gender dysphoria but applied the evidence
11 was lacking for depression, anxiety, and
12 suicidality and not of the core gender dysphoria
13 symptoms. That leads me to believe that there's
14 some differentiation of how Dr. Cass is measuring
15 effect based upon symptom inventories that were not
16 designed to track core symptoms of gender
17 dysphoria.
18 Q. Could you explain that a little more?
19 A. Sure. I think in kind of plain
20 language, treatment for gender dysphoria aims to
21 improve gender dysphoria. Whether or not treatment
22 for gender dysphoria impacts measures that were
23 specifically designed for tracking the treatment of
24 major depressive disorder and anxiety disorders is

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1 not an appropriate outcome when we are looking at
2 the impact of a treatment specific for gender
3 dysphoria.
4 We should be looking at treatment
5 outcomes for gender dysphoria, quality of life,
6 body alignment, et cetera.
7 Q. And those relate to the distress from
8 gender dysphoria? That is the point?
9 A. Correct.
10 Q. And the fault or the flaw that you are
11 describing is that, what did they assess?
12 A. Depression, anxiety, suicidality.
13 Q. Can the distress from gender dysphoria
14 ever be perceived as anxiety or depression?
15 A. It certainly can exacerbate underlying
16 depressive, anxiety, and suicidality symptoms. The
17 diagnosis of depression, major depressive disorder,
18 a diagnosis of generalize anxiety disorder or
19 social anxiety disorder or separation anxiety
20 disorder is different from the symptoms of
21 depression, anxiety, and suicidality.
22 Q. Can we go to Exhibit 7, which is your
23 expert report, and page 15, first full paragraph,
24 Gender dysphoria, by definition, is accompanied by

1 clinically significant psychological stress. That
2 distress can take on many different forms, e.g.,
3 anxiety, mood disorders, and depression and vary
4 greatly in severity resulting in co-occurring
5 conditions.
6 Can you explain the distinction between
7 what you say there and what you just said?
8 A. Sure. So there's a whole category of
9 disorders called adjustment disorders, meaning that
10 you can have symptoms of anxiety or depression
11 secondary to a life stressor that is separate from
12 a diagnosis of major depressive disorder or
13 generalized anxiety disorder.
14 Measurements that are looking at
15 diagnoses of depression and anxiety are not the
16 same as looking at outcomes of factors of mood or
17 anxiety adjustment secondary to diagnosis of gender
18 dysphoria. It's a bit of an apples and oranges,
19 which makes it difficult to draw conclusions.
20 If I may, a majority of the data that
21 Dr. Cass is looking at to even make this false
22 assertion about the lack of relationship between
23 gender dysphoria and improvement, specifically
24 around mood, anxiety, and suicidality through the

1 use of the CBCL, the Child Behavior Check List,
2 developed by Achenbach, which is, I think, about a
3 130-question screening document. It's not a
4 document that is meant to be used as a substitute
5 for clinical practice.
6 And in my work back in New York, we
7 frequently used the CBCL as a screening instrument.
8 We don't use the CBCL in isolation. The CBCL is
9 one part of a component. We would never make a
10 diagnosis of depression, anxiety, or seek to define
11 somebody's functioning based upon the CBCL alone.
12 So it's concerning when I read -- and I
13 read this kind of broad generalization about impact
14 on -- of treatment on mood, anxiety, and
15 suicidality using solely something like a CBCL,
16 which is not designed to do that.
17 Q. And what -- sorry -- in Exhibit 15 --
18 was it on the page that we were previously
19 discussing and you saw what you were describing?
20 A. Yeah, it was in that conclusion
21 paragraph. It looks like page 45.
22 Q. 45, yeah. And can you point to where it
23 is that you are describing?
24 A. Sure. So the results of the studies

1 that reported impact on the critical outcomes of
2 gender dysphoria and mental health, depression,
3 anger, and anxiety.
4 To me, that reads as, The critical
5 outcomes of gender dysphoria are the impacts on
6 depression, anxiety, and anger and not on core
7 gender dysphoria symptoms.
8 Q. So what do you do with studies that
9 assess the effectiveness of pubertal suppression on
10 things like depression and anxiety and show
11 improvement in those areas but do not report the
12 findings with respect to gender dysphoria? Are
13 those articles irrelevant?
14 A. I have not seen those articles. The
15 majority of the articles that I have seen, when
16 looking at outcomes specific to gender dysphoria,
17 have shown clear and consistent improvements of the
18 core symptoms of gender dysphoria with treatments
19 for gender dysphoria.
20 Q. And the core symptoms of gender
21 dysphoria are?
22 A. The symptoms of gender dysphoria that we
23 reviewed in the DSM-5.
24 Q. Distress?

1 A. Distress.
2 Q. And so does -- quality of life, is that
3 a measurement of distress?
4 A. It can be. Certainly your quality of
5 life is diminished by significant distress, and
6 when you have the privilege of working with these
7 patients, you hear these stories of distress that
8 are incredibly difficult to understand for folks
9 who are not living through it. The description of
10 people who every day there is just torment that
11 people are describing.
12 Q. So improvement in quality of life can be
13 a measurement of distress, but improvement in
14 depression cannot be a measure of distress
15 associated with gender dysphoria?
16 A. It can be. It's an element. The
17 question is, do you substitute one for the other,
18 or do you recognize that this is one component of a
19 whole and provide and assign a degree of attention
20 or focus to this one specific symptom? To me it
21 seems like Dr. Cass has substituted evidence for
22 improvement on depression and anxiety measures for
23 evidence of improvement for gender dysphoria, and I
24 don't think that is a fair comparison.

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1 Q. And so if there were a study that was
2 assessing the effectiveness of puberty blockers or
3 cross-sex hormones and that study did not report on
4 improvements in gender dysphoria itself, but rather
5 on depression and anxiety, would that be -- would
6 that study be of diminished relevance?
7 A. It depends upon the question, and if the
8 question is to puberty-blocking agents or the
9 intervention at hand, significantly impact these
10 measures and you have a clear sense of what those
11 measures are and what they are measuring, it's
12 absolutely valuable. And there have been quite
13 valuable studies that have looked at that exact
14 question, but to say that an impact on -- if
15 there's not a demonstrable impact on improvements
16 in depression and anxiety, is not the same as
17 saying that those medications or those
18 interventions don't work for gender dysphoria.
19 Q. But it's also not saying that they do
20 work for gender dysphoria?
21 A. It depends upon the study, but yes. You
22 can't make a statement about whether or not an
23 intervention is useful for gender dysphoria solely
24 based on depression or anxiety measures alone.

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1 Q. And so going back to Exhibit 16, which
2 is the gender-affirming hormone systematic review.
3 I would like to go to page 13, and about halfway
4 down under Discussion, the third paragraph, first
5 full sentence says, The included studies have
6 relatively short follow-up with an average duration
7 of treatment with gender-affirming hormones between
8 around one year and 5.8 years. Further studies
9 with a longer follow-up are needed to determine the
10 long-term effect of gender-affirming hormones for
11 children and adolescents with gender dysphoria.
12 Did I read that correctly?
13 A. You did.
14 Q. Do you agree that it would take longer
15 than 5.8 years for some of the effects associated
16 with these hormonal interventions to become
17 apparent?
18 A. Averages can be rendered meaningless,
19 and so you really need to look at the individual
20 studies to recognize it. If you had two studies or
21 three studies that followed these patients for
22 25 years but you happen to have a bunch of
23 fledgling gender programs start to release data
24 that all had been following their patients for one

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1 year, it would make the average quite low. But it
2 does not diminish the value of the three studies
3 that have followed patients for 20, 25 years. So
4 looking at just an average, I can't draw any
5 conclusion from this.
6 Q. And the three studies that you were
7 talking about, was that the Dutch and Belgium, or
8 what was it?
9 A. These were hypothetical studies. I'm
10 saying, unless I know the studies and have a link
11 to the studies, that just seeing an average on its
12 own is not going to give me any information that is
13 useful.
14 Q. Let's put it in the context of an
15 individual. Do you agree that with an individual,
16 you will not have an understanding of what the
17 long-term effects of the hormonal interventions
18 will be within 5.8 years?
19 A. Thankfully, on an individual level, we
20 have decades and decades and decades of experience
21 because transgender people have existed for a very
22 long time and have had access to this care for a
23 very long time. So if we are looking at an
24 individual's experience of their own impact, we

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1 have many, many decades of personal experience and
2 individual experience to draw from.
3 Q. You are talking about adults?
4 A. Uh-huh.
5 Q. So next paragraph, same page, it says,
6 Most studies included in this review did not report
7 comorbidities, physical or mental health, and no
8 study reported concomitant treatments in detail.
9 Did I read that correctly?
10 A. You did.
11 Q. What do you understand -- actually, I'll
12 read the second sentence as well. Because of this,
13 it is not clear whether any changes seen were due
14 to gender-affirming hormones or other treatments
15 the participants may have received. Did I read
16 that correctly?
17 A. Yes, you did.
18 Q. And what do you understand that
19 paragraph to be saying there?
20 A. What do I understand it to be saying, or
21 what is my conclusion from that paragraph?
22 Q. Both.
23 A. Sure. So what I mean it to say is that
24 in the published literature, the description of

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1 treatments that happened outside of the specific
2 study protocols were not included, and, thus, it's
3 difficult for an outside reviewer to make an
4 assessment of the potential impact of those
5 theoretical outside treatments on care.
6 My reaction, as I read it, is this is
7 part of the reason why we want people who have
8 experience in the field to do systematic reviews
9 because we can talk to some of the providers and
10 gather more information, whenever possible, to
11 understand what kind of treatments were happening.
12 I happen to know from the Dutch clinics
13 and the Belgium clinics that they have all of this
14 data, just that it was not published in the course
15 of these studies, and so there's a difference
16 between data that is not published and data that is
17 somehow nefariously hidden.
18 Q. What data are you referring to?
19 A. The other treatments that people had
20 access to during this care.
21 Q. And what are the other treatments?
22 A. You would have to ask the study sites,
23 that has that information, whether it was published
24 or not.

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1 Q. But I thought you said you know it?
2 A. No, not for all of the studies. I'm
3 saying it is a knowable -- it is a knowable
4 question, but not one that Dr. Cass appeared to
5 investigate.
6 Q. In the Dutch studies, do you think that
7 psychotherapy was a confounding variable?
8 A. For what?
9 Q. What do you mean, for what?
10 A. For what outcome?
11 Q. Gender dysphoria.
12 A. There's many aspects of gender
13 dysphoria. For the improvement of gender
14 dysphoria, is that your question?
15 Q. I think so. Can you answer that, if
16 that is the question?
17 A. Confounding means, to me, involved in,
18 not necessarily causative of. Do I think it was
19 confounding? Not in particular. I don't think
20 that the evidence supports that, but I think it's
21 certainly possible, in my experience, and I have a
22 bias as a mental health professional, that
23 generally therapy is a good thing and helps most
24 people understand and articulate experiences.

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1 But the data that we have that
2 supplements the Dutch data includes the
3 cross-sectional and also the survey-based data that
4 looks at people that did not have access to therapy
5 and people who had access to therapy but not to
6 medical interventions, and in those cases the
7 people who have access to therapy but not medical
8 interventions, when indicated, did worse and felt
9 worse.
10 So to me it's -- the preponderance of
11 the evidence, when you actually take it as a whole,
12 is that it's certainly not sufficient as a
13 treatment for gender dysphoria to do psychotherapy
14 alone when medical interventions are necessary.
15 Q. When you say that they did worse just
16 now, are you referring to compared to the other
17 group?
18 A. Yes.
19 Q. Are you referring to the Costa study?
20 A. It was the Costa study and the Turban
21 study.
22 Q. The Turban study based on the USTS data?
23 A. That is correct.
24 Q. And are you aware that health

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1 authorities in Sweden have taken steps to restrict
2 the use of puberty blockers and cross-sex hormones
3 for adolescents with gender dysphoria?
4 A. Yes.
5 Q. And did you ever attempt to review the
6 evidentiary basis for those decisions?
7 A. I have not read the Swedish reports that
8 I can recall, but it's possible that I have. But,
9 again, similar to the Cass report, the underlying
10 data that all of these folks have been drawing from
11 has been published and reviewed.
12 (WHEREUPON, a certain document was
13 marked Janssen Deposition Exhibit
14 No. 17, for identification.)
15 BY MR. RAMER:
16 Q. Dr. Janssen, you have been handed what
17 has been marked as Exhibit 17, and the title is A
18 Systematic Review of Hormone Treatment for Children
19 with Gender Dysphoria and Recommendations for
20 Research; is that correct?
21 A. That is what it says.
22 Q. And have you seen this article before?
23 A. I have seen this article before. I
24 can't recall when I read it.

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1 Q. And do you understand this to be a
2 systematic review commissioned by the Swedish
3 government?
4 A. I don't see where it says it was
5 commissioned by the Swedish government, but if that
6 is what you are saying, I'm happy to stipulate
7 that.
8 Q. We can put it on the record. Go to
9 2280, which is the second page of the study, and
10 the right column under 2.1, the first sentence
11 says, This systematic review originated from a
12 two-year commissioned work from the governmental
13 body of The Swedish Agency for Health Technology
14 Assessment and Assessment of Social Services, SBU;
15 is that right?
16 A. Yes. That is what it says. I cannot
17 testify to being an expert on the governmental
18 structures of health care delivery in Sweden.
19 Q. That is fair. On the same page, up
20 toward the top in the gray box, there's the
21 conclusion, and the first sentence says, Evidence
22 to assess the effects of hormone treatment on the
23 above fields in children with gender dysphoria is
24 insufficient. Do you see that?

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1 A. I see that.
2 Q. And do you disagree with that
3 conclusion?
4 A. I disagree with the structure of the
5 sentence. Insufficient for what? It's unclear.
6 Q. Insufficient -- you don't think that
7 sentence is talking about whether the evidence is
8 sufficient to assess the effects of hormone
9 treatment?
10 A. Yeah. It's not defined clearly to me.
11 If I were editing this paper, I would say,
12 Insufficient in what way? Please expand.
13 Q. Going back to the first page, which is
14 2279. Again, in the gray box, the first category,
15 the aim says, The aim of this systematic review was
16 to assess the effects on psychosocial and mental
17 health, cognition, body composition, and metabolic
18 markers, hormone treatment in children with gender
19 dysphoria; is that right?
20 A. That's correct.
21 Q. So then if we go back to 2208 and read
22 the conclusion again, that says, Evidence to assess
23 the effects of hormone treatment on the above
24 fields in children with gender dysphoria is

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1 insufficient. My question is, do you disagree with
2 that conclusion?
3 A. So on page 2282, Section 3.3, the
4 authors define what outcomes they are looking at
5 for psychosocial and mental health. They identify
6 the CGAS, which is the Childrens Global Assessment
7 Scale, which is just a gestalt view of functioning,
8 and then they define the other things that we are
9 looking at, including the Child Behavior Checklist
10 and the Youth Self-Report, which are looking at
11 core symptoms of externalizing and internalizing
12 symptoms, primarily depression and anxiety. There
13 are no measures of gender dysphoria that are
14 included in psychosocial and mental health.
15 Working with patients, when they come and describe
16 their experience of gender dysphoria, gender
17 dysphoria symptoms significantly impact mental
18 health.
19 So when I read something that says it is
20 insufficient to demonstrate efficacy on mental
21 health but the measurements used are specifically
22 looking at depression and anxiety and not at gender
23 dysphoria, I think that is incomplete.
24 Q. Do you know -- I mean, that paragraph

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1 that you just read, that is the authors describing
2 the studies that were in the systematic review,
3 correct?
4 A. That's correct.
5 Q. Do you know what any of those studies
6 are that they are citing there?
7 A. Going back through 14 through 19, I
8 would have to go back and look. Some of the
9 studies did not include and some of the studies did
10 include symptoms of gender dysphoria.
11 Q. Is Footnote 14 the de Vries study?
12 A. Yes.
13 Q. Switching gears a little bit.
14 A. So sorry. I apologize. To go back --
15 Q. No, please.
16 A. If we look at that table.
17 Q. Which table?
18 A. Table 1. Many of them do have
19 measurements of core symptoms of gender dysphoria,
20 and it's notable to me that the authors neglected
21 to include those in the analysis.
22 Q. Which --
23 A. Anything that says UGDS has a measure of
24 gender dysphoria.

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1 Q. And how is the UGDS used in the Dutch
2 studies?
3 A. To track severity of gender dysphoria
4 symptoms over time.
5 Q. Do you know specifically in the study
6 how they deployed it with the subjects?
7 A. I don't know the frequency with which
8 they deployed it in their studies. I would have to
9 look at the specific methodology of each published
10 study to know.
11 Q. If they had flipped the UGDS scales for
12 the subjects, so let me just -- it's going to be a
13 longwinded explanation and then I'll ask the
14 question.
15 Suppose that when these subjects entered
16 the study, they gave natal males the UGDS
17 questionnaire that is intended for males, and then
18 after transition, they gave now transgender females
19 the UGDS scale or questionnaire for females. Would
20 that tell us anything about the effect of the
21 treatment on gender dysphoria?
22 A. I'm not sure I'm following the question.
23 It's not tracking the patient experience in any
24 meaningful way. The appreciation and experience of

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1 individuals with gender dysphoria is because of the
2 incongruence, and so if you are having a measure
3 that you want to track longitudinally, you want to
4 use as much as possible the same measure over time.
5 So to switch measures at the end just does not make
6 sense psychometrically, but it also doesn't make
7 sense clinically for the actual clinical experience
8 of the patients and the questions that are asked in
9 the Utrecht Gender Dysphoria Scale.
10 Q. Why does it not make sense clinically?
11 A. Because it's not what the patients are
12 experiencing.
13 Q. So how would you use it? How would you
14 use the UGDS to measure the outcome when you are
15 testing the efficacy of pubertal suppression and
16 cross-sex hormones?
17 A. The Utrecht Gender Dysphoria Scale -- I
18 can't say that I would vouch for it in all
19 situations for all people, but the Utrecht Gender
20 Dysphoria Scale measures severity, intensity, and
21 types of symptoms of gender dysphoria. One would
22 hope that as you treat gender dysphoria, that
23 intensity of distress would improve over time.
24 That is what we are measuring with the Utrecht

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1 Gender Dysphoria Scale.
2 Q. Is it a questionnaire?
3 A. It's a guided questionnaire. The
4 provider or the clinician fills it out.
5 Q. And are there two forms of the guided
6 questionnaire, one for natal females and one for
7 natal males?
8 A. That is correct.
9 Q. So then how do you use that to measure
10 the improvement? Which one do you give the patient
11 on the other side of the transition?
12 A. The same as you did before.
13 Q. The male one -- sorry. If you had a
14 natal male, you will give them the male
15 questionnaire?
16 A. Yes.
17 Q. And then they will go through transition
18 and you would give them the male questionnaire
19 again?
20 A. Yes.
21 Q. Isn't -- wouldn't the male questionnaire
22 be asking them, How does it feel when people call
23 you a male, et cetera?
24 A. We can -- if you have a copy, we could

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1 go through it, but that is not what the -- you
2 would have to go line by line and see how it
3 impacts it. What it measures is severity of
4 distress in multiple different domains. We would
5 anticipate that if a treatment is effective for
6 gender dysphoria, a degree of distress would
7 improve over time. And if you more misalignment of
8 your body that leads to distress, that is going to
9 lead to an elevated score. As you get more
10 congruence, less distress, your scores would go
11 down.
12 Q. More congruence with what though?
13 A. Congruence between your sense of self
14 and your lived experience and your body alignment.
15 Q. But so you would be giving transgender
16 females the questionnaire that is written for natal
17 males, correct?
18 A. Correct. That is how the study was --
19 that is how the instrument was designed, so that is
20 the appropriate use of the instrument. It was not
21 designed or tested to do the opposite, so it would
22 not be an appropriate use of that instrument.
23 Q. So switching gears now. Do you agree
24 that social media can play a powerful role in the

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1 contagion of suicidal behavior among youth?
2 MR. RAY: Object to form.
3 BY THE WITNESS:
4 A. We would have to break that down in
5 terms of what you mean by "contagion" and what you
6 mean by "powerful."
7 BY MR. RAMER:
8 Q. We'll just do it this way, I guess.
9 (WHEREUPON, a certain document was
10 marked Janssen Deposition Exhibit
11 No. 18, for identification.)
12 BY MR. RAMER:
13 Q. Dr. Janssen, you have been handed what
14 has been marked as Exhibit 18, and the title is,
15 Editorial: Dialectical Behavior Therapy: More is
16 Not Always Better When Different is Required,
17 correct?
18 A. Yes.
19 Q. Did you help author this?
20 A. I did.
21 Q. In the first paragraph towards the very
22 bottom, you discuss recent research suggesting the
23 powerful role of social media in supporting
24 contagion of suicidal behavior among youth,

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1 correct?
2 A. Yes.
3 Q. Can you explain what you mean by
4 "powerful" and "contagion" in that sentence?
5 A. I would have to get the Sedgwick article
6 to tell you the specifics.
7 Q. Can you clarify what you mean by that?
8 A. That the authors of the Sedgwick article
9 documented their impact, the impact of social media
10 contagion on suicidality in youth, but they have
11 the details in that paper. I don't have them here
12 in front of me. I don't recall them specifically.
13 Q. Do you think that social media plays a
14 role in supporting contagion suicidal behavior in
15 youth?
16 A. It can certainly.
17 Q. How so?
18 A. There has actually been a robust amount
19 of evidence that how suicide is talked about can
20 influence whether or not members of a peer group
21 may act on concurrent suicidal thoughts.
22 Q. What did the research tell us?
23 A. Part of it -- I would have to go back
24 and look at all of the specifics, but by and large,

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1 from my recollection of the research, doing things
2 like having pictures of where the suicide happened,
3 overly extolling the victim of the death by
4 suicide, valorizing that patient, normalizing it
5 can increase the risk of others in the same social
6 network acting on suicidal thoughts.
7 Q. Then same page, same column, the third
8 paragraph, the first sentence says, Contagion of
9 suicidal behavior among youth and their high level
10 of engagement with social media are particularly
11 concerning; is that right?
12 A. Uh-huh.
13 Q. So do you think that high level of
14 engagement with social media plays a role in the
15 contagion of suicidal behavior among youth?
16 A. I think normalization of suicide in the
17 context of a social media space is not a positive
18 development.
19 Q. Then two sentences later, it says,
20 Children now have in their pockets access to
21 communities and information that encourage
22 exploration of suicide and teach children how to
23 access more lethal means online, correct?
24 A. Yes.

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1 Q. And do you agree with that statement?
2 A. I do.
3 Q. So did you think that social media can
4 play a role in contagion of gender dysphoria among
5 youth?
6 A. Of the diagnosis of gender dysphoria, I
7 do not.
8 Q. Do you think that contagion of gender
9 dysphoria among youth and youth's level of
10 engagement with social media is concerning?
11 A. I would not use the word "contagion" to
12 describe an identity development process.
13 Q. Do you agree that minors have access to
14 communities and information that encourage
15 exploration of their gender?
16 A. Yes.
17 Q. Do you agree that minors have access to
18 communities and information that teach minors how
19 to access medical interventions for gender
20 transitioning?
21 A. Yes.
22 Q. For adults, do you agree that therapy or
23 mental health care should not be required as part
24 of the transition process?

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1 A. That is context dependent.
2 Q. And can you explain what the context is
3 that it depends upon?
4 A. Yeah. Psychotherapy is an intervention
5 like any other intervention, in that you have to
6 understand what are your treatment goals and what
7 are the risks and benefits and alternatives to that
8 treatment.
9 For some people, there are no treatment
10 goals that would be indicated for psychotherapy,
11 and in those cases psychotherapy is not indicated.
12 Q. And that would not be the case -- do you
13 think that -- do you agree that mental health care
14 should not be required as part of the transition
15 process for adolescents?
16 A. It's not indicated in all cases. A
17 mental health evaluation is recommended as a part
18 of this process, but ongoing psychotherapy is not a
19 required element for all cases.
20 Q. All right. I would like to go back to
21 Exhibit 7, which is your report. I would like to
22 go to page 3 and third paragraph, it looks like the
23 third sentence, you write, The WPATH SOC has been
24 recognized and adopted as the prevailing standard

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1 of care by the major professional associations,
2 medical and mental health providers in the United
3 States, including the American Medical Association,
4 American Academy of Pediatrics, and then a few
5 other organizations; is that right?
6 A. Yes.
7 Q. And how do you know that?
8 A. From my recollection, it is from seeing
9 statements of endorsement.
10 Q. You have seen statements of endorsement
11 from the American Medical Association of the WPATH
12 SOC 8?
13 A. That is my recollection.
14 Q. Is there any place where somebody in the
15 public could go find that statement and verify it?
16 A. I do not know.
17 Q. And you have also seen statements of
18 endorsement of the SOC 8 from the American Medical
19 Association?
20 A. From my recollection, yes.
21 Q. Go to page 9. So on page 9, first full
22 paragraph, second sentence, you write, Following
23 transition transgender young people are often able
24 to reduce dosage of psychiatric medications,

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1 correct?
2 A. Correct.
3 Q. And is that based on your clinical
4 experience?
5 A. Yeah.
6 Q. Do you agree that the data in the
7 Glintborg study says the opposite?
8 A. I would have to see the Glintborg study.
9 MR. RAY: I bet he's got it.
10 (WHEREUPON, a certain document was
11 marked Janssen Deposition Exhibit
12 No. 19, for identification.)
13 BY MR. RAMER:
14 Q. And you have been handed what has been
15 marked as Exhibit 19, and is this the supplemental
16 expert report that you submitted in this case?
17 A. It is, yes.
18 Q. I would like to go to page 7.
19 A. Sure.
20 Q. And just a few lines up from the bottom,
21 where you are describing the Glintborg study, you
22 say, Correspondingly, the proportion of transgender
23 individuals prescribed psychopharmacological agents
24 increased significantly from baseline to diagnosis;

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1 is that right?
2 A. That's right.
3 Q. And so do you agree that the data in
4 this study contradicts what you say in page 9 of
5 your report?
6 A. I do not.
7 Q. What is the distinction I'm missing?
8 A. The distinction is between the
9 difference of a class effect and an individual
10 effect. As a class of folks, transgender
11 individuals, just like any other individuals who
12 are required to have a mental health assessment,
13 are going to have identification of mental illness
14 that requires treatment, and you'll see increases
15 of rates of prescribing.
16 That is different from the question of,
17 in an individual who has psychiatric medication at
18 baseline, who has access to gender-affirming
19 treatments, whether that individual patient will
20 see improvements in mental health care, such that
21 they are able to see reduction of medication doses
22 or medication numbers.
23 Q. So are you distinguishing between dosage
24 and number of prescribed agents?

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1 A. Yes.
2 Q. Still on page 9, you cite a study by
3 Diane Chen, correct?
4 A. I do, yeah.
5 (WHEREUPON, a certain document was
6 marked Janssen Deposition Exhibit
7 No. 20, for identification.)
8 BY MR. RAMER:
9 Q. And you have been handed what has been
10 marked as Exhibit 20, and about partway down this
11 first page, there's a title that says, Growing
12 Evidence and Remaining Questions in Adolescent
13 Transgender Care; is that right?
14 A. Yes.
15 Q. And the lead author of this editorial is
16 Annelou de Vries, correct?
17 A. Yes.
18 Q. And that is the de Vries who helped with
19 the Dutch studies, correct?
20 A. That is correct.
21 Q. And do you agree, de Vries is an expert
22 in the field of transgender medicine?
23 A. I do.
24 Q. And if you could go page 277, which is

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1 the third page, and you look at Footnote 1, this
2 editorial is discussing the Chen article that you
3 cite, correct?
4 A. It is, yes.
5 Q. And have you seen this before?
6 A. I have.
7 Q. Okay. What did you think when you read
8 it?
9 A. Oh, I don't recall what I thought about
10 when I read it.
11 Q. I would like to go to page 276, and left
12 column, second full paragraph, second sentence, it
13 says, Although overall psychological functioning in
14 the study participants improved, there was
15 substantial variation among participants. A
16 considerable number still had depression, anxiety,
17 or both at 24 months and two died by suicide. Did
18 I read that correctly?
19 A. You did, yeah.
20 Q. And were you aware of these facts before
21 you cited the Chen article in your report?
22 A. Yes.
23 Q. And did these facts concern you?
24 A. Death by suicide always concerns me.

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1 Q. Do you think that -- does that concern
2 extend to the reliability of the study?
3 A. It does not.
4 Q. Why not?
5 A. Because outcomes that are -- outcomes
6 such as this are not an indication of poor study
7 design. Again, what we are looking at are the
8 outcomes that are studied and the interventions
9 based upon those outcomes. Treatment of
10 suicidality is a different process than treatment
11 of gender dysphoria.
12 Q. But does gender dysphoria lead to
13 suicidality?
14 A. In my clinical experience, it's how many
15 of my patients describe it.
16 Q. But does it -- apart from the
17 description, does gender dysphoria lead to
18 suicidality?
19 A. So there's many reasons for suicidality,
20 and the good data that we have on adolescent
21 suicidality in particular demonstrate that the
22 majority of adolescents who die by suicide have no
23 co-occurring mental health disorders and yet they
24 die by suicide.

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1 Why do they die by suicide? Because
2 there are in-the-moment challenges, distresses,
3 et cetera, plus access to lethal means, and that is
4 the combination that leads to death by suicide
5 among this population.
6 Reducing gender dysphoria does not
7 reduce access to lethal means nor does it reduce
8 access to adverse events that can often trigger
9 intense suicidal thoughts. Evidence-based
10 interventions, like collaborative assessment and
11 management of suicidality or DBT are effective
12 interventions for suicidality. Stanley Brown's
13 safety plan, lethal means counseling, these are
14 evidence-based interventions that reduce outcomes
15 of suicidality.
16 We would hope that some of the milieu
17 that leads to increased suicidal thinking would
18 improve with treatment of the gender dysphoria, but
19 we can't anticipate that treatment of dysphoria is
20 going to specifically treat suicidality because
21 it's a different phenomenology.
22 Q. So same paragraph, two sentences later,
23 it says, However, other possible determinants of
24 outcomes were not reported, particularly the extent

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1 of mental health care provided throughout GAH
2 treatment. Did I read that correctly?
3 A. You read that correctly.
4 Q. And what is your understanding of what
5 de Vries is saying there?
6 A. She's saying because it was not
7 reported, we can't really comment on it.
8 Q. She's saying we can't comment on it, or
9 she's saying that this mental health care could be
10 a possible determinant of outcome?
11 A. From my read of it, it's that we can't
12 draw any conclusions because it was not included in
13 the analysis.
14 Q. And would that preclude drawing
15 conclusions about the medical interventions as
16 well?
17 A. I don't think it would, no.
18 Q. Why not?
19 A. It's not how the study was designed.
20 Q. What do you mean by that?
21 A. You would have to go back and look at
22 the specific Chen study itself to review the
23 specifics of the study design.
24 Q. But you think there's a zero percent

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1 chance that any improvements were due to mental
2 health care?
3 A. Well, you are talking to a psychiatrist,
4 so I'm never going to say that there's a zero
5 percent impact. And I think that mental health
6 interventions are often incredibly beneficial, so I
7 would never say that it is a zero percent.
8 Q. 10 percent?
9 A. I could not tell you. There's no
10 specific percentage that I would feel comfortable
11 without data.
12 Q. Do you feel comfortable thinking that
13 the measures of improvements from the medical
14 interventions are attributable to the medical
15 interventions?
16 A. When that is combined with the rest of
17 the extant literature with the clinical experience
18 and the reports of the patients that have been
19 through this process, as well as the other research
20 types that have looked at longer term outcomes,
21 yes, I feel confident that this reflects my
22 clinical experience in working with these patients.
23 Q. And so just to confirm, you do not think
24 that de Vries is talking about mental health care

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1 as a possible confounding variable in this
2 sentence; is that correct?
3 A. I think she is talking about, but it's
4 not possible to draw conclusions when the
5 description of the additional mental health care
6 delivery was not included in the analysis.
7 Q. What do you think a confounding variable
8 is?
9 A. Something that contributes to the
10 outcome.
11 Q. And why is it labelled confounding?
12 A. Because it's an additional element that
13 can potentially impact outcome.
14 MR. RAMER: Maybe take a short one, short
15 break, does that work?
16 MR. RAY: Absolutely.
17 (WHEREUPON, a recess was had.)
18 MR. FLETCHER: I was saying, the United States
19 is going to order a copy of the transcript,
20 whenever it's available.
21 BY MR. RAMER:
22 Q. Dr. Janssen, I would like to go back to
23 Exhibit 7, which is your expert report, and,
24 specifically, I would like to go to page 15.

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1 A. Okay.
2 Q. And in the first full paragraph, kind of
3 a couple sentences from the bottom of that
4 paragraph, you say, The distress associated with
5 gender dysphoria can also amplify co-occurring
6 conditions that develop independently of the gender
7 dysphoria; is that correct?
8 A. That is correct.
9 Q. And can you just explain what you mean
10 by that?
11 A. Sure. So a concrete example, you have
12 an adolescent with major depressive disorder. One
13 of the treatments for major depressive disorder is
14 called behavioral activation, essentially being
15 around people, doing things that you enjoy.
16 If the gender dysphoria is such that
17 your distress makes it feel uncomfortable to be
18 around friends or to go to school or to engage in
19 sports or other activities, then you don't have
20 access to that same degree of behavior activation,
21 and depressive symptoms can worsen.
22 Q. Can symptoms from co-occurring
23 conditions that developed independently from gender
24 dysphoria ever amplify the distress associated with

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1 gender dysphoria?
2 A. I think that's accurate. I think more
3 often what we see in clinical practice is that the
4 co-occurring mental health disorders interfere with
5 the capacity to tolerate the distress from gender
6 dysphoria.
7 Q. And in that situation, which issue do
8 you target first?
9 A. That's not how it works in clinical
10 practice. If a patient comes to me with ADHD and
11 depression, I'm going to treat both ADHD and
12 depression.
13 Q. But what if the treatment of one would
14 help resolve and, thus, negate the need for the
15 treatment of the other?
16 A. That is a part of your assessment that
17 you would do prior to initiating a treatment plan.
18 If your treatment plan and your agreement that you
19 have worked with your patient and family is to do
20 treatment consecutively as opposed to concurrently,
21 you test the efficacy of the treatment on the core
22 symptoms that you are working to improve.
23 Q. Would you ever take into account the
24 degree of intrusiveness for the interventions for

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1 one versus the interventions for the other when
2 making that decision?
3 A. The families make the decision, and
4 there's a number of factors that are involved that
5 families often draw from. The intensity of the
6 intervention, the frequency of the intervention.
7 There's many, many factors that parents engage in
8 around making these decisions.
9 Q. When you are making a recommendation, do
10 you ever take into account the intrusiveness of the
11 interventions for one versus the other when
12 deciding how to proceed?
13 A. I offer and discuss what the
14 implications of all of the interventions are, so
15 that families can make an informed decision.
16 Q. But you make a suggestion, don't you?
17 A. I make a suggestion based upon the best
18 available evidence, but the suggestion is couched
19 within multiple options.
20 Q. I guess I'm not sure I understand. I
21 mean, when the family is coming to you, are you --
22 you don't just, like, say, Here is -- here are
23 these options, go forth and choose. Don't you come
24 up with a suggestion of, Based on what I'm seeing

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1 and what I know, I think you should go this route,
2 these are other options you can consider? Which
3 one sounds more accurate?
4 A. Neither. It's a collaborative
5 discussion that you have with the patients and
6 families, many of whom already come into care with
7 thoughts about what might be appropriate. My job,
8 as a physician working with these patients and
9 their families, is to make my assessment and
10 provide the options of care.
11 I will often describe what level of
12 support for the various options that we have are.
13 Outside of the world of gender, this is not
14 different from patients that I'm treating with
15 depression or anxiety. We know that for severe
16 depression, medication in addition to therapy is
17 what is recommended as the likeliest to improve
18 outcomes in the quickest way possible.
19 Many families don't want medication, and
20 so they opt not to do that. So even though I might
21 make a recommendation, ultimately the decision is
22 the patient and the family's.
23 Q. And when you say "describe the level of
24 support," are you referring to evidentiary support?

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1 A. Yes.
2 Q. So sticking with your declar- -- your
3 report, Exhibit 7, same page, towards the bottom,
4 you say, It is often seen that the gender dysphoria
5 would eclipse the person's co-occurring conditions.
6 Do you see that?
7 A. I do.
8 Q. What does it mean for one condition to
9 eclipse another?
10 A. I think in the example that I gave about
11 a lack of access to behavioral activation because
12 of the gender dysphoria symptoms would be an
13 example of that.
14 Q. Could you remind me of what behavioral
15 activation is?
16 A. So if a patient needs to be out and
17 about, do some exercise, be with friends as a way
18 of treating depression, and they are not able to do
19 that because of gender dysphoria symptoms, it makes
20 it hard to treat the depression.
21 Q. And in that situation -- it's a
22 hypothetical, I understand -- you would start with
23 treating the gender dysphoria as opposed to finding
24 ways to help with the activation; is that right?

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1 A. We would do it concurrently.
2 Q. On the next page, you say -- first full
3 sentence on the page, you say, The increased
4 distress from their gender dysphoria would
5 translate to self-harm; is that correct?
6 A. Yes, it can. Yes.
7 Q. You say "would"?
8 A. Yes. It would resort to negative coping
9 mechanisms, as an example, self-harm. It's not --
10 Q. So the i.e. should be an e.g.? I mean,
11 not to be pedantic?
12 A. No, please be pedantic. Yes, it should
13 be an e.g. there.
14 Q. So you do not think it has been
15 established that delaying treatment will cause
16 self-harm; is that right?
17 A. If we are talking about individual or
18 population-based studies, there's a difference.
19 Absolutely in my clinical experience, I have seen
20 delays in accessing gender dysphoria medical
21 interventions leading to increased frequency and
22 severity of self-harm. There have not been
23 published studies looking at large populations
24 because there has not been a study on rates of

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1 self-harm in this context.
2 Q. But, presumably, they would show that
3 based on the individual; is that right?
4 A. We don't know. That would be a testable
5 hypothesis that we would like to -- we would be
6 happy to study, but the studies have not yet been
7 done.
8 Q. But you observed it in this individual?
9 A. Yes.
10 Q. And you can say that the delaying of the
11 treatment caused the self-harm?
12 A. That has been the experience that I have
13 had clinically, yes.
14 Q. Why would that not be guaranteed to hold
15 constant with a large population, if you have
16 concluded that it caused the self-harm?
17 A. Because that is not how studies work. I
18 have a hypothesis, and I would imagine that it
19 would hold up if we looked at a population of
20 patients who utilized self-harm as a maladaptive
21 coping tool for gender dysphoria. My hypothesis
22 would be that withholding treatment for gender
23 dysphoria would likely exacerbate intensity and
24 frequency of self-harm. But that is a testable

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1 hypothesis, so I'm not going to presuppose what the
2 conclusion of a study is that has not yet been
3 done.
4 Q. But then doesn't that also preclude you
5 from saying that in this individual, the delaying
6 of treatment caused the self-harm?
7 A. No, because there's a difference between
8 individual evaluations and assessment, which is
9 core clinical care in a population-based study.
10 Q. I guess I don't know -- my question
11 is -- why is the distinction between individual
12 versus population, as opposed to the distinction is
13 between deciding something has caused something
14 else and merely stating that you have observed this
15 association?
16 A. There might be a distinction without a
17 difference here. My patients have told me, I can't
18 manage this distress. I can't wait any longer, and
19 I don't know what else to do and resort to
20 self-harm. Those same patients I have seen improve
21 when they have access to the medical interventions
22 for gender dysphoria. That is separate from
23 looking at a class of patients and doing
24 evaluations about an intervention on a class of

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1 patients.
2 Q. Do you think the use of pubertal
3 suppression to treat gender dysphoria is beyond
4 debate?
5 A. Nothing is beyond debate.
6 Q. Do you think that reasonable experts
7 could dispute that pubertal suppression is
8 effective for treating gender dysphoria?
9 A. I mean, reasonableness and evaluating
10 reasonableness, I don't know how you want me to do
11 that. I think that the evidentiary -- let me
12 figure out how to say this.
13 I think pairing the evidentiary support
14 with clinical experience, it would be hard to find
15 an expert who can reasonably combine those two
16 things and say that there is not robust support
17 that puberty blockers are safe and effective
18 treatments for gender dysphoria.
19 Q. And is it the same answer for the use of
20 cross-sex hormones to treat gender dysphoria in
21 adolescents?
22 A. Yes.
23 Q. Okay. Going to Exhibit 19, which is
24 your supplemental expert report, and page 4,

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1 paragraph 7 starts, and you are excusing the
2 Morandini study, but I have a question for you on
3 page 5, where that paragraph carries over.
4 A. Uh-huh.
5 Q. And I think it is relevant to what we
6 were discussing earlier, but I just want to make
7 sure that I understand the concept.
8 You are faulting -- so page 5, the end
9 of paragraph 7, last two sentences. You are
10 faulting the Morandini study because the authors
11 used anxiety, depression, and suicidality measures
12 as opposed to gender dysphoria, correct?
13 A. That is essentially correct, that the
14 authors have used those three criteria exclusively
15 as a definition for mental health, at the exclusion
16 of the core symptoms of mental health that the
17 intervention is aimed to be treating, which is
18 gender dysphoria.
19 Q. And for that reason -- I guess, what if
20 they had included the measurements of gender
21 dysphoria and they were just neutral, no changes
22 either way?
23 A. Then that would be useful information to
24 understand and to learn, and you would analyze the

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1 strengths and benefits of the study designed to be
2 able to give weight to that conclusion.
3 Q. And next paragraph, next sentence, you
4 also fault the study for being a cross-sectional
5 design; is that right?
6 A. Correct.
7 Q. And what is the significance of that?
8 A. I would not fault it for being a
9 cross-sectional design, so I would not say that
10 that is accurate. So I apologize for saying yep to
11 that, but it comes with its own set of limitations.
12 Q. And what kind of limitations?
13 A. It's hard to prove causality in a
14 cross-sectional designed study, particularly in
15 this cross-sectional designed study that was
16 looking at indicators of mental health at the time
17 of initiation of care and not at the time of
18 completion of care.
19 Q. Do you think that we have established
20 causation for the effectiveness -- sorry. Let me
21 back up.
22 Given the state of the literature, do
23 you think that research has established causation
24 for the effectiveness of pubertal suppression in

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1 treating gender dysphoria?
2 A. I think causation is a tricky word in
3 the medical literature. I think that it took
4 decades of epidemiologic research to say
5 conclusively that smoking causes lung cancer, even
6 though the preponderance of the evidence was very
7 clear about that for many decades before the
8 statistical power was developed to be able to make
9 that very firm conclusion.
10 So the definition of causation or not is
11 a little bit tricky in this context. Do we have a
12 preponderance of the evidence that suggests this is
13 safe and effective care for the core symptoms of
14 gender dysphoria and improves functioning and
15 quality of life? Yes, we do.
16 Q. And on pages -- sticking with
17 Exhibit 19, on pages 7 through 11.
18 A. Uh-huh.
19 Q. You analyze the Kaltiala and Glintborg
20 studies, correct?
21 A. That is correct.
22 Q. And are there any flaws in those studies
23 that you did not describe in your report?
24 A. I'm sure there are, but --

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1 Q. You are sure there are?
2 A. There are flaws in every study. I can't
3 categorize every single flaw of every single study,
4 but I would have to look at the studies again more
5 carefully.
6 Q. And so when you say that you are sure
7 there are, that is just applicable to every study,
8 not something specific to Kaltiala and Glintborg;
9 is that correct?
10 A. Correct.
11 Q. Okay. And are you a member of the
12 American Academy of Child and Adolescent
13 Psychiatry?
14 A. Yes.
15 Q. And the acronym for that, do you say
16 AACAP?
17 A. AACAP.
18 Q. Just AACAP?
19 A. Yeah.
20 Q. And in your role at AACAP, have you ever
21 interacted with Kristopher Kaliebe?
22 A. Yes, I have.
23 Q. In what context?
24 A. He asked if I would be -- my initial

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1 interaction with him was when he asked if I would
2 be a discussant on a panel that he was proposing
3 for one of the AACAP annual meetings.
4 Q. And what was the substance of that
5 discussion?
6 A. The thing I remember most about that
7 discussion is his description of himself as
8 somebody with an interest in but not expertise in
9 gender dysphoria, and that -- it was a lovely
10 back-and-forth conversation about the state of
11 affairs in the world of gender dysphoria research,
12 and it was left with me saying that I would
13 consider being on the panel, depending upon the
14 content of the panel.
15 Q. And what was the content that he wanted
16 to discuss?
17 A. From my recollection, it was about
18 skepticism towards research in transgender health.
19 Q. Did you read his expert report that he
20 submitted in this case?
21 A. I did.
22 Q. Did you read the part of the report that
23 suggests you suppressed a panel at an AACAP
24 conference?

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1 A. I did read that.
2 Q. And what is your response to that?
3 A. It's not true.
4 Q. Which part of it is not true?
5 A. I would have to look at the specific
6 report to give you specifics on my response to it.
7 Q. Do you remember him approaching you
8 about a panel?
9 A. I was not involved in the selection of
10 any of the panels that he was involved in.
11 Q. And do you think that members of AACAP
12 suppress ideas that they disagree with?
13 A. No, I do not.
14 Q. Are you familiar with the research of
15 Dr. Littman?
16 A. Yes.
17 Q. And what are your thoughts on the
18 articles that she has published?
19 A. It depends upon the specific article. I
20 think that her initial foray into the world of
21 transgender health research was low quality and
22 poorly designed and unethical. The second one was
23 better but still had significant problems in
24 design.

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1 Q. When you say "low quality," are you
2 using specific --
3 A. Not a specific methodology or grading
4 criteria.
5 Q. And did you review the medical records
6 of any of the plaintiffs in this case?
7 A. No.
8 Q. Are you a neurologist?
9 A. No. I'm boarded by the American -- the
10 ABPN.
11 Q. And what is that?
12 A. I'm trying to remember the specific
13 acronym. American Board of Psychiatrists and
14 Neurologists.
15 Q. And so are you only under the P part of
16 that acronym?
17 A. We both get the same licensure, but, no,
18 I'm not a neurologist.
19 Q. Are you a surgeon?
20 A. No.
21 Q. Are you a urologist?
22 A. I am not.
23 Q. Are you a gynecologist?
24 A. I am not.

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1 Q. Are you a bioethicist?
2 A. I'm not.
3 Q. Are you a social worker?
4 A. I'm not.
5 MR. RAMER: Dr. Janssen, I think that those
6 are all of the questions that I have for you. I'll
7 thank you very much for your time, and I'll turn it
8 over to your counsel, if counsel has questions.
9 MR. RAY: I don't have any questions. I don't
10 also think that there was anything confidential --
11 MR. RAMER: Correct.
12 MR. RAY: -- today, so I don't think that we
13 need to mark the transcript. The witness will
14 review and sign his transcript. I really
15 appreciate everyone's time on a Friday. Hope
16 everyone has safe travels home.
17 MR. RAMER: Thank you. Likewise.
18 FURTHER DEPONENT SAITH NOT.
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1 STATE OF ILLINOIS)
) SS:
2 COUNTY OF C O O K)
3
I, KRISTIN C. BRAJKOVICH, a Certified
4 Shorthand Reporter of said state, do hereby
certify:
5
That previous to the commencement of the
6 examination of the witness, the witness was duly
sworn to testify the whole truth concerning the
7 matters herein;
8 That the foregoing deposition transcript
was reported stenographically by me,
9 was thereafter reduced to typewriting under my
personal direction and constitutes a true record
10 of the testimony given and the proceedings had;
11 That the said deposition was taken
before me at the time and place specified;
12
That I am not a relative or employee
13 or attorney or counsel, nor a relative or
employee of such attorney or counsel for any of
14 the parties hereto, nor interested directly or
indirectly in the outcome of this action.
15
IN WITNESS WHEREOF, I do hereunto set my
16 hand and affix my seal of office at Chicago,
Illinois, this 3rd of May, 2024.
17
18
19
20
21 KRISTIN C. BRAJKOVICH
C.S.R. Certificate No. 84-3810.
22
23
24

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3 Case Caption: Brianna Boe, United States of
4 America v. Hon. Steve Marshall,
5 et al.
6
7 DECLARATION UNDER PENALTY OF PERJURY
8
9 I declare under penalty of perjury that
10 I have read the entire transcript of my deposition
11 taken in the captioned matter or the same has been
12 read to me, and the same is true and accurate, save
13 and except for changes and/or corrections, if any,
14 as indicated by me on the DEPOSITION ERRATA SHEET
15 hereof, with the understanding that I offer these
16 changes as if still under oath.
17
18 Signed on the ___________ day of
19 ________________, 20_______.
20
21
22
23 ______________________________________
24 ARON JANSSEN, M.D.

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EXHIBIT 67

CHAPTER 7 Children

These Standards of Care pertain to prepubescent gender diverse children and are based on research, ethical principles, and accumulated expert knowledge. The principles underlying these standards include the following 1) childhood gender diversity is an expected aspect of general human development (Endocrine Society and Pediatric Endocrine Society, 2020; Telfer et al., 2018); 2) childhood gender diversity is not a pathology or mental health disorder (Endocrine Society and Pediatric Endocrine Society, 2020; Oliphant et al., 2018; Telfer et al., 2018); 3) diverse gender expressions in children cannot always be assumed to reflect a transgender identity or gender incongruence (Ehrensaft, 2016; Ehrensaft, 2018; Rael et al., 2019); 4) guidance from mental health professionals (MHPs) with expertise in gender care for children can be helpful in supporting positive adaptation as well as discernment of gender-related needs over time (APA, 2015; Ehrensaft, 2018; Telfer et al., 2018); 5) conversion therapies for gender diversity in children (i.e., any "therapeutic" attempts to compel a gender diverse child through words, actions, or both to identify with, or behave in accordance with, the gender associated with the sex assigned at birth are harmful and we repudiate their use (APA, 2021; Ashley, 2019b, Paré, 2020; SAMHSA, 2015; Telfer et al., 2018; UN Human Rights Council, 2020).

Throughout the text, the term "health care professional" (HCP) is used broadly to refer to professionals working with gender diverse children. Unlike pubescent youth and adults, prepubescent gender diverse children are not eligible to access medical intervention (Pediatric Endocrine Society, 2020); therefore, when professional input is sought, it is most likely to be from an HCP specialized in psychosocial supports and gender development. Thus, this chapter is uniquely focused on developmentally appropriate psychosocial practices, although other HCPs, such as pediatricians and family practice HCPs may also find these standards useful as they engage in professional work with gender diverse children and their families.

This chapter employs the term "gender diverse" given that gender trajectories in prepubescent children cannot be predicted and may evolve over time (Steensma, Kreukels et al., 2013). At the same time, this chapter recognizes some children will remain stable in a gender identity they articulate early in life that is discrepant from the sex assigned at birth (Olson et al., 2022). The term, "gender diverse" includes transgender binary and nonbinary children, as well as gender diverse children who will ultimately not identify as transgender later in life. Terminology is inherently culturally bound and evolves over time. Thus, it is possible terms used here may become outdated and we will find better descriptors.

This chapter describes aspects of medical necessary care intended to promote the well-being and gender-related needs of children (see medically necessary statement in the Global Applicability chapter, Statement 2.1). This chapter advocates everyone employs these standards, to the extent possible. There may be situations or locations in which the recommended resources are not fully available. HCPs/teams lacking resources need to work toward meeting these standards. However, if unavoidable limitations preclude components of these recommendations, this should not hinder providing the best services currently available. In those locations where some but not all recommended services exist, choosing not to implement potentially beneficial care services risks harm to a child (Murchison et al., 2016; Telfer et al., 2018; Riggs et al., 2020). Overall, it is imperative to prioritize a child's best interests.

A vast empirical psychological literature indicates early childhood experiences frequently set the stage for lifelong patterns of risk and/or resilience and contribute to a trajectory of development more or less conducive to well-being and a positive quality of life (Anda et al., 2010; Masten & Cicchetti, 2010; Shonkoff & Garner, 2012). The available research indicates, in general, gender diverse youth are at greater risk for experiencing psychological difficulties (Ristori & Steensma, 2016) than age- matched cisgender peers as a result of encountering destructive experiences, including trauma and maltreatment stemming from gender diversity-related rejection and other harsh, non-accepting interactions (Barrow & Apostle, 2018; Giovanardi et al., 2018; Gower, Rider, Brown et al., 2018; Grossman & D'Augelli, 2006; Hendricks & Testa, 2012; Reisner, Greytak

et al., 2015; Roberts et al., 2014; Tishelman & Neumann-Mascis, 2018). Further, literature indicates prepubescent children who are well accepted in their gender diverse identities are generally well-adjusted (Malpas et al., 2018; Olson et al., 2016). Assessment and treatment of children typically emphasizes an *ecological* approach, recognizing children need to be safe and nurtured in each setting they frequent (Belsky, 1993; Bronfenbrenner, 1979; Kaufman & Tishelman, 2018; Lynch & Cicchetti, 1998; Tishelman et al., 2010; Zielinski & Bradshaw, 2006). Thus, the perspective of this chapter draws on basic psychological literature and knowledge of the unique risks to gender diverse children and emphasizes the integration of an ecological approach to understanding their needs and to facilitating positive mental health in all gender care. This perspective prioritizes fostering well-being and quality of life for a child throughout their development. Additionally, this chapter also embraces the viewpoint, supported by the substantial psychological research cited above, that psychosocial gender-affirming care (Hidalgo et al., 2013) for prepubescent children offers a window of opportunity to promote a trajectory of well-being that will sustain them over time and during the transition to adolescence. This approach potentially can mitigate some of the common mental health risks faced by transgender and gender diverse (TGD) teens, as frequently described in literature (Chen et al., 2021; Edwards-Leeper et al., 2017; Haas et al., 2011; Leibowitz & de Vries, 2016; Reisner, Bradford et al., 2015; Reisner, Greytak et al., 2015).

Developmental research has focused on understanding various aspects of gender development in the earliest years of childhood based on a general population of prepubescent children. This research has typically relied on the assumption that child research participants are cisgender (Olezeski et al., 2020) and has reported gender identity stability is established in the preschool years for the general population of children, most of whom are likely not gender diverse (Kohlberg, 1966; Steensma, Kreukels et al., 2013). Recently, developmental research has demonstrated gender diversity can be observed and identified in young prepubescent children (Fast & Olson, 2018; Olson & Gülgöz, 2018; Robles et al., 2016). Nonetheless, empirical study in this area is limited, and at this time there are no psychometrically sound assessment measures capable of reliably and/or fully ascertaining a prepubescent child's self-understanding of their own gender and/or gender-related needs and preferences (Bloom et al., 2021). Therefore, this chapter emphasizes the importance of a nuanced and individualized clinical approach to gender assessment, consistent with the recommendations from various guidelines and literature (Berg & Edwards-Leeper, 2018; de Vries & Cohen-Kettenis, 2012; Ehrensaft, 2018; Steensma & Wensing-Kruger, 2019). Research and clinical experience have indicated gender diversity in prepubescent children may, for some, be fluid; there are no reliable means of predicting an individual child's gender evolution (Edwards-Leeper et al., 2016; Ehrensaft, 2018; Steensma, Kreukels et al., 2013), and the gender-related needs for a particular child may vary over the course of their childhood.

It is important to understand the meaning of the term "assessment" (sometimes used synonymously with the term "evaluation"). There are multiple contexts for assessment (Krishnamurthy et al., 2004) including rapid assessments that take place during an immediate crisis (e.g., safety assessment when a child may be suicidal) and focused assessments when a family may have a circumscribed question, often in the context of a relatively brief consultation (Berg & Edwards-Leeper, 2018). The term assessment is also often used in reference to "diagnostic assessment," which can also be called an "intake" and is for the purpose of determining whether there is an issue that is diagnosable and/or could benefit from a therapeutic process. This chapter focus on comprehensive assessments, useful for understanding a child and family's needs and goals (APA, 2015; de Vries & Cohen-Kettenis, 2012; Srinath et al., 2019; Steensma & Wensing-Kruger, 2019). This type of psychosocial assessment is not necessary for all gender diverse children, but may be requested for a number of reasons. Assessments may present a useful opportunity to start a process of support for a gender diverse child and their family, with the understanding that gender diverse children benefit when their family dynamics include

Statements of Recommendations

7.1- We recommend health care professionals working with gender diverse children receive training and have expertise in gender development and gender diversity in children and possess a general knowledge of gender diversity across the life span.
7.2- We recommend health care professionals working with gender diverse children receive theoretical and evidenced-based training and develop expertise in general child and family mental health across the developmental spectrum.
7.3- We recommend health care professionals working with gender diverse children receive training and develop expertise in autism spectrum disorders and other neurodiversity or collaborate with an expert with relevant expertise when working with autistic/neurodivergent, gender diverse children.
7.4- We recommend health care professionals working with gender diverse children engage in continuing education related to gender diverse children and families.
7.5- We recommend health care professionals conducting an assessment with gender diverse children access and integrate information from multiple sources as part of the assessment.
7.6- We recommend health care professionals conducting an assessment with gender diverse children consider relevant developmental factors, neurocognitive functioning, and language skills.
7.7- We recommend health care professionals conducting an assessment with gender diverse children consider factors that may constrain accurate reporting of gender identity/gender expression by the child and/or family/caregiver(s).
7.8- We recommend health care professionals consider consultation, psychotherapy, or both for a gender diverse child and family/caregivers when families and health care professionals believe this would benefit the well-being and development of a child and/or family.
7.9- We recommend health care professionals offering consultation, psychotherapy, or both to gender diverse children and families/caregivers work with other settings and individuals important to the child to promote the child's resilience and emotional well-being.
7.10- We recommend health care professionals offering consultation, psychotherapy, or both to gender diverse children and families/caregivers provide both parties with age-appropriate psychoeducation about gender development.
7.11- We recommend that health care professionals provide information to gender diverse children and their families/caregivers as the child approaches puberty about potential gender affirming medical interventions, the effects of these treatments on future fertility, and options for fertility preservation.
7.12- We recommend parents/caregivers and health care professionals respond supportively to children who desire to be acknowledged as the gender that matches their internal sense of gender identity.
7.13- We recommend health care professionals and parents/caregivers support children to continue to explore their gender throughout the pre-pubescent years, regardless of social transition.
7.14- We recommend the health care professionals discuss the potential benefits and risks of a social transition with families who are considering it.
7.15- We suggest health care professionals consider working collaboratively with other professionals and organizations to promote the well-being of gender diverse children and minimize the adversities they may face.

acceptance of their gender diversity and parenting guidance when requested. Comprehensive assessments are appropriate when solicited by a family requesting a full understanding of the child's gender and mental health needs in the context of gender diversity.

In these circumstances, family member mental health issues, family dynamics, and social and cultural contexts, all of which impact a gender diverse child, should be taken into consideration (Barrow & Apostle, 2018; Brown & Mar, 2018; Cohen-Kettenis et al., 2003; Hendricks & Testa, 2012; Kaufman & Tishelman, 2018; Ristori & Steensma, 2016; Tishelman & Neumann-Mascis, 2018). This is further elaborated upon in the text below.

It is important HCPs working with gender diverse children strive to understand the child and the family's various aspects of identity and experience: racial, ethnic, immigrant/refugee status, religious, geographic, and socio-economic, for example, and be respectful and sensitive to cultural context in clinical interactions (Telfer et al., 2018). Many factors may be relevant to culture and gender, including religious beliefs, gender-related expectations, and the degree to which gender diversity is accepted (Oliphant et al., 2018). Intersections between gender diversity, sociocultural diversity, and minority statuses can be sources of strength, social stress, or both (Brown & Mar, 2018; Oliphant et al., 2018; Riggs & Treharne, 2016).

Each child, family member, and family dynamic is unique and potentially encompasses multiple cultures and belief patterns. Thus, HCPs of all disciplines should avoid stereotyping based on preconceived ideas that may be incorrect or biased (e.g., that a family who belongs to a religious organization that is opposed to appreciating gender diversity will necessarily be unsupportive of their child's gender diversity) (Brown & Mar, 2018). Instead, it is essential to approach each family openly and understand each family member and family pattern as distinct.

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 7.1

We recommend the health care professionals working with gender diverse children receive training and have expertise in gender development and gender diversity in children and possess general knowledge of gender diversity across the life span.

HCPs working with gender diverse children should acquire and maintain the necessary training and credentials relevant to the scope of their role as professionals. This includes licensure, certification, or both by appropriate national and/or regional accrediting bodies. We recognize the specifics of credentialing and regulation of professionals vary globally. Importantly, basic licensure, certification, or both may be insufficient in and of itself to ensure competency working with gender diverse children, as HCPs specifically require in-depth training and supervised experience in childhood gender development and gender diversity to provide appropriate care.

Statement 7. 2

We recommend health care professionals working with gender diverse children receive theoretical and evidenced-based training and develop expertise in general child and family mental health across the developmental spectrum.

HCPs should receive training and supervised expertise in general child and family mental health across the developmental spectrum from toddlerhood through adolescence, including evidence-based assessment and intervention approaches. Gender diversity is not a mental health disorder; however, as cited above, we know mental health can be adversely impacted for gender diverse children (e.g., through gender minority stress) (Hendricks & Testa, 2012) that may benefit from exploration and support; therefore, mental health expertise is highly recommended. Working with children is a complex endeavor, involving an understanding of a child's developmental needs at various ages, the ability to comprehend the forces impacting a child's well-being both inside and outside the family (Kaufman & Tishelman, 2018), and an ability to fully assess when a child is unhappy or experiencing significant mental health difficulties, related or unrelated to gender. Research has indicated high levels of adverse experiences and trauma in the gender diverse community of children, including susceptibility to rejection or even maltreatment (APA, 2015; Barrow & Apostle, 2018; Giovanardi et al., 2018; Reisner, Greytak et al., 2015; Roberts et al., 2012; Tishelman & Neumann-Mascis, 2018). HCPs need to be cognizant of the potential for adverse experiences and be able to initiate effective interventions to prevent harm and promote positive well-being.

Statement 7.3

We recommend health care professionals working with gender diverse children receive training and develop expertise in autism spectrum disorders and other neurodiversity or collaborate with an expert with relevant expertise when working with autistic/neurodivergent, gender diverse children.

The experience of gender diversity in autistic children as well as in children with other forms of neurodivergence may present extra clinical complexities (de Vries et al., 2010; Strang, Meagher et al., 2018). For example, autistic children may find it difficult to self-advocate for their gender-related needs and may communicate in highly individualistic ways (Kuvalanka et al., 2018; Strang, Powers et al., 2018). They may have varied interpretations of gender-related experiences given common differences in communication and thinking style. Because of the unique needs of gender diverse neurodivergent children, they may be at high risk for being misunderstood (i.e., for their communications to be misinterpreted). Therefore, professionals providing support to these children can best serve them by receiving training and developing expertise in autism and related neurodevelopmental presentations and/or collaborating with autism specialists (Strang, Meagher et al., 2018). Such training is especially relevant as research has documented

higher rates of autism among gender diverse youth than in the general population (de Vries et al., 2010; Hisle-Gorman et al., 2019; Shumer et al., 2015).

Statement 7.4

We recommend health care professionals working with gender diverse children engage in continuing education related to gender diverse children and families.

Continuing professional development regarding gender diverse children and families may be acquired through various means, including through readings (journal articles, books, websites associated with gender knowledgeable organizations), attending on-line and in person trainings, and joining peer supervision/consultation groups (Bartholomaeus et al., 2021).

Continuing education includes 1) maintaining up-to-date knowledge of available and relevant research on gender development and gender diversity in prepubescent children and gender diversity across the life span; 2) maintaining current knowledge regarding best practices for assessment, support, and treatment approaches with gender diverse children and families. This is a relatively new area of practice and health care professionals need to adapt as new information emerges through research and other avenues (Bartholomaeus et al., 2021).

Statement 7.5

We recommend health care professionals conducting an assessment with gender diverse children access and integrate information from multiple sources as part of the assessment.

A comprehensive assessment, when requested by a family and/or an HCP can be useful for developing intervention recommendations, as needed, to benefit the well-being of the child and other family members. Such an assessment can be beneficial in a variety of situations when a child and/or their family/guardians, in coordination with providers, feel some type of intervention would be helpful. Neither assessments nor interventions should ever be used as a means of covertly or overtly discouraging a child's gender diverse expressions or identity. Instead, with appropriately trained providers, assessment can be an effective means of better understanding how to support a child and their family without privileging any particular gender identity or expression. An assessment can be especially important for some children and their families by collaborating to promote a child's gender health, well-being, and self-fulfillment.

A comprehensive assessment can facilitate the formation of an individualized plan to assist a gender diverse prepubescent children and family members (de Vries & Cohen-Kettenis, 2012; Malpas et al., 2018; Steensma & Wensing-Kruger, 2019; Telfer et al., 2018; Tishelman & Kaufman, 2018). In such an assessment, integrating information from multiple sources is important to 1) best understand the child's gender needs and make recommendations; and 2) identify areas of child, family/caregiver, and community strengths and supports specific to the child's gender status and development as well as risks and concerns for the child, their family/caregivers and environment. Multiple informants for both evaluation and support/intervention planning purposes may include the child, parents/caregivers, extended family members, siblings, school personnel, HCPs, the community, broader cultural and legal contexts and other sources as indicated (Berg & Edwards-Leeper, 2018; Srinath, 2019).

An HCP conducting an assessment of gender diverse children needs to explore gender-related issues but must also take a broad view of the child and the environment, consistent with the ecological model described above (Bronfenbrenner, 1979) to fully understand the factors impacting a child's well-being and areas of gender support and risk (Berg & Edwards-Leeper, 2018; Hendricks & Testa, 2012; Kaufman & Tishelman, 2018; Tishelman & Neumann-Mascis, 2018). This includes understanding the strengths and challenges experienced by the child/family and that are present in the environment. We advise HCPs conducting an assessment with gender diverse children to consider incorporating multiple assessment domains, depending on the child and the family's needs and circumstances. Although some of the latter listed domains below do not directly address the child's gender (see items 7–12 below), they need to be accounted for in a gender assessment, as indicated by clinical judgment, to understand the complex web of factors

that may be affecting the child's well-being in an integrated fashion, including gender health, consistent with evaluation best practices a (APA, 2015; Berg & Edwards-Leeper, 2018; Malpas et al., 2018) and develop a multi-pronged intervention when needed.

Summarizing from relevant research and clinical expertise, assessment domains often include 1) a child's asserted gender identity and gender expression, currently and historically; 2) evidence of dysphoria, gender incongruence, or both; 3) strengths and challenges related to the child, family, peer and others' beliefs and attitudes about gender diversity, acceptance and support for child; 4) child and family experiences of gender minority stress and rejection, hostility, or both due to the child's gender diversity; 5) level of support related to gender diversity in social contexts (e.g., school, faith community, extended family); 6) evaluation of conflict regarding the child's gender and/or parental/caregiver/sibling concerning behavior related to the child's gender diversity; 7) child mental health, communication and/or cognitive strengths and challenges, neurodivergence, and/or behavioral challenges causing significant functional difficulty; 8) relevant medical and developmental history; 9) areas that may pose risks (e.g., exposure to domestic and/or community violence, any form of child maltreatment; history of trauma; safety and/or victimization with peers or in any other setting; suicidality); 10) co-occurring significant family stressors, such as chronic or terminal illness, homelessness or poverty; 11) parent/caregiver and/or sibling mental health and/or behavioral challenges causing significant functional difficulty; and 12) child's and family's strengths and challenges.

A thorough assessment incorporating multiple forms of information gathering is helpful for understanding the needs, strengths, protective factors, and risks for a specific child and family across environments (e.g., home/school). Methods of information gathering often include 1) interviews with the child, family members and others (e.g., teachers), structured and unstructured; 2) caregiver and child completed standardized measures related to gender; general child well-being; child cognitive and communication skills and developmental disorders/disabilities; support and acceptance by parent/caregiver, sibling, extended family and peers; parental stress; history of childhood adversities; and/or other issues as appropriate (APA, 2020; Berg & Edwards-Leeper, 2018; Kaufman & Tishelman, 2018; Srinath, 2019).

Depending on the family characteristics, the developmental profile of the child, or both, methods of information gathering also may also benefit from including the following 1) child and/or family observation, structured and unstructured; and 2) structured and visually supported assessment techniques (worksheets; self-portraits; family drawings, etc.) (Berg & Edwards-Leeper, 2018).

Statement 7.6

We recommend that health care professionals conducting an assessment with gender diverse children consider relevant developmental factors, neurocognitive functioning and language skills.

Given the complexities of assessing young children who, unlike adults, are in the process of development across a range of domains (cognitive, social, emotional, physiological), it is important to consider the developmental status of a child and gear assessment modalities and interactions to the individualized abilities of the child. This includes tailoring the assessment to a child's developmental stage and abilities (preschoolers, school age, early puberty prior to adolescence), including using language and assessment approaches that prioritize a child's comfort, language skills, and means of self-expression (Berg & Edwards-Leeper, 2018; Srinath, 2019). For example, relevant developmental factors, such as neurocognitive differences (e.g., autism spectrum conditions), and receptive and expressive language skills should be considered in conducting the assessment. Health care professionals may need to consult with specialists for guidance in cases in which they do not possess the specialized skills themselves (Strang et al., 2021).

Statement 7.7

We recommend health care professionals conducting an assessment with gender diverse children consider factors that may constrain accurate reporting of gender identity/gender expression by the child and/or family/caregiver(s).

HCPs conducting an assessment with gender diverse children and families need to account for developmental, emotional, and environmental factors that may constrain a child's, caregiver's, sibling or other's report or influence their belief systems related to gender (Riggs & Bartholomaeus, 2018). As with all child psychological assessments, environmental and family/caregiver reactions (e.g., punishment), and/or cognitive and social factors may influence a child's comfort and/or ability to directly discuss certain factors, including gender identity and related issues (Srinath, 2019). Similarly, family members may feel constrained in freely expressing their concerns and ideas depending on family conflicts or dynamics and/or other influences (e.g., cultural/religious; extended family pressure) (Riggs & Bartholomaeus, 2018).

Statement 7.8

We recommend health care professionals consider consultation, psychotherapy, or both for a gender diverse child and family/caregivers when families and health care professionals believe this would benefit the well-being and development of a child and/or family.

The goal of psychotherapy should never be aimed at modifying a child's gender identity (APA, 2021; Ashley, 2019b; Paré, 2020; SAMHSA, 2015; UN Human Rights Council, 2020), either covertly or overtly. Not all gender diverse children or their families need input from MHPs as gender diversity is not a mental health disorder (Pediatric Endocrine Society, 2020; Telfer et al., 2018). Nevertheless, it is often appropriate and helpful to seek psychotherapy when there is distress or concerns are expressed by parents to improve psychosocial health and prevent further distress (APA, 2015). Some of the common reasons for considering psychotherapy for a gender diverse child and family include the following 1) A child is demonstrating significant conflicts, confusion, stress or distress about their gender identity or needs a protected space to explore their gender (Ehrensaft, 2018; Spivey and Edwards-Leeper, 2019); 2) A child is experiencing external pressure to express their gender in a way that conflicts with their self-knowledge, desires, and beliefs (APA, 2015); 3) A child is struggling with mental health concerns, related to or independent of their gender (Barrow & Apostle, 2018); 4) A child would benefit from strengthening their resilience in the face of negative environmental responses to their gender identity or presentation (Craig & Auston, 2018; Malpas et al., 2018); 5) A child may be experiencing mental health and/or environmental concerns, including family system problems that can be misinterpreted as gender congruence or incongruence (Berg & Edwards-Leeper, 2018); and 6) A child expresses a desire to meet with an MHP to get gender-related support. In these situations, the psychotherapy will focus on supporting the child with the understanding that the child's parent(s)/caregiver(s) and potentially other family members will be included as necessary (APA, 2015; Ehrensaft, 2018; McLaughlin & Sharp, 2018). Unless contraindicated, it is extremely helpful for parents/guardians to participate in some capacity in the psychotherapy process involving prepubescent children as family factors are often central to a child's well-being. Although relatively unexplored in research involving gender diverse children, it may be important to attend to the relationship between siblings and the gender diverse child (Pariseau et al., 2019; Parker & Davis-McCabe, 2021).

HCPs should employ interventions tailor-made to the individual needs of the child that are designed to 1) foster protective social and emotional coping skills to promote resilience in the face of potential negative reactions to the child's gender identity, expressions, or both (Craig & Austin, 2016; Malpas et al., 2018; Spencer, Berg et al., 2021); 2) collaboratively problem-solve social challenges to reduce gender minority stress (Barrow & Apostle, 2018; Tishelman & Neumann-Mascis, 2018); 3) strengthen environmental supports for the child and/or members of the immediate and extended family (Kaufman & Tishelman, 2018); and 4) provide the child an opportunity to further understand their internal gender experiences (APA, 2015; Barrow& Apostle, 2018; Ehrensaft, 2018; Malpas et al., 2018; McLaughlin & Sharp, 2018). It is helpful for HCPs to develop a relationship with a gender diverse child and family that can endure over time as needed. This enables the child/family to establish a long-term trusting relationship throughout childhood whereby the HCP can offer support and guidance as a child matures and as potentially

different challenges or needs emerge for the child/family (Spencer, Berg et al., 2021; Murchison et al., 2016). In addition to the above and within the limits of available resources, when a child is neurodivergent, an HCP who has the skill set to address both neurodevelopmental differences and gender is most appropriate (Strang et al., 2021).

As outlined in the literature, there are numerous reasons parents/caregivers, siblings, and extended family members of a prepubescent child may find it useful to seek psychotherapy for themselves (Ehrensaft, 2018; Malpas et al., 2018; McLaughlin & Sharp, 2018). As summarized below, some of these common catalysts for seeking such treatment occur when one or more *family members* 1) desire education around gender development (Spivey & Edwards-Leeper, 2019); 2) are experiencing significant confusion or stress about the child's gender identity, expression, or both (Ashley, 2019c; Ehrensaft, 2018); 3) need guidance related to emotional and behavioral concerns regarding the gender diverse child (Barrow & Apostle, 2018; 4) need support to promote affirming environments outside of the home (e.g., school, sports, camps) (Kaufman & Tishelman, 2018); 5) are seeking assistance to make informed decisions about social transition, including how to do so in a way that is optimal for a child's gender development and health (Lev & Wolf-Gould, 2018); 6) are seeking guidance for dealing with condemnation from others, including political entities and accompanying legislation, regarding their support for their gender diverse child (negative reactions directed toward parents/caregivers can sometimes include rejection and/or harassment/abuse from the social environment arising from affirming decisions (Hidalgo & Chen, 2019); 7) are seeking to process their own emotional reactions and needs about their child's gender identity, including grief about their child's gender diversity and/or potential fears or anxieties for their child's current and future well-being (Pullen Sansfaçon et al., 2019); and 8) are emotionally distressed and/or in conflict with other family members regarding the child's gender diversity (as needed, HCPs can provide separate sessions for parents/caregivers, siblings and extended family members for support, guidance, and/or psychoeducation) (McLaughlin & Sharp, 2018; Pullen Sansfaçon et al., 2019; Spivey & Edwards-Leeper, 2019).

Statement 7.9

We recommend health care professionals offering consultation, psychotherapy, or both to gender diverse children and families/caregivers work with other settings and individuals important to the child to promote the child's resilience and emotional well-being.

Consistent with the ecological model described above and, as appropriate, based on individual/family circumstances, it can be extremely helpful for HCPs to prioritize coordination with important others (e.g., teachers, coaches, religious leaders) in a child's life to promote emotional and physical safety across settings (e.g., school settings, sports and other recreational activities, faith-based involvement) (Kaufman & Tishelman, 2018). Therapeutic and/or support groups are often recommended as a valuable resource for families/caregivers and/or gender diverse children themselves (Coolhart, 2018; Horton et al., 2021; Malpas et al., 2018; Murchison et al., 2016).

Statement 7.10

We recommend HCPs offering consultation, psychotherapy, or both to gender diverse children and families/caregivers provide both parties with age appropriate psycho-education about gender development.

Parents/caregivers and their gender diverse child should have the opportunity to develop knowledge regarding ways in which families/caregivers can best support their child to maximize resilience, self-awareness, and functioning (APA, 2015; Ehrensaft, 2018; Malpas, 2018; Spivey & Edwards-Leeper, 2019). It is neither possible nor is it the role of the HCP to predict with certainty the child's ultimate gender identity; instead, the HCP's task is to provide a safe space for the child's identity to develop and evolve over time without attempts to prioritize any particular developmental trajectory with regard to gender (APA, 2015; Spivey & Edwards-Leeper, 2019). Gender diverse children and early adolescents have different needs and experiences than older adolescents, socially and physiologically, and those differences should be reflected in the individualized approach HCPs

provide to each child/family (Keo-Meir & Ehrensaft, 2018; Spencer, Berg et al., 2021).

Parents/caregivers and their children should also have the opportunity to develop knowledge about gender development and gender literacy through age-appropriate psychoeducation (Berg & Edwards-Leeper, 2018; Rider, Vencill et al., 2019; Spencer, Berg et al., 2021). Gender literacy involves understanding the distinctions between sex designated at birth, gender identity, and gender expression, including the ways in which these three factors uniquely come together for a child (Berg & Edwards-Leeper, 2018; Rider, Vencill et al., 2019; Spencer, Berg et al., 2021). As a child gains gender literacy, they begin to understand their body parts do not necessarily define their gender identity and/or their gender expression (Berg & Edwards-Leeper, 2018; Rider, Vencill et al., 2019; Spencer, Berg et al., 2021). Gender literacy also involves learning to identify messages and experiences related to gender within society. As a child gains gender literacy, they may view their developing gender identity and gender expression more positively, promoting resilience and self-esteem, and diminishing risk of shame in the face of negative messages from the environment. Gaining gender literacy through psychoeducation may also be important for siblings and/or extended family members who are important to the child (Rider, Vencill et al., 2019; Spencer, Berg et al., 2021).

Statement 7.11

We recommend health care professionals provide information to gender diverse children and their families/caregivers as the child approaches puberty about potential gender-affirming medical interventions, the effects of these treatments on future fertility, and options for fertility preservation.

As a child matures and approaches puberty, HCPs should prioritize working with children and their parents/caregivers to integrate psychoeducation about puberty, engage in shared decision-making about potential gender-affirming medical interventions, and discuss fertility-related and other reproductive health implications of medical treatments (Nahata, Quinn et al., 2018; Spencer, Berg et al., 2021). Although only limited empirical research exists to evaluate such interventions, expert consensus and developmental psychological literature generally support the notion that open communication with children about their bodies and preparation for physiological changes of puberty, combined with gender-affirming acceptance, will promote resilience and help to foster positive sexuality as a child matures into adolescence (Spencer, Berg et al., 2019). All these discussions may be extended (e.g., starting earlier) to include neurodivergent children, to ensure there is enough time for reflection and understanding, especially as choices regarding future gender- affirming medical care potentially arise (Strang, Jarin et al., 2018). These discussions could include the following topics:

- Review of body parts and their different functions;
- The ways in which a child's body may change over time with and without medical intervention;
- The impact of medical interventions on later sexual functioning and fertility;
- The impact of puberty suppression on potential later medical interventions;
- Acknowledgment of the current lack of clinical data in certain areas related to the impacts of puberty suppression;
- The importance of appropriate sex education prior to puberty.

These discussions should employ developmentally appropriate language and teaching styles, and be geared to the specific needs of each individual child (Spencer, Berg et al., 2021).

Statement 7.12

We recommend parents/caregivers and health care professionals respond supportively to children who desire to be acknowledged as the gender that matches their internal sense of gender identity.

Gender social transition refers to a process by which a child is acknowledged by others and has the opportunity to live publicly, either in all situations or in certain situations, in the gender identity they affirm and has no singular set of parameters or actions (Ehrensaft et al., 2018).

Gender social transition has often been conceived in the past as binary—a girl transitions to a boy, a boy to a girl. The concept has expanded to include children who shift to a nonbinary or individually shaped iteration of gender identity (Chew et al., 2020; Clark et al., 2018). Newer research indicates the social transition process may serve a protective function for some prepubescent children and serve to foster positive mental health and well-being (Durwood et al., 2017; Gibson et al., 2021; Olson et al., 2016). Thus, recognition that a child's gender may be fluid and develop over time (Edwards-Leeper et al., 2016; Ehrensaft, 2018; Steensma, Kreukels et al., 2013) is not sufficient justification to negate or deter social transition for a prepubescent child when it would be beneficial. Gender identity evolution may continue even after a partial or complete social transition process has taken place (Ashley, 2019e; Edwards-Leeper et al., 2018; Ehrensaft, 2020; Ehrensaft et al., 2018; Spivey & Edwards-Leeper, 2019). Although empirical data remains limited, existing research has indicated children who are most assertive about their gender diversity are most likely to persist in a diverse gender identity across time, including children who socially transition prior to puberty (Olson et al., 2022; Rae et al., 2019; Steensma, McGuire et al., 2013). Thus, when considering a social transition, we suggest parents/caregivers and HCPs pay particular attention to children who consistently and often persistently articulate a gender identity that does not match the sex designated at birth. This includes those children who may explicitly request or desire a social acknowledgement of the gender that better matches the child's articulated gender identity and/or children who exhibit distress when their gender as they know it is experienced as incongruent with the sex designated at birth (Rae et al., 2019; Steensma, Kreukels et al., 2013).

Although there is a dearth of empirical literature regarding best practices related to the social transition process, clinical literature and expertise provides the following guidance that prioritizes a child's best interests (Ashley, 2019e; Ehrensaft, 2018; Ehrensaft et al, 2018; Murchison et al., 2016; Telfer et al., 2018): 1) social transition should originate from the child and reflect the child's wishes in the process of making the decision to initiate a social transition process; 2) an HCP may assist exploring the advantages/benefits, plus potential challenges of social transition; 3) social transition may best occur in all or in specific contexts/settings only (e.g., school, home); and 4) a child may or may not choose to disclose to others that they have socially transitioned, or may designate, typically with the help of their parents/caregivers, a select group of people with whom they share the information.

In summary, social transition, when it takes place, is likely to best serve a child's well-being when it takes place thoughtfully and individually for each child. A child's social transition (and gender as well) may evolve over time and is not necessarily static, but best reflects the cross-section of the child's established self-knowledge of their present gender identity and desired actions to express that identity (Ehrensaft et al., 2018).

A social transition process can include one or more of a number of different actions consistent with a child's affirmed gender (Ehrensaft et al., 2018), including:

- Name change;
- Pronoun change;
- Change in sex/gender markers (e.g., birth certificate; identification cards; passport; school and medical documentation; etc.);
- Participation in gender-segregated programs (e.g., sports teams; recreational clubs and camps; schools; etc.);
- Bathroom and locker room use;
- Personal expression (e.g., hair style; clothing choice; etc.);
- Communication of affirmed gender to others (e.g., social media; classroom or school announcements; letters to extended families or social contacts; etc.).

Statement 7.13

We recommend health care professionals and parents/caregivers support children to continue to explore their gender throughout the pre-pubescent years, regardless of social transition.

It is important children who have engaged in social transition be afforded the same opportunities as other children to continue considering

meanings and expressions of gender throughout their childhood years (Ashley 2019e; Spencer, Berg et al., 2021). Some research has found children may experience gender fluidity or even detransition after an initial social transition. Research has not been conclusive about when in the life span such detransition is most likely to occur, or what percentage of youth will eventually experience gender fluidity and/or a desire to detransition—due to gender evolution, or potentially other reasons (e.g., safety concerns; gender minority stress) (Olson et al., 2022; Steensma, Kreukels et al., 2013). A recent research report indicates in the US, detransition occurs with only a small percentage of youth five years after a binary social transition (Olson et al., 2022); further follow-up of these young people would be helpful. Replication of these findings is important as well since this study was conducted with a limited and self-selected participant pool in the US and thus may not be applicable to all gender diverse children. In summary, we have limited ability to know in advance the ways in which a child's gender identity and expressions may evolve over time and whether or why detransition may take place for some. In addition, not all gender diverse children wish to explore their gender (Telfer et al., 2018). Cisgender children are not expected to undertake this exploration, and therefore attempts to force this with a gender diverse child, if not indicated or welcomed, can be experienced as pathologizing, intrusive and/or cisnormative (Ansara & Hegarty, 2012; Bartholomaeus et al., 2021; Oliphant et al., 2018).

Statement 7.14

We recommend health care professionals discuss the potential benefits and risks of a social transition with families who are considering it.

Social transition in prepubescent children consists of a variety of choices, can occur as a process over time, is individualized based on both a child's wishes and other psychosocial considerations (Ehrensaft, 2018), and is a decision for which possible benefits and challenges should be weighted and discussed.

A social transition may have potential benefits as outlined in clinical literature (e.g., Ehrensaft et al., 2018) and supported by research (Fast & Olson, 2018; Rae et al., 2019). These include facilitating gender congruence while reducing gender dysphoria and enhancing psychosocial adjustment and well-being (Ehrensaft et al., 2018). Studies have indicated socially transitioned gender diverse children largely mirror the mental health characteristics of age matched cisgender siblings and peers (Durwood et al., 2017). These findings differ markedly from the mental health challenges consistently noted in prior research with gender diverse children and adolescents (Barrow & Apostle, 2018) and suggest the impact of social transition may be positive. Additionally, social transition for children typically can only take place with the support and acceptance of parents/caregivers, which has also been demonstrated to facilitate well-being in gender diverse children (Durwood et al., 2021; Malpas et al., 2018; Pariseau et al., 2019), although other forms of support, such as school-based support, have also been identified as important (Durwood et al., 2021; Turban, King et al., 2021). HCPs should discuss the potential benefits of a social transition with children and families in situations in which 1) there is a consistent, stable articulation of a gender identity that is incongruent with the sex assigned at birth (Fast & Olson, 2018). This should be differentiated from gender diverse expressions/behaviors/interests (e.g., playing with toys, expressing oneself through clothing or appearance choices, and/or engaging in activities socially defined and typically associated with the other gender in a binary model of gender) (Ehrensaft, 2018; Ehrensaft et al., 2018); 2) the child is expressing a strong desire or need to transition to the gender they have articulated as being their authentic gender (Ehrensaft et al., 2018; Fast & Olson, 2018; Rae et al., 2019); and 3) the child will be emotionally and physically safe during and following transition (Brown & Mar, 2018). Prejudice and discrimination should be considerations, especially in localities where acceptance of gender diversity is limited or prohibited (Brown & Mar, 2018; Hendricks & Testa, 2012; Turban, King et al., 2021). Of note, there can also be possible risks to a gender diverse child who does not socially transition, including 1) being ostracized or bullied for being perceived as not conforming to prescribed community

gender roles and/or socially expected patterns of behavior; and 2) living with the internal stress or distress that the gender they know themselves to be is incongruent with the gender they are being asked to present to the world.

To promote gender health, the HCP should discuss the potential challenges of a social transition. One concern often expressed relates to fear that a child will preclude considering the possible evolution of their gender identity as they mature or be reluctant to initiate another gender transition even if they no longer feel their social transition matches their current gender identity (Edwards-Leeper et al., 2016; Ristori & Steensma, 2016). Although limited, recent research has found some parents/caregivers of children who have socially transitioned may discuss with their children the option of new gender iterations (for example, reverting to an earlier expression of gender) and are comfortable about this possibility (Olson et al., 2019). Another often identified social transition concern is that a child may suffer negative sequelae if they revert to the former gender identity that matches their sex designated at birth (Chen et al., 2018; Edwards-Leeper et al., 2019; Steensma & Cohen-Kettenis, 2011). From this point of view, parents/caregivers should be aware of the potential developmental effect of a social transition on a child.

HCPs should provide guidance to parents/caregivers and supports to a child when a social gender transition is being considered or taking place by 1) providing consultation, assessment, and gender supports when needed and sought by the parents/caregivers; 2) aiding family members, as needed, to understand the child's desires for a social transition and the family members' own feelings about the child's expressed desires; 3) exploring with, and learning from, the parents/caregivers whether and how they believe a social transition would benefit their child both now and in their ongoing development; 4) providing guidance when parents/caregivers are not in agreement about a social transition and offering the opportunity to work together toward a consistent understanding of their child's gender status and needs; 5) providing guidance about safe and supportive ways to disclose their child's social transition to others and to facilitate their child transitioning in their various social environments (e.g., schools, extended family); 6) facilitating communication, when desired by the child, with peers about gender and social transition as well as fortifying positive peer relationships; 7) providing guidance when social transition may not be socially accepted or safe, either everywhere or in specific situations, or when a child has reservations about initiating a transition despite their wish to do so; there may be multiple reasons for reservations, including fears and anxieties; 8) working collaboratively with family members and MHPs to facilitate a social transition in a way that is optimal for the child's unfolding gender development, overall well-being, and physical and emotional safety; and 9) providing psychoeducation about the many different trajectories the child's gender may take over time, leaving pathways open to future iterations of gender for the child, and emphasizing there is no need to predict an individual child's gender identity in the future (Malpas et al., 2018).

All of these tasks incorporate enhancing the quality of communication between the child and family members and providing an opportunity for the child to be heard and listened to by all family members involved. These relational processes in turn facilitate the parents/caregivers' success in making informed decisions about the advisability and/or parameters of a social transition for their child (Malpas et al., 2018).

One role of HCPs is to provide guidance and support in situations in which children and parents/caregivers wish to proceed with a social transition but conclude that the social environment would not be accepting of those choices, by 1) helping parents/caregivers define and extend safe spaces in which the child can express their authentic gender freely; 2) discussing with parents/caregivers ways to advocate that increase the likelihood of the social environment being supportive in the future, if this is a realistic goal; 3) intervening as needed to help the child/family with any associated distress and/or shame brought about by the continued suppression of authentic gender identity and the need for secrecy; and 4) building both the child's and the family's resilience, instilling the understanding that if the social environment is having difficulty accepting a child's social transition and affirmed gender identity, it is not because of some shortcoming in the child but because of

insufficient gender literacy in the social environment (Ehrensaft et al., 2018).

Statement 7.15

We suggest health care professionals consider working collaboratively with other professionals and organizations to promote the well-being of gender diverse children and minimize the adversities they may face.

All children have the right to be supported and respected in their gender identities (Human Rights Campaign, 2018; Paré, 2020; SAMHSA, 2015). As noted above, gender diverse children are a particularly vulnerable group (Barrow & Apostle, 2018; Cohen-Kettenis et al., 2003; Giovanardi et al., 2018; Gower, Rider, Coleman et al., 2018; Grossman & D'Augelli, 2007; Hendricks & Testa, 2012; Reisner, Greytak et al., 2015; Ristori & Steensma, 2016; Roberts et al., 2012; Tishelman & Neumann-Mascis, 2018). The responsibilities of HCPs as advocates encompass acknowledging social determinants of health are critical for marginalized minorities (Barrow & Mar, 2018; Hendricks & Testa, 2012). Advocacy is taken up by all HCPs in the form of child and family support (APA, 2015; Malpas et al., 2018).

Some HCPs may be called on to move beyond their individual offices or programs to advocate for gender diverse children in the larger community, often in partnership with stakeholders, including parents/caregivers, allies, and youth (Kaufman & Tishelman, 2018; Lopez et al., 2017; Vanderburgh, 2009). These efforts may be instrumental in enhancing children's gender health and promoting their civil rights (Lopez et al., 2017).

HCP's voices may be essential in schools, in parliamentary bodies, in courts of law, and in the media (Kuvalanka et al., 2019; Lopez et al., 2017; Whyatt-Sames, 2017; Vanderburgh, 2009). In addition, HCPs may have a more generalized advocacy role in acknowledging and addressing the frequent intentional or unintentional negating of the experience of gender diverse children that may be transmitted or communicated by adults, peers, and in media (Rafferty et al., 2018). Professionals who possess the skill sets and find themselves in appropriate situations can provide clear de-pathologizing statements on the needs and rights of gender diverse children and on the damage caused by discriminatory and transphobic rules, laws, and norms (Rafferty et al., 2018).

CHAPTER 18 Mental Health

This chapter is intended to provide guidance to health care professionals (HCPs) and mental health professionals (MHPs) who offer mental health care to transgender and gender diverse (TGD) adults. It is not meant to be a substitute for chapters on the assessment or evaluation of people for hormonal or surgical interventions. Many TGD people will not require therapy or other forms of mental health care as part of their transition, while others may benefit from the support of mental health providers and systems (Dhejne et al., 2016).

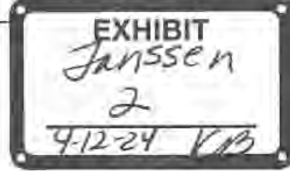
Some studies have shown a higher prevalence of depression (Witcomb et al., 2018), anxiety (Bouman et al., 2017), and suicidality (Arcelus et al., 2016; Bränström & Pachankis, 2022; Davey et al., 2016; Dhejne, 2011; Herman et al., 2019) among TGD people (Jones et al., 2019; Thorne, Witcomb et al., 2019) than in the general population, particularly in those requiring medically necessary gender-affirming medical treatment (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1). However, transgender identity is not a mental illness, and these elevated rates have been linked to complex trauma, societal stigma, violence, and discrimination (Nuttbrock et al., 2014; Peterson et al., 2021). In addition, psychiatric symptoms lessen with appropriate gender-affirming medical and surgical care (Aldridge et al., 2020; Almazan and Keuroghlian; 2021; Bauer et al., 2015; Grannis et al., 2021) and with interventions that lessen discrimination and minority stress (Bauer et al., 2015; Heylens, Verroken et al., 2014; McDowell et al., 2020).

Mental health treatment needs to be provided by staff and implemented through the use of systems that respect patient autonomy and recognize gender diversity. MHPs working with transgender people should use active listening as a method to encourage exploration in individuals who are uncertain about their gender identity. Rather than impose their own narratives or preconceptions, MHPs should assist their clients in determining their own paths. While many transgender people require medical or surgical interventions or seek mental health care, others do not (Margulies et al., 2021). Therefore, findings from research involving clinical populations should not be extrapolated to the entire transgender population.

Addressing mental illness and substance use disorders is important but should not be a barrier to transition-related care. Rather, these interventions to address mental health and substance use disorders can facilitate successful outcomes from

Statements of Recommendations

18.1- We recommend mental health professionals address mental health symptoms that interfere with a person's capacity to consent to gender-affirming treatment before gender-affirming treatment is initiated.
18.2- We recommend mental health professionals offer care and support to transgender and gender diverse people to address mental health symptoms that interfere with a person's capacity to participate in essential perioperative care before gender-affirmation surgery.
18.3- We recommend when significant mental health symptoms or substance abuse exists, mental health professionals assess the potential negative impact that mental health symptoms may have on outcomes based on the nature of the specific gender-affirming surgical procedure.
18.4- We recommend health care professionals assess the need for psychosocial and practical support of transgender and gender diverse people in the perioperative period surrounding gender- affirmation surgery.
18.5- We recommend health care professionals counsel and assist transgender and gender diverse people in becoming abstinent from tobacco/nicotine prior to gender-affirmation surgery.
18.6- We recommend health care professionals maintain existing hormone treatment if a transgender and gender diverse individual requires admission to a psychiatric or medical inpatient unit, unless contraindicated.
18.7- We recommend health care professionals ensure if transgender and gender diverse people need in-patient or residential mental health, substance abuse or medical care, all staff use the correct name and pronouns (as provided by the patient), as well as provide access to bathroom and sleeping arrangements that are aligned with the person's gender identity.
18.8- We recommend mental health professionals encourage, support, and empower transgender and gender diverse people to develop and maintain social support systems, including peers, friends, and families.
18.9- We recommend health care professionals should not make it mandatory for transgender and gender diverse people to undergo psychotherapy prior to the initiation of gender-affirming treatment, while acknowledging psychotherapy may be helpful for some transgender and gender diverse people.
18.10- We recommend "reparative" and "conversion" therapy aimed at trying to change a person's gender identity and lived gender expression to become more congruent with the sex assigned at birth should not be offered.



transition-related care, which can improve quality of life (Nobili et al., 2018).

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 18.1

We recommend mental health professionals address mental health symptoms that interfere with a person's capacity to consent to gender-affirming treatment before gender-affirming treatment is initiated.

Because patients generally are assumed to be capable of providing consent for care, whether the presence of cognitive impairment, psychosis, or other mental illness impairs the ability to give informed consent is subject to individual examination (Applebaum, 2007). Informed consent is central to the provision of health care. The health care provider must educate the patient about the risks, benefits, and alternatives to any care that is offered so the patient can make an informed, voluntary choice (Berg et al., 2001). Both the primary care provider or endocrinologist prescribing hormones and the surgeon performing surgery must obtain informed consent. Similarly, MHPs obtain informed consent for mental health treatment and may consult on a patient's capacity to give informed consent when this is in question. Psychiatric illness and substance use disorders, in particular cognitive impairment and psychosis, may impair an individual's ability to understand the risks and benefits of the treatment (Hostiuc et al., 2018). Conversely, a patient may also have significant mental illness, yet still be able to understand the risks and benefits of a particular treatment (Carpenter et al., 2000). Multidisciplinary communication is important in challenging cases, and expert consultation should be utilized as needed (Karasic & Fraser, 2018). For many patients, difficulty understanding the risks and benefits of a particular treatment can be overcome with time and careful explanation. For some patients, treatment of the underlying condition that is interfering with the capacity to give informed consent—for example treating an underlying psychosis—will allow the patient to gain the capacity to consent to the required treatment. However, mental health symptoms such as anxiety or depressive symptoms that do not affect the capacity to give consent should not be a barrier for gender-affirming medical treatment, particularly as this treatment has been found to reduce mental health symptomatology (Aldridge et al., 2020).

Statement 18.2

We recommend mental health professionals offer care and support to transgender and gender diverse people to address mental health symptoms that interfere with a person's capacity to participate in essential perioperative care before gender-affirmation surgery.

The inability to adequately participate in perioperative care due to mental illness or substance use should not be viewed as an obstacle to needed transition care, but should be seen as an indication mental health care and social support be provided (Karasic, 2020). Mental illness and substance use disorders may impair the ability of the patient to participate in perioperative care (Barnhill, 2014). Visits to health care providers, wound care, and other aftercare procedures (e.g., dilation after vaginoplasty) may be necessary for a good outcome. A patient with a substance use disorder might have difficulty keeping necessary appointments to the primary care provider and the surgeon. A patient with psychosis or severe depression might neglect their wound or not be attentive to infection or signs of dehiscence (Lee, Marsh et al., 2016). Active mental illness is associated with a greater need for further acute medical and surgical care after the initial surgery (Wimalawansa et al., 2014).

In these cases, treatment of the mental illness or substance use disorder may assist in achieving successful outcomes. Arranging more support for the patient from family and friends or a home health care worker may help the patient participate sufficiently in perioperative care for surgery to proceed. The benefits of mental health treatments that may delay surgery should be weighed against the risks of delaying surgery and should

include an assessment of the impact on the patients' mental health delays may cause in addressing gender dysphoria (Byne et al., 2018).

Statement 18.3

We recommend when significant mental health symptoms or substance abuse exists, mental health professionals assess the potential negative impact mental health symptoms may have on outcomes based on the nature of the specific gender-affirming surgical procedure.

Gender-affirming surgical procedures vary in terms of their impact on the patient. Some procedures require a greater ability to follow preoperative planning as well as engage in peri- and postoperative care to achieve the best outcomes (Tollinche et al., 2018). Mental health symptoms can influence a patient's ability to participate in the planning and perioperative care necessary for any surgical procedure (Paredes et al., 2020). The mental health assessment can provide an opportunity to develop strategies to address the potential negative impact mental health symptoms may have on outcomes and to plan support for the patient's ability to participate in the planning and care. Gender-affirming surgical procedures have been shown to relieve symptoms of gender dysphoria and improve mental health (Owen-Smith et al., 2018; van de Grift, Elaut et al., 2017). These benefits are weighed against the risks of each procedure when the patient and provider are deciding whether to proceed with the treatment. HCPs can assist TGD people in reviewing preplanning and perioperative care instructions for each surgical procedure (Karasic, 2020). Provider and patient can collaboratively determine the necessary support or resources needed to assist with keeping appointments for perioperative care, obtaining necessary supplies, addressing financial issues, and handling other preoperative coordination and planning. In addition, issues surrounding appearance-related and functional expectations, including the impact of these various factors on gender dysphoria, can be explored.

Statement 18.4

We recommend health care professionals assess the need for psychosocial and practical support of transgender and gender diverse people in the perioperative period surrounding gender-affirmation surgery.

Regardless of specialty, all HCPs have a responsibility to support patients in accessing medically necessary care. When HCPs are working with TGD people as they prepare for gender-affirming surgical procedures, they should assess the levels of psychosocial and practical support required (Deutsch, 2016b). Assessment is the first step in recognizing where additional support may be needed and enhancing the ability to work collaboratively with the individual to successfully navigate the pre-, peri-, and postsurgical periods (Tollinche et al., 2018). In the perioperative period, it is important to help patients optimize functioning, secure stable housing, when possible, build social and family supports by assessing their unique situation, plan ways of responding to medical complications, navigate the potential impact on work/income, and overcome additional hurdles some patients may encounter, such as coping with electrolysis and tobacco cessation (Berli et al., 2017). In a complex medical system, not all patients will be able to independently navigate the procedures required to obtain care, and HCPs and peer navigators can support patients through this process (Deutsch, 2016a).

Statement 18.5

We recommend health care professionals counsel and assist transgender and gender diverse people in becoming abstinent from tobacco/nicotine prior to gender-affirmation surgery.

Transgender populations have higher rates of tobacco and nicotine use (Kidd et al., 2018). However, many are unaware of the well-documented smoking-associated health risks (Bryant et al., 2014). Tobacco consumption increases the risk of developing health problems (e.g., thrombosis) in individuals receiving gender-affirming hormone treatment, particularly estrogens (Chipkin & Kim, 2017).

Tobacco use has been associated with worse outcomes in plastic surgery, including overall complications, tissue necrosis, and the need for surgical revision (Coon et al., 2013). Smoking also increases the risk for postoperative infection (Kaoutzanis et al., 2019). Tobacco use has been shown to affect

the healing process following any surgery, including gender-related surgeries (e.g., chest reconstructive surgery, genital surgery) (Pluvy, Garrido et al., 2015). Tobacco users have a higher risk of cutaneous necrosis, delayed wound healing, and scarring disorders due to hypoxia and tissue ischemia (Pluvy, Panouilleres et al., 2015). In view of this, surgeons recommend stopping the use of tobacco/nicotine prior to gender-affirmation surgery and abstaining from smoking up to several weeks postoperatively until the wound has completely healed (Matei & Danino, 2015). Despite the risks, cessation may be difficult. Tobacco smoking and nicotine use is addictive and is also used as a coping mechanism (Matei et al., 2015). HCPs who see patients longitudinally before surgery, including mental health and primary care providers, should address the use of tobacco/nicotine with individuals in their care, and either assist TGD people in accessing smoking cessation programs or provide treatment directly (e.g., varenicline or bupropion).

Statement 18.6

We recommend health care professionals maintain existing hormone treatment if a transgender and gender diverse individual requires admission to a psychiatric or medical inpatient unit, unless contraindicated.

TGD people entering inpatient psychiatric, substance use treatment, or medical units should be maintained on their current hormone regimens. There is an absence of evidence supporting routine cessation of hormones prior to medical or psychiatric admissions. Rarely, a newly admitted patient may be diagnosed with a medical complication necessitating suspension of hormone treatment, for example an acute venous thromboembolism (Deutsch, 2016a). There is no strong evidence for routinely stopping hormone treatment prior to surgery, and the risks and benefits for each individual patient should be assessed before doing so (Boskey et al., 2018).

Hormone treatment has been shown to improve quality of life and to decrease depression and anxiety (Aldridge et al., 2020; Nguyen et al., 2018; Nobili et al., 2018; Owen-Smith et al., 2018, Rowniak et al., 2019). Access to gender-affirming medical treatment is associated with a substantial reduction in the risk of suicide attempt (Bauer et al., 2015). Halting a patient's regularly prescribed hormones denies the patient of these salutary effects, and therefore may be counter to the goals of hospitalization.

Some providers may be unaware of the low risk of harm and the high potential benefit of continuing transition-related treatment in the inpatient setting. A study of US and Canadian medical schools revealed that students received an average of 5 hours of LGBT-related course content over their entire four years of education (Obedin-Maliver et al., 2011). According to a survey of Emergency Medicine physicians, who are often responsible for making quick decisions about medications as patients are being admitted, while 88% reported caring for transgender patients, only 17.5% had received any formal training about this population (Chisolm-Straker et al., 2018). As education about transgender topics increases, more providers will become aware of the importance of maintaining transgender patients on their hormone regimens during hospitalization.

Statement 18.7

We recommend health care professionals ensure if transgender and gender diverse people need inpatient or residential mental health, substance abuse, or medical care, all staff use the correct name and pronouns (as provided by the patient), as well as provide access to bathroom and sleeping arrangements that are aligned with the person's gender identity.

Many TGD patients encounter discrimination in a wide range of health settings, including hospitals, mental health treatment settings, and drug treatment programs (Grant et al., 2011). When health systems fail to accommodate TGD individuals, they reinforce the longstanding societal exclusion many have experienced (Karasic, 2016). Experiences of discrimination in health settings lead to avoidance of needed health care due to anticipated discrimination (Kcomt et al., 2020).

The experience of discrimination experienced by TGD individuals is predictive of suicidal ideation (Rood et al., 2015; Williams et al., 2021). Gender minority stress associated with rejection and nonaffirmation has also been associated with suicidality (Testa et al., 2017). Denial of access to gender appropriate bathrooms has been

associated with increased suicidality (Seelman, 2016). However, the use of chosen names for TGD people has been associated with lower depression and suicidality (Russell et al., 2018). Structural as well as internalized transphobia must be addressed to reduce the incidence of suicide attempts in TGD people (Brumer et al., 2015). To successfully provide care, health settings must minimize the harm done to patients because of transphobia by respecting and accommodating TGD identities.

Statement 18.8

We recommend mental health professionals encourage, support, and empower transgender and gender diverse people to develop and maintain social support systems, including peers, friends, and families.

While minority stress and the direct effects of discriminatory societal discrimination can be harmful to the mental health of TGD people, strong social support can help lessen this harm (Trujillo et al., 2017). TGD children often internalize rejection from family and peers as well as the transphobia that surrounds them (Amodeo et al., 2015). Furthermore, exposure to transphobic abuse may be impactful across a person's lifespan and may be particularly acute during the adolescent years (Nuttbrock et al., 2010).

The development of affirming social support is protective of mental health. Social support can act as a buffer against the adverse mental health consequences of violence, stigma, and discrimination (Bockting et al., 2013), can assist in navigating health systems (Jackson Levin et al., 2020), and can contribute to psychological resilience in TGD people (Bariola et al., 2015; Başar and Öz, 2016). Diverse sources of social support, especially LGBTQ + peers and family, have been found to be associated with better mental health outcomes, well-being, and quality of life (Bariola et al., 2015; Başar et al., 2016; Kuper, Adams et al., 2018; Puckett et al., 2019). Social support has been proposed to facilitate the development of coping mechanisms and lead to positive emotional experiences throughout the transition process (Budge et al., 2013).

HCPs can support patients in developing social support systems that allow them to be recognized and accepted as their authentic identity and help them cope with symptoms of gender dysphoria. Interpersonal problems and lack of social support have been associated with a greater incidence of mental health difficulties in TGD people (Bouman, Davey et al., 2016; Davey et al., 2015) and have been shown to be an outcome predictor of gender-affirming medical treatment (Aldridge et al., 2020). Therefore, HCPs should encourage, support, and empower TGD people to develop and maintain social support systems. These experiences can foster the development of interpersonal skills and help with coping with societal discrimination, potentially reducing suicidality and improving mental health (Pflum et al., 2015).

Statement 18.9

We recommend health care professionals should not make it mandatory for transgender and gender diverse people to undergo psychotherapy prior to the initiation of gender-affirming treatment, while acknowledging psychotherapy may be helpful for some transgender and gender diverse people.

Psychotherapy has a long history of being used in clinical work with TGD people (Fraser, 2009b). The aims, requirements, methods and principles of psychotherapy have been an evolving component of the Standards of Care from the initial versions (Fraser, 2009a). At present, psychotherapeutic assistance and counseling with adult TGD people may be sought to address common psychological concerns related to coping with gender dysphoria and may also help some individuals with the coming-out process (Hunt, 2014). Psychological interventions, including psychotherapy, offer effective tools and provide context for the individual, such as exploring gender identity and its expression, enhancing self-acceptance and hope, and improving resilience in hostile and disabling environments (Matsuno and Israel, 2018). Psychotherapy is an established alternative therapeutic approach for addressing mental health symptoms that may be revealed during the initial assessment or later during the follow-up for gender-affirming medical interventions. Recent research shows, although mental health symptoms are reduced following gender-affirming medical treatment, levels of anxiety remain high (Aldridge et al., 2020) suggesting psychological therapy can play a role in helping

individuals suffering from anxiety symptoms following gender-affirming treatment.

In recent years, the uses and potential benefits of specific psychotherapeutic modalities have been reported (Austin et al., 2017; Budge, 2013; Budge et al., 2021; Embaye, 2006; Fraser, 2009b; Heck et al., 2015). Specific models of psychotherapy have been proposed for adult transgender and nonbinary individuals (Matsuno & Israel, 2018). However, more empiric data is needed on the comparative benefits of different psychotherapeutic models (Catelan et al., 2017). Psychotherapy can be experienced by transgender persons as a fearful as well as a beneficial experience (Applegarth & Nuttall, 2016) and presents challenges to the therapist and to alliance formation when it is associated with gatekeeping for medical interventions (Budge, 2015).

Experience suggests many transgender and nonbinary individuals decide to undergo gender-affirming medical treatment with little or no use of psychotherapy (Spanos et al., 2021). Although various modalities of psychotherapy may be beneficial for different reasons before, during, and after gender-affirming medical treatments and varying rates of desire for psychotherapy have been reported during different stages of transition (Mayer et al., 2019), a requirement for psychotherapy for initiating gender-affirming medical procedures has not been shown to be beneficial and may be a harmful barrier to care for those who do not need this type of treatment or who lack access to it.

Statement 18.10

We recommend "reparative" and "conversion" therapy aimed at trying to change a person's gender identity and lived gender expression to become more congruent with the sex assigned at birth should not be offered.

The use of "reparative" or "conversion" therapy or gender identity "change" efforts is opposed by many major medical and mental health organizations across the world, including the World Psychiatric Association, Pan American Health Organization, American Psychiatric and American Psychological Associations, Royal College of Psychiatrists, and British Psychological Society. Many states in the US have instituted bans on practicing conversion therapy with minors. Gender identity change efforts refers to interventions by MHPs or others that attempt to change gender identity or expression to be more in line with those typically associated with the person's sex assigned at birth (American Psychological Association, 2021).

Advocates of "conversion therapy" have suggested it could potentially allow a person to fit better into their social world. They also point out some clients specifically ask for help changing their gender identities or expressions and therapists should be allowed to help clients achieve their goals. However, "conversion therapy" has not been shown to be effective (APA, 2009; Przeworski et al., 2020). In addition, there are numerous potential harms. In retrospective studies, a history of having undergone conversion therapy is linked to increased levels of depression, substance abuse, suicidal thoughts, and suicide attempts, as well as lower educational attainment and less weekly income (Ryan et al., 2020; Salway et al., 2020; Turban, Beckwith et al., 2020). In 2021, the American Psychological Association resolutions states that "scientific evidence and clinical experience indicate that GICEs [gender identity change efforts] put individuals at significant risk of harm" (APA, 2021).

While there are barriers to ending gender identity "change" efforts, education about the lack of benefit and the potential harm of these practices may lead to fewer providers offering "conversion therapy" and fewer individuals and families choosing this option.

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Conflict of Interest

Conflict of interests were reviewed as part of the selection process for committee members and at the end of the process before publication. No conflicts of interest were deemed significant or consequential.

Ethical Approval

This manuscript does not contain any studies with human participants performed by any of the authors.

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Appendix A METHODOLOGY

1. Introduction

This version of the Standards of Care (SOC-8) is based upon a more rigorous and methodological evidence-based approach than previous versions. This evidence is not only based on the published literature (direct as well as background evidence) but also on consensus-based expert opinion. Evidence-based guidelines include recommendations intended to optimize patient care and are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options. Evidence-based research provides the basis for sound clinical practice guidelines and recommendations but must be balanced by the realities and feasibility of providing care in diverse settings. The process for development of the SOC-8 incorporated recommendations on clinical practice guideline development from the National Academies of Medicine and The World Health Organization that addressed transparency, the conflict-of-interest policy, committee composition and group process. (Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice, 2011; World Health Organization, 2019a).

The SOC-8 revision committee was multidisciplinary and consisted of subject matter experts, health care professionals, researchers and stakeholders with diverse perspectives and geographic representation. All committee members completed conflict of interest declarations.*

A guideline methodologist assisted with the planning and development of questions, and an independent team undertook systematic reviews that were used to inform some of the statements for recommendations. Additional input to the guidelines was provided by an international advisory committee, legal experts, and feedback received during a public comment period. Recommendations in the SOC-8 are based on available evidence supporting interventions, a discussion of risks and harms, as well as feasibility and acceptability within different contexts and country settings. Consensus of the final recommendations was attained using a Delphi process that included all members of the Standards of Care Revision committee and required that recommendation statements were approved by 75% of members. Supportive and explanatory text of the evidence for the statements were written by chapter members. Drafts of the chapters were reviewed by the Chair and the Co-Chairs of the SOC Revision Committee to ensure the format was consistent, evidence was properly provided, and recommendations were consistent across chapters. An independent team checked the references used in the SOC-8 before the guidelines were fully edited by a single professional. A detailed overview of the SOC-8 Methodology is described below.

2. Difference between the methodology of the SOC-8 and previous editions

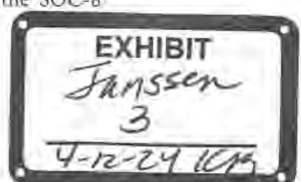
The main differences in the methodology of the SOC-8 when compared with other versions of the SOC are:

- The involvement of a larger group of professionals from around the globe;
- A transparent selection process to develop the guidelines steering committee as well as to select chapter leads and members;
- The inclusion of diverse stakeholders in the development of the SOC-8
- Management of conflicts of interest
- The use of a Delphi process to reach agreement on the recommendations among SOC-8 committee members
- The involvement of an independent body from a reputable university to help develop the methodology and undertake independent systematic literature reviews where possible
- Recommendations were graded as either "recommend" or "suggest" based upon the strength of the recommendations.
- The involvement of an independent group of clinical academics to review citations.
- The involvement of international organizations working with the transgender and gender diverse (TGD) community, members of WPATH and other professional organizations as well as the general public who provided feedback through a public comment period regarding the whole SOC-8.

3. Overview of SOC-8 development Process

The steps for updating the Standards of Care are summarized below:

1. Establishing Guideline Steering Committee including Chair, and Co-Chairs (July 19, 2017)
2. Determining chapters (scope of guidelines)
3. Selecting Chapter Members based upon expertise (March 2018)
4. Selecting the Evidence Review Team: John Hopkins University (May 2018)
5. Refining topics included in the SOC-8 and review questions for systematic reviews
6. Conducting systematic reviews (March 2019)
7. Drafting the recommendation statements
8. Voting on the recommendation statements using a Delphi process (September 2019–February 2022)
9. Grading of the recommendations statements
10. Writing the text supporting the statements
11. Independently validating the references used in the supportive text
12. Finalizing a draft SOC-8 (December 1, 2021)
13. Feedback on the statements by International Advisory Committee
14. Feedback on the entire draft of the SOC-8 during a public comment period (November 2021–January 2022)
15. Revision of Final Draft based on comments (January 2022- May 2022)
16. Approval of final Draft by Chair and Co-Chairs (June 10, 2022)
17. Approval by the WPATH Board of Directors
18. Publication of the SOC-8
19. Dissemination and translation of the SOC-8



3.1. Establishment of Guideline Steering Committee

The WPATH Guideline Steering Committee oversaw the guideline development process for all chapters of the Standards of Care. Except for the Chair (Eli Coleman) who was appointed by the WPATH board to maintain a continuity from previous SOC editions, members of the Guideline Steering Committee were selected by the WPATH Board from WPATH members applying for these positions. Job descriptions were developed for the positions of Co-Chairs, Chapter Leads, Chapter Members and Stakeholder. WPATH members were eligible to apply by completing an application form and submitting their CV. The Board of WPATH voted for the position of co-chair (one member of the board did not participate in view of conflict of interest). The chairs and co-chairs selected the chapter leads and members (as well as stakeholders) based on the application form and CVs.

The Guideline Steering Committee for Standards of Care 8th Version are:

- Eli Coleman, PhD (Chair) Professor, Director and Academic Chair, Institute for Sexual and Gender Health, Department of Family Medicine and Community Health, University of Minnesota Medical School (USA)
- Asa Radix, MD, PhD, MPH (Co-chair) Senior Director, Research and Education Callen-Lorde Community Health Center Clinical Associate Professor of Medicine New York University, USA
- Jon Arcelus, MD, PhD (Co-chair) Professor of Mental Health and Well-being Honorary Consultant in Transgender Health University of Nottingham, UK
- Karen A. Robinson, PhD (Lead, Evidence Review Team) Professor of Medicine, Epidemiology and Health Policy & Management Johns Hopkins University, USA

3.2. Determination of topics for chapters

The Guideline Steering Committee determined the chapters for inclusion in the Standards of Care by reviewing the literature and by reviewing the previous edition of the SOC. The chapters in the Standards of Care 8th Version:

1. Terminology
2. Global Applicability
3. Population estimates
4. Education*
5. Assessment of Adults
6. Adolescent
7. Children
8. Nonbinary
9. Eunuch
10. Intersex
11. Institutional environments
12. Hormone Therapy
13. Surgery and Postoperative Care
14. Voice and communication
15. Primary care
16. Reproductive Health
17. Sexual Health
18. Mental Health

* The Education Chapter was originally intended to cover both education and ethics. A decision was made to create a separate committee to write a chapter on ethics. In the course of writing the chapter, it was later determined topic of ethics was best placed external to the SOC8 and required further in-depth examination of ethical considerations relevant to transgender health.

3.3. Selection of chapter members

A call for applications to be part of the SOC-8 review committee (chapter lead or member) was sent to the WPATH membership. The Chairs of the Guideline Steering Committee appointed the members for each chapter, ensuring representation from a variety of disciplines and perspectives.

Chapter Leads and Members were required to be WPATH Full Members in good standing and content experts in transgender health, including in at least one chapter topic. Chapter Leads reported to the Guideline Steering Committee and were responsible for coordinating the participation of Chapter Members. Chapter members reported directly to the Chapter Lead.

Each chapter also included stakeholders as members who bring perspectives of transgender health advocacy or work in the community, or as a member of a family that included a transgender child, sibling, partner, parent, etc. Stakeholders were not required to be full members of WPATH.

The Chapter Members were expected to:

- Participate in the development refinement of review questions
- Read and provide comments on all materials from the Evidence Review Team
- Critically review draft documents, including the draft evidence report
- Review and assess evidence and draft recommendations
- Participate in the Delphi consensus process
- Develop the text to back up the recommendation statements
- Grade each statement to describe the strength of the recommendation
- Review and address the comments from the Chairs during the whole process
- Develop the content of the chapters
- Review comments from public comments and assist in the development of a revision of guidelines
- Provide input and participate in the dissemination of guidelines

Training and orientation for Chapter Leads and Members was provided, as needed. Training content included formulation and refinement of questions (i.e., use of PICO), reviewing the evidence, developing recommendation state-

ments, grading the evidence and the recommendations, and information about the guideline development program and process.

A total of 26 chapter-leads were appointed (some chapters required co-leads), 77 chapter members and 16 stakeholders. A total of 127 were selected. During the SOC process, 8 people left, due to personal or work-related issues. Therefore, there were 119 final authors of the SOC-8.

3.4. Selection of the evidence review team

The WPATH Board issued a request for applications to become the Evidence Review Team. For Standards of Care 8th Version the WPATH Board engaged the Evidence Review Team at Johns Hopkins University under the leadership of Karen Robinson.

- Karen A. Robinson, PhD (Lead, Evidence Review Team) Professor of Medicine, Epidemiology and Health Policy & Management Johns Hopkins University, USA

Dr Robinson also guided the steering committee in the development of the SOC-8 by providing advice and training in the development of PICO questions, statements, and the Delphi process as well as undertaking a very rigorous systematic literature review where direct evidence was available.

Conflict of interest

Members of the Guideline Steering Committee, Chapter Leads and Members, and members of the Evidence Review Team were asked to disclose any conflicts of interest. Also reported, in addition to potential financial and competing interests or conflicts, are personal or direct reporting relationships with a chair, co-chair or a WPATH Board Member or the holding of a position on the WPATH Board of Directors.

3.5. Refinement of topics and review of questions

The Evidence Review Team abstracted the recommendation statements from the prior version of the Standards of Care. With input from the Evidence Review Team, the Guideline Steering Committee and Chapter Leads determined:

- Recommendation statements that needed to be updated
- New areas requiring recommendation statements

3.6. Conduct the systematic reviews

Chapter Members developed questions to help develop recommendation statements. For the questions eligible for systematic review, the Evidence Review Team drafted review questions, specifying the Population, Interventions, Comparisons, and Outcomes (PICO elements). The Evidence Review Team undertook the systematic reviews. The Evidence Review Team presented evidence tables and other results of the systematic reviews to the members of the relevant chapter for feedback.

Protocol

A separate detailed systematic review protocol was developed for each review question or topic, as appropriate. Each protocol was registered on PROSPERO.

Literature search

The Evidence Review Team developed a search strategy appropriate for each research question including MEDLINE®, Embase™, and the Cochrane Central Register of Controlled Trials (CENTRAL). The Evidence Review Team searched additional databases as deemed appropriate for the research question. The search strategy included MeSH and text terms and was not limited by language of publication or date.

The Evidence Review Team hand searched the reference lists of all included articles and recent, relevant systematic reviews. The Evidence Review Team searched ClinicalTrials.gov for any additional relevant studies.

Searches were updated during the peer review process.

The literature included in the systematic review was mostly based on quantitative studies conducted in Europe, the US or Australia. We acknowledge a bias towards perspectives from the global north that does not pay sufficient attention to the diversity of lived experiences and perspectives within transgender and gender diverse (TGD) communities across the world. This imbalance of visibility in the literature points to a research and practice gap that needs to be addressed by researchers and practitioners in the future in order to do justice to the support needs of all TGD people independent of gender identification.

Study selection

The Evidence Review Team, with input from the Chapter Workgroup Leads, defined the eligibility criteria for each research question *a priori*.

Two reviewers from the Evidence Review Team independently screened titles and abstracts and full-text articles for eligibility. To be excluded, both reviewers needed to agree that the study met at least one exclusion criteria. Reviewers resolved differences regarding eligibility through discussion.

Data extraction

The Evidence Review Team used standardized forms to abstract data on general study characteristics, participant characteristics, interventions, and outcome measures. One reviewer abstracted the data, and a second reviewer confirmed the abstracted data.

Assessment of risk of bias

Two reviewers from the Evidence Review Team independently assessed the risk of bias for each included study. For

randomized controlled trials, the Cochrane Risk of Bias Tool was used. For observational studies, the Risk of Bias in Non-Randomized Studies—of Interventions (ROBINS-I) tool was used. Where deemed appropriate, existing recent systematic reviews were considered and evaluated using ROBIS.

Data synthesis and analysis

The Evidence Review Team created evidence tables detailing the data abstracted from the included studies. The members of the Chapter Workgroups reviewed and provided comments on the evidence tables.

Grading of the evidence

The Evidence Review Team assigned evidence grades using the GRADE methodology. The strength of the evidence was obtained using predefined critical outcomes for each question and by assessing the limitations to individual study quality/risk of bias, consistency, directness, precision, and reporting bias.

3.7. Drafting of the Recommendation Statements

Chapter Leads and Members drafted recommendation statements. The statements were crafted to be feasible, actionable, and measurable.

Evidence-based recommendation statements were based on the results of the systematic, and background literature reviews plus consensus-based expert opinions.

The Chair and Co-Chairs and Chapter Leads reviewed and approved all recommendation statements for clarity and consistency in wording. During this review and throughout the process any overlap between chapters was also addressed.

Many chapters had to work closely together to ensure consistency of their recommendations. For example, as there are now separate chapters for childhood and adolescence, to ensure consistency between both chapters, some authors were part of both chapters. For a similar reason, when applicable, a workgroup collaborated with other Chapter Workgroups on topics shared between the chapters (i.e., Assessment of Children, Assessment of Adults, Hormone Therapy, Surgery and Postoperative Care and Reproductive Health).

3.8. Approval of the recommendations using the Delphi process

Formal consensus for all statements was obtained using the Delphi process (a structured solicitation of expert judgements in three rounds). For a recommendation to be approved, a minimum of 75% of the voters had to approve the statement. A minimum of 65% of the SOC-8 members had to take part in the Delphi process for each statement. People who did not approve the statement had to provide information as to the reasons for their disapproval, so the statement could be modified (or removed) according to this feedback. Once modified, the statement was put through the Delphi process again. If after 3 rounds the statement was not approved, the statement was removed from the SOC. Every member of the SOC voted for each statement. There was a response rate between (74.79% and 94.96%) for the statements.

3.9. Grading criteria for statements

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

- The balance of potential benefits and harms
- Confidence in that balance or quality of evidence
- Values and preferences of providers and patients
- Resource use and feasibility

The statements were classified as:

- Strong recommendations ("we recommend") are for those interventions/therapy/strategies where:
  - the evidence is of high quality
  - estimates of the effect of an intervention/therapy/strategy (i.e., there is a high degree of certainty effects will be achieved in practice)
  - there are few downsides of therapy/intervention/strategy
  - there is a high degree of acceptance among providers and patients or those for whom the recommendation applies.
- Weak recommendations ("we suggest") are for those interventions/therapy/strategies where:
  - there are weaknesses in the evidence base
  - there is a degree of doubt about the size of the effect that can be expected in practice
  - there is a need to balance the potential upsides and downsides of interventions/therapy/strategies
  - there are likely to be varying degrees of acceptance among providers and patients or those for whom the recommendation applies.

3.10. Writing of the text supporting the statements

Following the grading of the statements, the Chapter Workgroups wrote the text providing the rationale or reasoning for the recommendation. This included providing the available evidence, providing details about potential benefits and harms, describing uncertainties, and information about implementation of the recommendation, including expected barriers or challenges among others. References use APA-7 style, to support the information in the text. Links to resources are also provided, as appropriate. The text, including whether a recommendation has been described as strong or weak, was reviewed and approved by the Chair and Co-Chairs.

3.11. External validation of references used to support the statements

A group of independent clinical academics working in the field of transgender health reviewed the references used in every chapter in order to validate that the references were appropriately used to support the text. Any queries regarding the references were sent back to the chapters for review.

3.12. Finalizing a draft SOC-8

A final SOC-8 draft was made available for comments.

3.13. Distribute Standards of Care for review by international advisors

The statements of the recommendations of Standards of Care 8th were circulated among the broader Standards of Care Revision Committee and the WPATH International Advisory Group, which included the Asia Pacific Transgender Network (APTN), the Global Action for Transgender Equality (GATE), the International Lesbian, Gay, Bisexual, Transgender, Intersex Association (ILGA), and Transgender Europe (TGEU).

3.14. Public comment period

The revised draft version of the Standards of Care document was posted online for comment from the public, including WPATH members, on the WPATH website. A 6-week period was allocated for comments. A total of 1,279 people made comments on the draft with a total of 2,688 comments.

3.15. Revision of final draft based on comments

The Chapter Leads and Guideline Steering Committee considered the feedback and made any necessary revisions. All public comments were read and, where appropriate, integrated into the background text.

As part of this process, 3 new Delphi statements were developed and 2 were modified enough to require a new vote by the SOC-8 committee. This meant a new Delphi process was initiated in January 2022. The results of this Delphi process were accepted by the chapters, and the new statements were added or modified accordingly. The new supportive text was added.

All the new versions of the chapters were reviewed again by the Chair and Co-Chairs and changes or modifications were suggested. Finally, once the Chairs and the Chapter Members were satisfied with the draft, the chapter was finalized.

All new references were double checked by an independent member.

3.16. Approval of final draft by Chair and Co-Chairs

Modifications were reviewed by the Chairs and were accepted by them.

3.17. Approval by the WPATH Board of Directors

The final document was presented to the WPATH Board of Directors for approval and it was approved on the 20th of June 2022.

3.18. Publication of the SOC-8 and dissemination of the Standards of Care

The Standards of Care was disseminated in a number of venues and in a number of formats including publication in the International Journal of Transgender Health (the official scientific journal of WPATH).

4. Plan to Update

A new edition of the SOC (SOC-9) will be developed in the future, when new evidence and/or significant changes in the field necessitating a new edition is substantial.

*The development of SOC-8 was a complex process at a time of COVID-19 and political uncertainties in many parts of the world. Members of the SOC-8 worked on the SOC-8 on top of their day-to-day job, and most of the meetings took place out of their working time and during their weekends via Zoom. There were very few face-to-face meetings, most of them linked to WPATH, USPATH or EPATH conferences. Committee members of the SOC-8 were not paid as part of this process.

SPECIAL ISSUE ARTICLE

Supporting the Mental Health of Transgender and Gender-Diverse Youth

Claire A. Coyne, PhD; T. Zachary Huit, PhD; Aron Janssen, MD; and Diane Chen, PhD

ABSTRACT

Increasing numbers of youth are identifying as transgender or gender diverse (TGD), meaning their gender identity or expression do not conform to culturally defined expectations for their designated sex at birth. The mental health needs of TGD youth are diverse, and to effectively address these needs requires knowledgeable general pediatric providers, who often are families' first resource for education and support around gender diversity. To help general pediatric providers work more effectively with TGD youth, we describe the role of mental health providers working with TGD youth and how best to support TGD youth's access to gender-affirming mental health and medical interventions. ***[Pediatr Ann*. 2023;52(12):e456–e461.]**

Transgender and gender-diverse (TGD) youth are those whose gender identity or expression does not conform to culturally defined expectations for their designated sex at birth. Recent population-based surveys estimate between 1.4%[1] and 9.2%[2] of high school-aged students identify as TGD in the United States. The increased prevalence of gender diversity among youth is likely attributable to multiple factors, including improved precision in gender terminology and assessment methods (eg, inclusion of nonbinary as a survey option), as well as cultural shifts in social norms about gender identity and expression. Gender development is an interactive and dynamic process that unfolds over time and is influenced by biological, social, and cultural factors.[3] Developing knowledgeable pediatric providers outside of gender specialty programs can reduce stigmatizing health

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care experiences for TGD youth.[4] Specifically, pediatric providers should understand the unique health care needs of TGD youth and principles of gender-affirming care that apply broadly in all service settings (eg, including chosen name in electronic medical records). The gender-affirmative model is the predominant evidence-based approach to gender care. Within this model, variation in gender identity and expression are nonpathological aspects of human diversity.[5] Gender-affirming providers thus focus on supporting people to live authentically without privileging any outcome other than prioritizing emotional well-being. This approach recognizes there is no "right way" to be TGD or single trajectory for youth exploring medical interventions.[6]

Although gender diversity is not inherently pathological, TGD youth do experience significant health disparities compared with their cisgender peers. Higher rates of depression, anxiety, suicidality, and substance use and poorer health status among TGD youth[7] are attributable in part to the effects of gender-related stigma and discrimination[7] and lack of access to quality health care.[8,9] Exposure to stigmatizing messages and discriminatory experiences (eg, nonaffirming school, community, or home environments) leads to negative internalized beliefs about gender diversity, which are linked to major depressive and generalized anxiety disorders in TGD youth.[10] That said, health care providers should be cautious not to attribute physical or mental health concerns solely to gender-related stigma and discrimination. This overgeneralization can occur when providers make assumptions about their patients' background and health needs, which subsequently can compound health disparities by delaying access to appropriate care.[11]

These health disparities highlight the need to improve access to high-quality and developmentally appropriate health care for TGD youth and their families. Providers who understand gender development and the range of available supports and interventions for gender dysphoria—ie, distress associated with incongruence between gender and designated sex at birth—can reduce stigma and the effect of gender minority stress in health care settings. Knowledgeable providers can identify when co-occurring psychopathology may be attributable to factors unrelated to gender diversity (eg, genetic risk) and provide appropriate treatment referrals. To help general pediatric providers work more effectively with TGD youth, we describe the role of mental health providers working with TGD youth and how best to support TGD youth's access to gender-affirming mental health and medical interventions.

GENDER-AFFIRMING SOCIAL, MEDICAL, AND SURGICAL INTERVENTIONS FOR GENDER DYSPHORIA

For TGD youth experiencing gender dysphoria, mental health support needs will likely vary over time and development.[4] At earlier stages, this may take the form of developing ways to describe and understand their own identity or identities, as well as finding self-acceptance. Providers may help youth and families explore social interventions that involve transitioning to live in line with their experienced gender rather than the gender aligned with designated sex at birth. Social interventions are generally considered reversible and may include changing clothing, hairstyles, name, and pronouns. As puberty progresses, nonmedical interventions such as chest binding, tucking, voice therapy, and hair removal are safe, reversible options that can help TGD youth explore their embodiment goals. These social interventions are associated with reduced mental health symptoms in both youth and adolescents, with evidence that socially transitioned prepubertal children (ie, from boy to girl or girl to boy) experience developmentally normative levels of depression and only minimally elevated levels of anxiety.[12] Similarly, use of chosen name and pronouns in more contexts (eg, at home, at school, with peers) is associated with less depression, suicidal ideation, and suicidal behavior among TGD adolescents.[13] Therapeutic support may also include assisting youth in navigating social environments (eg, school, peers), eventual transition into adulthood, and developing strategies for self-advocacy in various spaces (eg, college, health care, career). The frequency and intensity of mental health support is likely best tailored to each person's and family's needs.

Medical and surgical treatments for gender dysphoria vary based on a youth's age, developmental stage, and individualized treatment goals and are informed by clinical practice guidelines by the World Professional Association for Transgender Health (WPATH)[14] and the Endocrine Society.[15] Treatment options are provided in a staged manner, with treatments considered "reversible" typically offered before treatments considered "partially irreversible" or "irreversible." No medical or surgical treatments are indicated before pubertal onset. For pediatric populations, guidelines recommend a multidisciplinary approach to diagnosing gender dysphoria and ensuring that youth and their caregivers understand the benefits and potential risks of medical treatment and have accurate and appropriate expectations of treatment.[4] Support from a consenting parent or legal guardian is also required for minors.

In early puberty, medications to suppress endogenous sex hormone production may be offered. Gonadotropin-releasing hormone analogues (GnRHa), often referred to as "puberty blockers," suspend pubertal progression by suppressing the hypothalamic-pituitary-gonadal axis. This prevents gonadal sex hormone production (ie, testosterone and estrogen). GnRHa are considered reversible and are intended to provide time for TGD youth to mature and consider whether additional medical, surgical, or both types of interventions are aligned with their embodiment goals. Research suggests puberty blockers improve some aspects of mental health, although results are mixed. Three longitudinal studies have examined the psychosocial effect of puberty blockers, with two studies demonstrating improvement in psychosocial functioning[16,17] and a third demonstrating no change in overall emotional or behavioral problems after 36 months of treatment.[18] An additional cross-sectional study reported TGD youth treated with puberty blockers had fewer overall emotional and behavioral problems compared with gender clinic-referred, untreated youth.[19]

For TGD adolescents in later puberty, treatment with gender-affirming hormones (ie, testosterone or estrogen) will induce desired, gender-congruent secondary sex characteristics. Testosterone-mediated changes include facial and body hair growth and voice deepening; estrogen-mediated changes include breast development. Gender-affirming hormone treatment is considered partially irreversible—some physical changes (eg, fat distribution) are reversible, whereas others are irreversible (eg, breast development, voice deepening). There are five US-based, prospective, longitudinal studies examining psychosocial outcomes of gender-affirming hormone treatment.[20-24] Four studies reported improvements in depression,[20,22,23] anxiety,[22,23] body dissatisfaction,[22] appearance congruence,[22] suicidality,[21] positive affect,[22] life satisfaction,[22] and general well-being[21] after 1 to 2 years of treatment. A fifth study examined 104 youth, and during a 1-year period, 69 received puberty blockers, gender-affirming hormones, or both. Although mental health did not improve over time among treated youth, treated youth did report 60% lower odds of depression and 73% lower odds of suicidality compared with untreated youth.[24] Most surgical interventions, which are considered irreversible, are offered only to TGD adults and may involve removing undesired reproductive organs (eg, ovaries/uterus, testicles), surgical construction of desired genital anatomy (eg, vaginoplasty, phalloplasty/metoidioplasty), and other nongenital surgical interventions (eg, tracheal shave). A notable exception is breast/chest surgery, which may be offered to adolescents who experience significant and impairing chest dysphoria, desire chest surgery, and have parental support and consent.[25] A recent multicenter, prospective, matched-control study found that chest masculinization surgery was associated with low complication rates and significant improvement in chest dysphoria, gender congruence, and body image satisfaction 3 months after surgery.[26]

ROLES OF MENTAL HEALTH PROVIDERS IN SUPPORTING TGD YOUTH

Psychosocial Assessment

It is valuable for mental health providers to engage both TGD youth and their caregivers in psychosocial assessment to understand the social, cultural, and familial contexts affecting gender development. Some TGD youth recognize and share a non-cisgender identity early in childhood, and others may delay sharing because of concerns about social and familial acceptance or because they lack the language to describe their experience. For other youth, pubertal progression and accompanying distress about physical changes lead to gender exploration.

There are multiple aims of a psychosocial assessment, and the relative salience of each is determined by the goals of the youth and their family, as well as the youth's age and stage of pubertal development. The first aim is to understand the person's experience of their gender identity, gender expression, relationship to their body, and how these experiences have developed over time and across contexts. For some, incongruence between any of these domains can lead to distress. A second aim is to understand that distress and begin to differentiate the degree to which distress is related to gender dysphoria, anti-TGD stigma, and bias or to co-occurring mental health concerns. The third aim is to understand both resiliency and vulnerability of the young person and the systems that surround them. Family support is vital to building resilience and shaping positive outcomes; and holding space for differing beliefs and priorities for youth and caregivers is inherent to an effective process. Each caregiver will have their own observations about the child, and eliciting these observations provides a holistic picture of the family system and how the child functions within this system. For many families, this is their first encounter with a mental health provider and represents an opportunity to create a positive experience that is patient- and family-focused. Throughout the assessment process, there are opportunities for providers to learn the unique strengths and challenges faced by the youth and their family, provide psychoeducation about gender diversity, and augment familial support and acceptance.[14]

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For prepubertal youth for whom medical interventions are not indicated, the assessment should be tailored to the goals of the family. A comprehensive biopsychosocial assessment should include (1) the child's gender history, including statements of identity and observed play and peer preferences, and relationship to the body; (2) individual and family/system risk and resilience factors and the beliefs of the child and their family, peers, and community about gender diversity; (3) the child's mental health history and cognitive and communication abilities; (4) the experience of gender minority stress by the child, the family, or both; (5) relevant medical and developmental history; (6) salience of their gender identity/diversity on day-to-day life[27]; and (7) observed effect when the child's experienced gender is validated or invalidated (see **Table 1** for sample clinical interview questions).

For adolescents, the assessment is similar and, depending on the youth's stage of pubertal development and individualized treatment goals, can include discussions of medical, surgical, or both types of interventions. Both the WPATH[14] and Endocrine Society[15] guidelines recommend that TGD youth seeking puberty blockers or gender-affirming hormones complete a comprehensive biopsychosocial assessment before initiating medical treatment. The assessment process is not intended to evaluate youth's gender identity but rather to assess their overall mental health functioning and criteria consistent with a gender dysphoria diagnosis, understand their embodiment goals, ensure youth and caregivers understand the reversible and irreversible effects of the desired medical/surgical intervention and demonstrate appropriate expectations of treatment outcomes, and in the case of minors, confirm caregiver support and consent for treatment.

TABLE 1

Sample Assessment Questions for Mental Health Providers Working with Transgender and Gender-Diverse Youth

For children, consider altering phrasing to match child's developmental level and use visual aids as needed:

- What words would you use to describe your gender?
- How would you describe being a boy/girl/nonbinary person?
- Tell me about what your friends are like.
- What kinds of things do you and your friends do together?
- What are some things you like about your body? Are there things you don't like about your body? If yes, why don't you like those aspects of your body? Would you change them if you could? How would you change them?
- Who in your life have you talked to about your gender?
- Has anyone ever spoken to you or treated you poorly because of their own negative views about your gender identity?

For adolescents, consider questions about gender identity, expression, experiences with their body, and perceptions of gender expression in multiple contexts:

- How would you describe your own internal experience of your gender identity?
- Tell me about when you first started thinking about your gender identity.
- Are there changes you have made to how you dress or wear your hair that have made you feel more comfortable? Tell me what that was like for you.
- Can you explain why you feel more comfortable as a boy/girl/nonbinary person?
- What aspects of being masculine/feminine/gender fluid aligns more with how you see yourself?
- Tell me about what your relationship is like with your current body. Are there positive aspects about your body? Are there things that are particularly challenging about your body?
- What has been your experience with noticing changes in your body during puberty? How has that process felt for you?
- Are there parts of your body that you feel like do not align with your gender identity? What parts of your body are they?
- From your perspective, what advantages or disadvantages might people experience based on their gender identity or expression?

For caregivers, consider questions about their child's gender history, their response when their child shared their gender identity, their beliefs about gender identity and expression, and concerns caregivers may have:

- Tell me about your child's gender identity and expression.
- What was it like for you when your child shared their gender identity?
- How did you learn about gender identity and expression? What do you understand about gender diversity?

Assessing Co-occurring Mental Health Concerns

Mental health challenges among TGD youth can be grouped into three main categories.[27] The first category includes symptoms developed as a result of minority stress and challenges related to identifying as a member of a margin-

alized group (eg, anxiety around using public restrooms). The second includes gender dysphoria and body-related distress. Conversely, providers can also assess experiences of gender-related validation and affirmation, sometimes referred to as gender euphoria. The third includes co-occurring mental health issues that are independent from gender dysphoria but may affect care. Research has shown higher rates of depression, anxiety, self-harm, suicidality, autism spectrum disorders, eating disorders, and ADHD among transgender youth when compared with cisgender peers.[7]

Psychotherapeutic Treatment

For many TGD youth, therapy provides a safe place to explore gender fluidly and flexibly, in a youth-led approach. Notably, gender exploration is not a linear process and is highly individualized, oftentimes with questions and fluctuations as youth find what is most consistent with their own innate experience of gender. As every TGD youth presents in various stages within their own gender journey, the need for support can vary significantly from person to person, between families, and in the course of development. Mental health care serves as a crucial source of support for navigating these challenging processes.

In addition to diversity in individual gender identity processes, families are varied in their own journeys of understanding and accepting their child's gender identity. According to the WPATH Standards of Care,[14] providers should work with families and social environments to promote acceptance of gender diversity and support youth exploration and decision-making throughout development into young adulthood. As such, families who are earlier in the process toward acceptance or have significant challenges to supporting their child's gender diversity may need more structured family and parental support. This can be a helpful addition to individual therapy for TGD youth and allows each family member to receive individualized support for navigating complex processes that may be distinct. This allows space for family members to confront their own emotional experiences within the process (eg, grief, confusion, anger, shame) as well as receive support in navigating interpersonal challenges separately, reducing potential harm of conveying stigmatizing messages in settings where TGD youth are present. Other families who are more knowledgeable and accepting of their child's gender diversity may need further support in managing external challenges or navigating complex social environments. Supports that may be helpful to families can include combinations of individual therapy for youth, family therapy to address communication or other family-level processes, and parent-specific education and their own therapy space to understand challenges they face to accepting and advocating for their TGD youth. The level to which such recommendations are made should take into consideration the well-being and safety of the TGD youth and thoughtful assessment of where family members are at in their own spectrum of acceptance to determine which types of support may be most beneficial.

Additionally, the degree to which gender is foregrounded within treatment is highly individualized and will likely vary over time. Treatment of co-occurring diagnoses (eg, depression and anxiety) must consider salient aspects of gender identity and socioenvironmental factors that may relate to primary concerns outside of gender identity exploration. Practice guidelines for mental health care with TGD individuals recommend adapting existing evidence-based interventions to ensure they are affirming and consider the nuanced experience of TGD youth.[28] To address commonly co-occurring depression and anxiety, clinicians can adapt evidence-based cognitive-behavioral interventions to address relevant stressors associated with gender identity (eg, misgendering). Coyne et al.[29] summarized key factors in adapting evidence-based practice, including (1) normalizing the role of minority stress and its negative sequelae; (2) focusing on emotion processes and increasing distress tolerance skills; (3) restructuring cognitive biases in benign interactions; (4) building effective communication skills; (5) reducing unhelpful avoidance and promoting adaptive navigation of situations; (6) validating strengths and increasing resilience; and (7) building safe, affirming interpersonal spaces and relationships. Individualized approaches that consider the child, family, socioenvironmental factors, and developmental trajectory are crucial to ensure that TGD youth and families have the necessary support throughout their formative years, promoting well-being and facilitating better outcomes overall.

CONCLUSION

The mental health needs of TGD youth are diverse and knowledgeable clinicians who can provide developmentally informed assessment and treatment recommendations are essential. This includes general pediatric practitioners, who are uniquely positioned to support the mental health of TGD youth as trusted, familiar, and consistent health care professionals caring for youth across childhood and adolescence. Mental health supports must align with the individualized treatment needs of TGD youth and will change over time. For some youth, mental health support may comprise no more than caregiver education, coaching, and support, and an opportunity to transition socially. For other youth, the interplay between gender dysphoria,

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exposure to gender-related stress and stigma, and co-occurring mental health issues may require some combination of gender-affirming medical interventions and adaptations to evidence-based mental health interventions to adequately target sources of distress and impairment. General pediatric practitioners may be families' first resource for education and support around gender diversity, and thus, they play a critical role in early identification of gender dysphoria, screening for psychosocial risks, and referral for subspecialty gender care as indicated.

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HA40.4 **Aetiological considerations associated with relationship factors**

This category should be assigned when, in the clinician's judgment, relationship factors are important contributing factors to the Sexual Dysfunction or Sexual Pain Disorder. Examples include relationship conflict or lack of romantic attachment. This category may also be used when the Sexual Dysfunction or Sexual Pain Disorder is associated with a Sexual Dysfunction or Sexual Pain Disorder in the sexual partner

HA40.5 **Aetiological considerations associated with cultural factors**

This category should be assigned when, in the clinician's judgment, cultural factors are important contributing factors to the Sexual Dysfunction or Sexual Pain Disorder. Cultural factors may influence expectations or provoke inhibitions about the experience of sexual pleasure or other aspects of sexual activity. Other examples include strong culturally shared beliefs about sexual expression, for example a belief that loss of semen can lead to weakness, disease or death.

HA40.Y **Other specified aetiological considerations in sexual dysfunctions and sexual pain disorders**

Gender incongruence (HA60-HA6Z)

Gender incongruence is characterised by a marked and persistent incongruence between an individual's experienced gender and the assigned sex. Gender variant behaviour and preferences alone are not a basis for assigning the diagnoses in this group.

Exclusions: Paraphilic disorders (6D30-6D3Z)

HA60 **Gender incongruence of adolescence or adulthood**

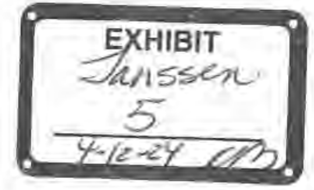
Gender Incongruence of Adolescence and Adulthood is characterised by a marked and persistent incongruence between an individual's experienced gender and the assigned sex, which often leads to a desire to 'transition', in order to live and be accepted as a person of the experienced gender, through hormonal treatment, surgery or other health care services to make the individual's body align, as much as desired and to the extent possible, with the experienced gender. The diagnosis cannot be assigned prior the onset of puberty. Gender variant behaviour and preferences alone are not a basis for assigning the diagnosis.

Exclusions: Paraphilic disorders (6D30-6D3Z)

HA61 **Gender incongruence of childhood**

Gender incongruence of childhood is characterised by a marked incongruence between an individual's experienced/expressed gender and the assigned sex in pre-pubertal children. It includes a strong desire to be a different gender than the assigned sex; a strong dislike on the child's part of his or her sexual anatomy or anticipated secondary sex characteristics and/or a strong desire for the primary and/or anticipated secondary sex characteristics that match the experienced gender; and make-believe or fantasy play, toys, games, or activities and playmates that are typical of the experienced gender rather than the assigned sex. The incongruence must have persisted for about 2 years. Gender variant behaviour and preferences alone are not a basis for assigning the diagnosis.

Exclusions: Paraphilic disorders (6D30-6D3Z)



HA6Z	**Gender incongruence, unspecified**
HA8Y	**Other specified conditions related to sexual health**
HA8Z	**Conditions related to sexual health, unspecified**

DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS

FIFTH EDITION
TEXT REVISION

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possibly co-occurring source of distress. *Transgender* refers to the broad spectrum of individuals whose gender identity is different from their birth-assigned gender. *Cisgender* describes individuals whose gender expression is congruent with their birth-assigned gender (also *nontransgender*). *Transsexual*, a historic term, denotes an individual who seeks, is undergoing,

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or has undergone a social transition from male to female or female to male, which in many, but not all, cases also involves a somatic transition by gender-affirming hormone treatment and genital, breast, or other gender-affirming surgery (historically referred to as *sex reassignment surgery*).

Although not all individuals will experience distress from incongruence, many are distressed if the desired physical interventions using hormones and/or surgery are not available. The current term is more descriptive than the previous DSM-IV term *gender identity disorder* and focuses on dysphoria as the clinical problem, not identity per se.

Gender Dysphoria

Diagnostic Criteria

Gender Dysphoria in Children F64.2

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by at least six of the following (one of which must be Criterion A1):

1. A strong desire to be of the other gender or an insistence that one is the other gender (or some alternative gender different from one's assigned gender).
2. In boys (assigned gender), a strong preference for cross-dressing or simulating female attire; or in girls (assigned gender), a strong preference for wearing only typical masculine clothing and a strong resistance to the wearing of typical feminine clothing.
3. A strong preference for cross-gender roles in make-believe play or fantasy play.
4. A strong preference for the toys, games, or activities stereotypically used or engaged in by the other gender.
5. A strong preference for playmates of the other gender.
6. In boys (assigned gender), a strong rejection of typically masculine toys, games, and activities and a strong avoidance of rough-and-tumble play; or in girls (assigned gender), a strong rejection of typically feminine toys, games, and activities.
7. A strong dislike of one's sexual anatomy.
8. A strong desire for the primary and/or secondary sex characteristics that

match one's experienced gender.

B. The condition is associated with clinically significant distress or impairment in social, school, or other important areas of functioning.

Specify if:

With a disorder/difference of sex development (e.g., a congenital adrenogenital disorder such as E25.0 congenital adrenal hyperplasia or E34.50 androgen insensitivity syndrome).

Coding note: Code the disorder/difference of sex development as well as gender dysphoria.

Gender Dysphoria in Adolescents and Adults F64.0

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by at least two of the following:

1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics).

2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics).
3. A strong desire for the primary and/or secondary sex characteristics of the other gender.
4. A strong desire to be of the other gender (or some alternative gender different from one's assigned gender).
5. A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender).
6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender).

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:

With a disorder/difference of sex development (e.g., a congenital adrenogenital disorder such as E25.0 congenital adrenal hyperplasia or E34.50 androgen insensitivity syndrome).

Coding note: Code the disorder/difference of sex development as well as gender dysphoria.

Specify if:

Posttransition: The individual has transitioned to full-time living in the experienced gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one gender-affirming medical procedure or treatment regimen—namely, regular gender-affirming hormone treatment or gender reassignment surgery confirming the experienced gender (e.g., breast augmentation surgery and/or vulvovaginoplasty in an individual assigned male at birth; transmasculine chest surgery and/or phalloplasty or metoidioplasty in an individual assigned female at birth).

Specifiers

The specifier "with a disorder/difference of sex development" should be used in the context of individuals who have a specific and codable disorder/difference of sex development documented in their medical record.

The "posttransition" specifier may be used in the context of continuing treatment procedures that serve to support the new gender assignment.

Diagnostic Features

Individuals with gender dysphoria have a marked incongruence between the gender to which they have been assigned (usually based on phenotypic sex at birth, referred to as *birth-assigned gender*) and their experienced/expressed gender. This discrepancy is the core component of the diagnosis. There must also be evidence of distress about this incongruence. Experienced gender may include alternative gender identities beyond binary stereotypes. Consequently, distress may involve not only the experience that the individual is a male or female gender other than the one assigned at birth but also an experience that the individual is an intermediate or alternative gender that differs from the individual's birth-assigned gender.

Gender dysphoria manifests itself differently in different age groups. The following examples may be less prominent in children raised in surroundings with fewer gender stereotypes.

Prepubertal individuals assigned female at birth with gender dysphoria may express a marked, persistent feeling or conviction that they are a boy, express aversion to the idea of

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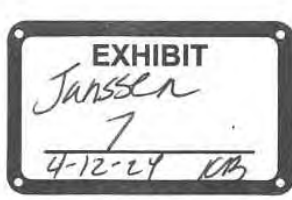
being a girl, or assert they will grow up to be a man. They often prefer boys' clothing and hairstyles, may be perceived by strangers as boys, and may ask to be called by a boy's name. Sometimes they display intense negative reactions to parental attempts to have them wear dresses or other feminine attire. Some may refuse to attend school or social events where such clothes are required. These children may demonstrate marked gender nonconformity in role-playing, dreams, gender-typed play and toy preferences, styles, mannerisms, fantasies, and peer preferences. Contact sports, rough-and-tumble play, traditional boyhood games, and boys as playmates are most often preferred. They show little interest in stereotypically feminine toys (e.g., dolls) or activities (e.g., feminine dress-up or role-play). Occasionally, they refuse to urinate in a sitting position. Some may express a desire to have a penis or claim to have a penis or that they will grow one when older. They may also state that they do not want to develop

IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

BRIANNA BOE, *et al.*, *Plaintiffs*, and UNITED STATES OF AMERICA, *Plaintiff-Intervenor*, v. STEVE MARSHALL, *et al.*, *Defendants*.	Case No. 2:22-cv-00184-LCB-SRW Honorable Liles C. Burke

EXPERT REPORT OF ARON JANSSEN, MD



My name is Aron Janssen, M.D. I am a board-certified child and adolescent psychiatrist. I specialize in the treatment of gender dysphoria in children and adolescents. I have been retained by counsel for Plaintiffs in the above-captioned lawsuit to provide an expert opinion on the standards of care for treating individuals diagnosed with gender dysphoria.

Background and Qualifications

The information provided regarding my professional background, experiences, publications, and presentations are detailed in my curriculum vitae. A true and correct copy of my CV is attached as Exhibit A.

I received my medical degree from the University of Colorado School of Medicine. I completed my residency in psychiatry and a fellowship in child and adolescent psychiatry at New York University Langone Medical Center.

In 2011, I founded the Gender and Sexuality Service at New York University, a clinical service dedicated to treating children and adolescents with gender dysphoria. In my last five years at NYU, that clinic served over 200 families, with 2-3 new referrals each week.

I am currently the Vice Chair of the Pritzker Department of Psychiatry and Behavioral Health and Chief Psychiatrist for the Gender Development Program at Ann and Robert H. Lurie Children's Hospital of Chicago. I am also a Clinical Associate Professor of Child and Adolescent Psychiatry at Northwestern University Feinberg School of Medicine. I maintain a clinical practice in Illinois where I treat patients from Illinois and the surrounding states.

I have been treating children and adolescents with gender dysphoria for over 10 years. I have treated over 300 children and adolescents with gender dysphoria during my medical career. Currently, approximately 90 percent of the patients in my clinical practice are transgender children and adolescents.

I am a contributing author to the Child and Adult Mental Health chapters of the Eighth Version of the World Professional Association for Transgender Health's (WPATH) *Standards of Care for the Health of Transgender and Gender Diverse People, Version 8* (hereafter, "WPATH SOC").

The WPATH SOC provides clinical guidance for health professionals based on the best available science and expert professional consensus. The purpose of the WPATH SOC is to assist health providers in delivering necessary and appropriate medical care to transgender and gender diverse people, in order to maximize their patients' overall health, psychological well-being, and self-fulfillment. The WPATH SOC has been recognized and adopted as the prevailing standard of care by the major professional associations medical and mental health providers in the United States, including the American Medical Association, American Academy of Pediatrics, American Psychiatric Association, American Psychological Association, and Pediatric Endocrine Society, among others.

In addition, I have written a number of peer-reviewed journal articles and chapters in professional textbooks about treatment of gender dysphoria in children and adolescents. In 2018, I co-edited *Affirmative Mental Health Care for Transgender and Gender Diverse Youth: A Clinical Casebook*, which is the first published clinical casebook on mental health

treatment for children and adolescents with gender dysphoria. A full and complete list of my publications is included in my CV.

I am an Associate Editor for the journal *Transgender Health*, and an Ad Hoc Reviewer for the journal *LGBT Health*. Each of these publications is a peer-reviewed medical journal.

I am actively involved in training other medical and mental health providers in the treatment of children and adolescents with gender dysphoria. I have conducted trainings for over 1,000 medical and mental health providers and have given dozens of public addresses, seminars, and lectures on the treatment of gender dysphoria in children and adolescents. I have also taught a number of courses through WPATH's Global Education Initiative, which provides training courses toward a member certification program in transgender health for practitioners around the world.

I am a member of the following professional organizations: American Psychiatric Association, American Academy of Child and Adolescent Psychiatry (AACAP), and World Professional Association for Transgender Health (WPATH). I am also a co-chair of the Sexual Orientation and Gender Identity Committee of AACAP and have participated in the Gender Dysphoria Working Group of the American Psychiatric Association, and the Transgender Health Committee of the Association of Gay and Lesbian Psychiatrists.

I am being compensated at an hourly rate of $400/hour plus expenses for my time spent in connection with this case. My compensation does not depend on the outcome of this litigation, the opinions I express, or the testimony I may provide.

In the previous four years, I was retained as an expert witness by the plaintiffs and deposed in *B.P.J. v. West Virginia State Board of Education* et al., No. 2:21-cv-00316 (S.D.W.V.), and *L.E. v. Lee* et al, No. 3.21-cv-00835 (M.D. Tenn).

Basis for Opinions

My opinions contained in this report are based on: (1) my clinical experience as a psychiatrist treating transgender patients, including adolescents and young adults; (2) my knowledge of the peer-reviewed research, including my own, regarding the treatment of gender dysphoria, which reflects the clinical advancements in the field of transgender health; (3) my work as a contributing author of the WPATH SOC; and (4) my review of the law challenged in this case.

Discussion

Gender Identity Development and Gender Dysphoria in Children and Adolescents

At birth, infants are assigned a sex, either male or female, based on the appearance of their external genitalia. For most people, their sex assigned at birth, or assigned sex, matches that person's gender identity. For transgender people, their assigned sex does not align with their gender identity.

Gender identity is a person's innate sense of their gender. It is a core and universal component of human identity.

It is essential to a person's mental health and well-being to be able to live consistent with their gender identity. This is true for transgender and non-transgender people

Gender identity has a biological basis and cannot be altered through medical or psychological interventions.

The evidence demonstrating that gender identity cannot be altered, either for transgender or for non-transgender individuals, underscores the innate nature of gender identity. Past attempts to "cure" transgender individuals by using talk therapy, and even aversive therapy, to change their gender identity to match their birth-assigned sex were ineffective and caused harm. The major associations of medical and mental health providers, such as the American Medical Association, the American Psychiatric Association, American Academy of Child and Adolescent Psychiatry, the American Psychological Association, and WPATH's standards of care, consider such efforts harmful and unethical.

Gender dysphoria is the medical diagnosis for the severe and unremitting psychological distress resulting from the incongruity between a transgender person's assigned sex and their gender identity. That distress can be alleviated when a transgender person is able to live consistent with their gender identity

It is a serious medical condition and is listed in the Diagnostic and Statistical Manual, Version 5 (DSM-5), the diagnostic and coding compendium for mental health professionals.

Standard of Care for Treatment of Gender Dysphoria in Youth

Like all children, transgender children can thrive, grow into healthy adults, and have the same capacity for happiness, achievement, and contribution to society as others. For this group of young people, that means supporting their need to live in a manner consistent with their gender identity in all aspects of their lives.

Accordingly, the goal of treatment for gender dysphoria is reduce distress and

improve functioning which often occurs through the process of enabling the individual to live consistent with their gender identity. The process of undergoing those treatments is often referred to as gender transition. The stages that make up a transgender person's gender transition will depend on that individual's medical and mental health needs.

The purpose of transition is to allow a transgender person to live congruently with their gender identity, including in many cases undergoing medical treatments to align the person's body with who they are.

Typically, transgender people start their transition with a series of steps that are commonly referred to as a "social transition." Those steps include, but are not limited to, changing their name, using different pronouns, wearing clothing and adopting grooming habits typically associated with their gender identity. Making those changes enable a transgender person to begin living their life consistent with their gender identity and helps ensure that they are treated as such by family, peers, and others in the community. It is important to note that there are no medical interventions for pre-pubertal transgender and gender-diverse children. For some children, social transition is an appropriate intervention, while for others, treatment for gender dysphoria may involve but not be limited to building family and social support or building resilience.

After the onset of puberty, transgender young people may also start taking puberty-delaying medication to prevent the development of unwanted and psychologically distressing secondary-sex characteristics that conflict with the person's identity.

Gender affirming hormone therapy is medically necessary for some transgender young people regardless of whether they have taken puberty-delaying medication. That

treatment causes their bodies to develop the secondary-sex characteristics more aligned with their gender identity, such as facial and body hair for boys who are transgender and female breast development in girls who are transgender.

Delaying any of these treatments, including puberty blockers or hormone therapy, when determined to be medically necessary will not only exacerbate a transgender young person's gender dysphoria, but also could lead to the development of other co-occurring mental health conditions, including depression, anxiety, and disordered eating. Those co-occurring mental health conditions may be accompanied by unhealthy coping behaviors such as self-harm, substance misuse, and suicide attempts.

Safe and Effective Treatments for Gender Dysphoria

Research and clinical experience repeatedly reaffirm that gender transition significantly improves the mental and physical health of transgender young people and is the only treatment that has been demonstrably effective for gender dysphoria.

This is true of each stage of a transgender young person's gender transition. Transgender young people who underwent a social transition in childhood demonstrated better mental health profiles than prior studies of gender nonconforming children. *See* Lily Durwood, et al., *Mental Health and Self-Worth in Socially Transitioned Transgender Youth*, 56 J. Am. Acad. of Child & Adol. Psychiatry 116 (2017); Kristina Olson, et al., *Mental Health of Transgender Children who are Supported in Their Identities*, 137 Pediatrics 1 (2016). This same outcome has also been seen in a longitudinal study of transgender young people who underwent each of the three stages of transition outlined above. Annelou L.C. de Vries, et al., *Young Adult Psychological Outcome After Puberty*

Suppression and Gender Reassignment, 134 Pediatrics 696 (2014).

Gender transition also can—and often does—alleviate co-occurring mental health issues a transgender young person experienced prior to transition. Following transition, transgender young people are often able to reduce dosage of psychiatric medications and see significant improvements in functioning and quality of life. Treating their gender dysphoria also increases a transgender young person's capacity to develop and maintain better coping strategies to manage any co-occurring conditions. For example, a recent study found that after two years of hormone treatment, transgender youth experienced increases in positive affect and life satisfaction and decreases in depression and anxiety symptoms. Diane Chen, et al., *Psychosocial Functioning in Transgender Youth after Two Years of Hormones,* 388 N. Engl. J. Med. 240 (2023).

Research shows that gender transition significantly improves the mental health of transgender young people, bringing their mental health profiles into alignment with their nontransgender peers. Kristina Olson, et al., *Mental health of transgender children who are supported in their identities*, 137 Pediatrics 1 (2016);[1] *see also* Jack Turban, et al., *Pubertal suppression for transgender youth and risk of suicidal ideation*, 145 Pediatrics 1 (2020) (transgender people who accessed puberty suppression treatment were 70% less likely to contemplate suicide).

Well-established research demonstrates the effectiveness of gender transition as

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[1] Anxiety was the only area where transgender young people differed from the non-transgender controls. On that measure, transgender young people showed slightly elevated levels of anxiety, but were still in the pre-clinical range.

treatment for gender dysphoria in adolescence. Jack Turban, Annelou DeVries & Kenneth Zucker, *Gender Incongruence & Gender Dysphoria*, in *Lewis's Child and Adolescent Psychiatry: A Comprehensive Textbook*, (A Martin, et al., eds., 5th ed., 2018).

The Role of Mental Health Providers in Assessing Necessity of Medical Treatments for Gender Dysphoria

The first objective of a mental health provider treating a child or adolescent who appears to be experiencing gender dysphoria is to conduct a careful and thorough assessment. That assessment allows the provider to accurately diagnose the patient, including whether the patient meets the stringent criteria for gender dysphoria and any co-occurring conditions. The foundation of the assessment process is building a detailed history of the patient, such as prior treatment, trauma, substance misuse, among many other factors. That assessment also requires a developmentally informed exploration of the patient's relationship to their gender identity over time that includes information obtained from multiple informants whenever possible.

To appropriately conduct that assessment, the mental health provider must draw from their professional training and experience in working with transgender young people, exercise professional judgment, and tailor the assessment to each individual patient and their family. The number of sessions that assessment requires will vary depending on the patient's presentation and the complexity of the issues the patient is navigating. The assessment process also goes beyond gathering information from the patient and their family. The mental health provider will typically gather and review information from the

patient's primary care provider, prior mental health providers, and other adult professionals who are part of the patient's care team.

A detailed history and assessment are important to provide the context for developing an appropriate treatment plan. That comprehensive assessment is also needed to help inform possible future care plans, such as the patient's need for puberty blockers or hormone therapy. Once this treatment plan is developed, the mental health provider remains involved in the treatment plan, ensuring that the plan continues to address the patient's individual needs. For example, mental health providers regularly assess the effects of gender dysphoria on a patient's life and functioning. The purpose of that ongoing evaluation is to identify the areas where the patient needs to develop resilience and coping strategies to minimize the effects of their gender dysphoria and to evaluate the mental health benefits of future treatment options.

Because of the thoroughness of this process, an assessment to determine the necessity of medical treatments typically occurs over several months. For patients who begin care as children, the assessment is based on years' worth of information.

A critical element of the standard of care is that it does not presume that being transgender is incompatible with a young person's short- and long-term health and wellbeing. That is consistent with DSM-5 diagnostic criteria which is "focus[ed] on dysphoria as the clinical problem, not identity per se." American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*, 451 (2013). As a result, therapists practicing consistent with the standard of care will create a space where the

patient can explore their gender identity, knowing that being transgender and not being transgender are both equally acceptable outcomes.[2]

Providing that individualized mental health treatment means that mental health providers are not simply a rubber-stamp in the process for accessing treatment for gender dysphoria. Instead, as is the case with all effective mental health treatment, the focus of the treatment is supporting overall health and wellbeing, regardless of whether the young person continues to identify as transgender. As a result, I have had patients who presented with some symptoms of gender dysphoria, but who ultimately did not meet the diagnostic criteria for a variety of reasons, and therefore I recommended treatments other than transition to alleviate their psychological distress. My experience in working with and speaking with other gender specialists is that this is routine throughout the profession. Part of the rigor of the diagnostic protocol is distinguishing between youth who are engaged in gender exploration from youth who are transgender and who do or will need treatment for gender dysphoria.

For young people who do meet the diagnostic criteria for gender dysphoria, mental health treatment often involves referring a patient for medical treatments. That process involves an assessment of the patient's gender dysphoria, co-occurring conditions, and the

[2] As observed in the context of research on gender identity conversion effort and family rejection, attempting to influence a young person's gender identity development is harmful, ineffective, and unethical. For example, a recent study found that being exposed to gender identity conversion efforts was associated with greater odds of attempting suicide, especially for those had those experiences in childhood. Jack Turban, et al., *Association between recalled exposure to gender identity conversion efforts and psychological distress and suicide attempts among transgender adults*, 77 JAMA Psychiatry 68 (2020).

medical treatment's likely effect on the patient's overall mental health and functioning. As part of that process, mental health providers also discuss the risks, benefits, and alternatives to treatment with transgender young people and their parents.

A patient's readiness to begin a particular course of medical treatment requires an evaluation of the patient's and the parent's/caregiver's understanding of the goals and potential limitations of the contemplated treatment. For example, for puberty-blocking medication, the provider will gauge the patient's ability to comprehend the effects of puberty on their body and mental health. An integral part of that discussion is evaluating a patient's grasp of the consequences of stopping those physical changes from occurring and alternatives to puberty-blocking treatment. And, in cases of the addition of hormone therapy in adolescence, the review of physical impact is explored over multiple meetings with the patient and parents. The provider will have those discussions with the patient and their parents both individually and together. As with the initial diagnosis, the amount of time required to complete this evaluation will depend on numerous factors including the length of their existing therapist-patient relationship and the complexity of the issues facing that patient.

The mental health provider will then document the results of their assessment in a letter to the patient's treating physician. The letter details the provider's diagnostic analysis as well as any professional opinions regarding the benefits of and readiness for the contemplated treatment. Ultimately, the appropriateness of any medical treatment is determined by a multidisciplinary team of expert mental and medical care providers.

Assessing Co-Occurring Conditions & Necessity of Medical Treatment for Gender Dysphoria

The existence—and prevalence—of co-occurring conditions among transgender young people is unsurprising. Transgender young people must cope with many stressors from the fear of rejection from family and peers to pervasive societal discrimination. In addition, their underlying gender dysphoria can cause significant psychological distress, which, if left untreated, can result in the development of co-occurring conditions.

Transgender young people, however, are not outliers in this regard. Research and clinical experience show that most psychiatric conditions are highly correlated with other co-occurring psychiatric conditions. For example, young people with depression are very likely to have at least one other diagnosable condition, most often anxiety. *See, e.g.*, E. Jane Costello, et al., *Prevalence and development of psychiatric disorders in childhood and adolescence*, 60 Archives of Gen. Psychiatry 837 (2003) ("There was strong heterotypic continuity from depression to anxiety" and finding approximately 30% of participants diagnosed with a depressive disorder were also diagnosed with an anxiety disorder). Likewise, a study on children diagnosed with Attention-Deficit/Hyperactivity Disorder found between 74-79% participants had additional co-occurring psychiatric conditions. Timothy Wilens, et al., *Psychiatric Comorbidity and Functioning in Clinically Referred Preschool Children and School-Age Youths With ADHD*, 41 J. of Am. Academy of Child & Adol. Psychiatry 262 (2002).

A comprehensive assessment—the cornerstone of the prevailing standards of care for the treatment of gender dysphoria—not only seeks to identify any co-occurring

conditions, but also to evaluate the effect those conditions have on a transgender person's functioning. This is equally true when assessing whether medical treatment for gender dysphoria is necessary from a mental health perspective.

The standards of care recognize that it is not possible for a transgender patient to resolve all co-occurring conditions prior to undergoing medical treatment, nor would it be ethical to impose such a requirement. Resolving all co-occurring conditions before medical treatment is not a requirement for other conditions. Gender dysphoria, by definition, is accompanied by clinically significant psychological distress. That distress can take on many different forms (*e.g.*, anxiety, mood disorders, and depression) and vary greatly in severity, resulting in co-occurring conditions. Because psychological distress is not easily compartmentalized, the distress associated with gender dysphoria can also amplify co-occurring conditions that developed independently of the gender dysphoria. In either situation, gender dysphoria limits the effectiveness of treatment of any co-occurring mental health conditions. Thus, treating the underlying gender dysphoria is essential to alleviating the psychological distress associated with co-occurring conditions.

Even assuming that it was possible to cure a patient's co-occurring conditions, delaying medical treatment can cause very real harms to a transgender person's physical and mental health. Without medical treatment, their gender dysphoria would continue to persist and often worsen. At a minimum, that increased distress would interfere with the treatment for the person's co-occurring conditions, subjecting them unnecessarily to a longer course of treatment. It is often seen that the gender dysphoria would eclipse the person's co-occurring conditions, not only entirely impeding treatment of those co-

occurring conditions, but also resulting in an overall deterioration of their mental health. The increased distress from their gender dysphoria would translate to resorting to negative coping mechanisms (*i.e.*, self-harm), suicidal ideation, and suicide attempts—just as it could if that increased distress was attributable to a co-occurring condition.

Gender dysphoria is a real and serious medical condition that is highly treatable. There is a rigorous and comprehensive protocol for diagnosing an individual with the condition. There is also a well-established standard of care for the treatment of gender dysphoria, including for treatment of gender dysphoria in transgender youth with puberty blockers and hormone therapy. When that treatment is provided, transgender youth can thrive. There are studies that have demonstrated that, and my own experience confirms it. In my experience, I have seen mental health providers carefully assess and work with youth, their parents, and other doctors that care for the youth to create a treatment plan that includes continuing mental health care and ongoing assessments.

Medical treatment for gender dysphoria has immense psychological benefits for youth, bringing their mental health to a level similar to their non-transgender peers. My understanding is that the law challenged in this case will prevent transgender youth in Alabama who are diagnosed with gender dysphoria from getting essential medical care that they need. In my professional opinion, if transgender youth cannot get the medical care that they need, including puberty blockers and hormone therapy, they will suffer and their mental health will deteriorate.

I hold each of the opinions expressed in this report with a reasonable degree of scientific certainty, based on the materials I have reviewed and on my education, experience, and knowledge. I reserve the right to supplement, amend, or modify my opinions upon review of further information, including, but not limited to, testimony, documents, and reports I receive after the date of this report.

Dated: February 10, 2023

Aron Janssen, M.D.

EXHIBIT A

Curriculum Vitae

Aron Janssen, M.D.

Personal Data

Born	Papillion, Nebraska
Citizenship	USA

Academic Appointments

2011-2017	Clinical Assistant Professor of Child and Adolescent Psychiatry
2011-2019	Founder & Clinical Director, NYU Gender and Sexuality Service Director, LGBT Mental Health Elective, NYULMC
2015-2019	Co-Director, NYU Pediatric Consultation Liaison Service New York University Department of Child and Adolescent Psychiatry
2017-present	Clinical Associate Professor of Child and Adolescent Psychiatry
2019-present	Vice Chair, Pritzker Department of Psychiatry and Behavioral Health Ann and Robert H. Lurie Children's Hospital of Chicago
2020-present	Medical Director, Outpatient Psychiatric Services Ann and Robert H. Lurie Children's Hospital of Chicago

Education

Year	**Degree**	**Field**	**Institution**
6/97	Diploma		Liberty High School
5/01	B.A.	Biochemistry	University of Colorado
5/06	M.D.	Medicine	University of Colorado

Postdoctoral Training

2006-2009 Psychiatry Residency Ze'ev Levin, M.D. NYU Department of Psychiatry
2009-2011 Child and Adolescent Psychiatry Fellowship – Fellow and Clinical Instructor
Jess Shatkin, M.D. NYU Dept of Child/Adolescent Psychiatry

Licensure and Certification

2007-2018	New York State Medical License
2017-present	Illinois Medical License
2011-present	Certification in Adult Psychiatry, American Board of Psychiatry and Neurology
2013-present	Certification in Child and Adolescent Psychiatry, ABPN

Academic Appointments

2009-2011	Clinical Instructor, NYU Department of Child and Adolescent Psychiatry
2011-2017	Clinical Asst Professor, NYU Dept of Child and Adolescent Psychiatry
2017-2019	Clinical Assoc Professor, NYU Dept of Child and Adolescent Psychiatry
2011-2019	Clinical Director, NYU Gender and Sexuality Service
2015-2019	Co-Director, NYU Pediatric Consultation-Liaison Service
2019-present	Associate Professor of Child and Adolescent Psychiatry, Northwestern University
2019-present	Vice Chair of Clinical Affairs, Pritzker Department of Psychiatry and Behavioral Health, Lurie Children's Hospital of Chicago

Major Committee Assignments

International, National and Regional

2021-present	Sexual Orientation and Gender Identity Committee, Chair, AACAP
2019-present	WPATH Standards of Care Revision Committee, Children
2019-present	WPATH Standards of Care Revision Committee, Adult Mental Health
2015-2019	Department of Child Psychiatry Diversity Ambassador
2013-2021	Sexual Orientation and Gender Identity Committee Member, AACAP
2012-2019	Founder and Director, Gender Variant Youth and Family Network
2012-present	Association of Gay and Lesbian Psychiatrists, Transgender Health Committee
2012-2019	NYULMC, Chair LGBTQ Advisory Council
2012-2019	NYULMC, Child Abuse and Protection Committee
2013-2015	NYULMC, Pediatric Palliative Care Team
2003-2004	American Association of Medical Colleges (AAMC), Medical Education Delegate
2004-2006	AAMC, Western Regional Chair
Psychiatry Residency	
2006-2009	Resident Member, Education Committee
2007-2008	Resident Member, Veterans Affairs (VA) Committee
Medical School	
2002-2006	Chair, Diversity Curriculum Development Committee
2002-2006	AAMC, Student Representative
2003-2004	American Medical Student Assoc. (AMSA) World AIDS Day Coordinator
2003-2004	AMSA, Primary Care Week Coordinator
2004-2006	Chair, Humanism in Medicine Committee

Memberships, Offices, and Committee Assignments in Professional Societies

2006-present	American Psychiatric Association (APA)
2009-present	American Academy of Child and Adolescent Psychiatry (AACAP)
2011-present	World Professional Association for Transgender Health (WPATH)
2011-2019	Director, Gender Variant Youth and Family Network, NYC
2013-2019	Chair, NYU Langone Medical Center LGBTQ Council

Editorial Positions

2016-2018	Clinical Assistant Editor, *Transgender Health*
2014-present	Ad Hoc Reviewer, *LGBT Health*.
2016-present	Ad Hoc Reviewer, *JAACAP*
2018-present	Associate Editor, *Transgender Health*
2020-present	Ad Hoc Reviewer, *Pediatrics*

Principal Clinical and Hospital Service Responsibilities

2011-2019	Staff Psychiatrist, Pediatric Consultation Liaison Service
2011-2019	Faculty Physician, NYU Child Study Center
2011-2019	Founder and Clinical Director, NYU Gender & Sexuality Service

2015-2019	Co-Director, Pediatric Consultation Liaison Service
2019-present	Vice Chair, Pritzker Dept of Psychiatry and Behavioral Health
2019-present	Chief Psychiatrist, Gender Development Program
2020-present	Medical Director, Outpatient Psychiatry Services

Relevant Program Development

Gender and Sexuality Service

-founded by Aron Janssen in 2011, who continues to direct the service

-first mental health service dedicated to transgender youth in NYC

-served over 200 families in consultation, with 2-3 referrals to the gender clinic per week

-trained over 500 mental health practitioners in transgender mental health – 1 or 2 full day trainings in partnership with the Ackerman Institute's Gender and Family Project (GFP) and with WPATH Global Educational Initiative (GEI)

-New hires in Adolescent Medicine, Psychology, Plastic Surgery, Urology, Gynecology, Endocrinology, Social Work, Department of Population Health with focus on transgender care has led to expansion of available services for transgender youth at NYULMC in partnership with the Gender and Sexuality Service

-development of partnerships with Ackerman Institute, Callen-Lorde Health Center – both institutions have been granted access to our IRB and have agreed to develop shared research and clinical priorities with the Gender and Sexuality Service.

-multiple IRB research projects underway, including in partnership with national and international clinics

-model has been internationally recognized

Clinical Specialties/Interests

Gender and Sexual Identity Development

Co-Occurring Mental Health Disorders in Transgender children, adolescents and adults

Pediatric Consultation/Liaison Psychiatry

Psychotherapy

Gender Affirmative Therapy, Supportive Psychotherapy, CBT, MI

Teaching Experience

2002-2006	Course Developer and Instructor, LGBT Health (University of Colorado School of Medicine
2011-2019	Instructor, Cultural Competency in Child Psychiatry (NYU Department of Child and Adolescent Psychiatry) – 4 hours per year
2011-2019	Course Director, Instructor "Sex Matters: Identity, Behavior and Development" – 100 hours per year
2011-2019	Course Director, LGBT Mental Health Elective (NYU Department of Psychiatry) - 50 hours of direct supervision/instruction per year
2011-2019	Course Director, Transgender Mental Health (NYU Department of Child and Adolescent Psychiatry – course to begin in Spring 2018.
2015-2019	Instructor, Gender & Health Selective (NYU School of Medicine) – 4 hours per year.

Academic Assignments/Course Development

New York University Department of Child and Adolescent Mental Health Studies

-Teacher and Course Director: "Sex Matters: Identity, Behavior and Development."

A full semester 4 credit course, taught to approximately 50 student per year since 2011, with several students now in graduate school studying sexual and gender identity development as a result of my mentorship.

NYU Department of Child and Adolescent Psychiatry

-Instructor: Cultural Competency in Child and Adolescent Psychiatry

-Director: LGBTQ Mental Health Elective

World Professional Association of Transgender Health

-Official Trainer: Global Education Initiative – one of two child psychiatrists charged with training providers in care of transgender youth and adults.

Peer Reviewed Publications

1. Janssen, A., Erickson-Schroth, L., "A New Generation of Gender: Learning Patience from our Gender Non-Conforming Patients," Journal of the American Academy of Child and Adolescent Psychiatry, Volume 52, Issue 10, pp. 995-997, October, 2013.
2. Janssen, A., et. al. "Theory of Mind and the Intolerance of Ambiguity: Two Case Studies of Transgender Individuals with High-Functioning Autism Spectrum
3. Janssen A, Huang H, and Duncan C., Transgender Health. February 2016, "Gender Variance Among Youth with Autism: A Retrospective Chart Review." 1(1): 63-68. doi:10.1089/trgh.2015.0007.
4. Goedel WC, Reisner SL, Janssen AC, Poteat TC, Regan SD, Kreski NT, Confident G, Duncan DT. (2017). Acceptability and Feasibility of Using a Novel Geospatial Method to Measure Neighborhood Contexts and Mobility Among Transgender Women in New York City. Transgender Health. July 2017, 2(1): 96-106.
5. Janssen A., et. al., "Gender Variance Among Youth with ADHD: A Retrospective Chart Review," in review
6. Janssen A., et. al., "Initial Clinical Guidelines for Co-Occurring Autism Spectrum Disorder and Gender Dysphoria or Incongruence in Adolescents," Journal of Child & Adolescent Psychology, 105-115, January 2018.
7. Janssen A., et. al., "A Review of Evidence Based Treatments for Transgender Youth Diagnosed with Social Anxiety Disorder," Transgender Health, 3:1, 27–33, DOI: 10.1089/ trgh.2017.0037.
8. Janssen A., et. al., "'The Complexities of Treatment Planning for Transgender Youth with Co-Occurring Severe Mental Illness: A Literature Review and Case Study," Archives of Sexual Behavior, 2019. # 3563492
9. Kimberly LL, Folkers KM, Friesen P, Sultan D, Quinn GP, Bateman-House A, Parent B, Konnoth C, Janssen A, Shah LD, Bluebond-Langner R, Salas-Humara C., "Ethical Issues in Gender-Affirming Care for Youth," Pediatrics, 2018 Dec;142(6).
10. Strang JF, Janssen A, Tishelman A, Leibowitz SF, Kenworthy L, McGuire JK, Edwards-Leeper L, Mazefsky CA, Rofey D, Bascom J, Caplan R, Gomez-Lobo V, Berg D, Zaks Z, Wallace GL, Wimms H, Pine-Twaddell E, Shumer D, Register-Brown K, Sadikova E, Anthony LG., "Revisiting the Link: Evidence of the Rates of

Autism in Studies of Gender Diverse Individuals," Journal of the American Academy of Child and Adolescent Psychiatry, 2018 Nov;57(11):885-887.

11. Goedel William C, Regan Seann D, Chaix Basile, Radix Asa, Reisner Sari L, Janssen Aron C, Duncan Dustin T, "Using global positioning system methods to explore mobility patterns and exposure to high HIV prevalence neighbourhoods among transgender women in New York City," Geospatial Health, 2019 Jan; 14(2): 351-356.
12. Madora, M., Janssen, A., Junewicz, A., "Seizure-like episodes, but is it really epilepsy?" Current Psychiatry, 2019 Aug; 18(8): 42-47.
13. Janssen, A., Busa, S., Wernick, J., "The Complexities of Treatment Planning for Transgender Youth with Co-Occurring Severe Mental Illness: A Literature Review and Case Study," Archives of Sexual Behavior, 2019 Oct; 48(7): 2003-2009.
14. Wernick Jeremy A, Busa Samantha, Matouk Kareen, Nicholson Joey, Janssen Aron, "A Systematic Review of the Psychological Benefits of Gender-Affirming Surgery," Urol Clin North Am. 2019 Nov; 46(4): 475-486.
15. Strang, J.F., Knauss, M., van der Miesen, A.I.R., McGuire, J., Kenworthy, L., Caplan, R., Freeman, A.J., Sadikova, E., Zacks, Z., Pervez, N., Balleur, A., Rowlands, D.W., Sibarium, E., McCool, M.A., Ehrbar, R.D., Wyss, S.E., Wimms, H., Tobing, J., Thomas, J., Austen, J., Pine, E., Willing, L., Griffin, A.D., Janssen, A., Gomez-Lobo, A., Brandt, A., Morgan, C., Meagher, H., Gohari, D., Kirby, L., Russell, L., Powers, M., & Anthony, L.G., (in press 2020). A clinical program for transgender and gender-diverse autistic/neurodiverse adolescents developed through community-based participatory design. *Journal of Clinical Child and Adolescent Psychology.* DOI 10.1080/15374416.2020.1731817
16. Coyne, C. A., Poquiz, J. L., Janssen, A., & Chen, D. Evidence-based psychological practice for transgender and non-binary youth: Defining the need, framework for treatment adaptation, and future directions. Evidence-based Practice in Child and Adolescent Mental Health.
17. Janssen, A., Voss, R., Policies sanctioning discrimination against transgender patients flout scientific evidence and threaten health and safety. Transgender Health.
18. Dubin, S., Cook, T., Liss, A., Doty, G., Moore, K., Janssen, A. (In press 2020). Comparing Electronic Health Records Domains' Utility to Identify Transgender Patients. Transgender Health, DOI 10.1089/trgh.2020.0069

Published Abstracts

1. Thrun, M., Janssen A., et. al. "Frequency of Patronage and Choice of Sexual Partners may Impact Likelihood of HIV Transmission in Bathhouses," original research poster presented at the 2007 Conference on Retroviruses and Opportunistic Infections, February, 2007.
2. Janssen, A., "Advocating for the mental health of Lesbian, Gay, Bisexual and Transgender (LGBT) population: The Role of Psychiatric Organizations." Workshop for the American Psychiatric Association Institute of Psychiatric Services Annual Meeting, October 2012.
3. Janssen, A., "Gender Variance in Childhood and Adolescents: Training the Next Generation of Psychiatrists," 23rd Symposium of the World Professional Association for Transgender Health, Amsterdam, The Netherlands, February 2014.

4. Janssen, A., "When Gender and Psychiatric Acuity/Comorbidities Overlap: Addressing Complex Issues for Gender Dysphoric and Non-Conforming Youth," AACAP Annual Meeting, October 2014.
5. Janssen, A., "Patient Experiences as Drivers of Change: A unique model for reducing transgender health disparities as an academic medical center," Philadelphia Transgender Health Conference, June 2016.
6. Janssen, A., "How much is too much? Assessments & the Affirmative Approach to TGNC Youth," 24th Symposium of the World Professional Association for Transgender Health, Amsterdam, The Netherlands, June 2016.
7. Janssen, A., "Trauma, Complex Cases and the Role of Psychotherapy," 24th Symposium of the World Professional Association for Transgender Health, Amsterdam, The Netherlands, June 2016.
8. Janssen, A., "Gender Variance Among Youth with Autism: A Retrospective Chart Review," Research Poster, 24th Symposium of the World Professional Association for Transgender Health, Amsterdam, The Netherlands, June 2016.
9. Janssen, A., "Gender Fluidity and Gender Identity Development," Center for Disease Control – STD Prevention Conference, September 2016.
10. Janssen, A., "Transgender Identities Emerging During Adolescents' Struggles With Mental Health Problems," AACAP Annual Conference, October 2016.
11. Janssen, A., "How Much is Too Much? Assessments and the Affirmative Approach to Transgender and Gender Diverse Youth," US Professional Association for Transgender Health Inaugural Conference, Los Angeles, February 2017.
12. Janssen, A., "Trauma, Complex Cases and the Role of Psychotherapy," US Professional Association for Transgender Health Inaugural Conference, Los Angeles, February 2017.
13. Sutter ME, Bowman-Curci M, Nahata L, Tishelman AC, Janssen AC, Salas-Humara C, Quinn GP. Sexual and reproductive health among transgender and gender-expansive AYA: Implications for quality of life and cancer prevention. Oral presentation at the Oncofertility Consortium Conference, Chicago, IL. November 14, 2017.
14. Janssen, A., Sidhu, S., Gwynette, M., Turban, J., Myint, M., Petersen, D., "It's Complicated: Tackling Gender Dysphoria in Youth with Autism Spectrum Disorders from the Bible Belt to New York City," AACAP Annual Conference, October 2017.
15. May 2018: "A Primer in Working with Parents of Transgender Youth," APA Annual Meeting.
16. October 2018: "Gender Dysphoria Across Development" – Institute for AACAP Annual Conference.
17. November 2018: "Gender Variance Among Youth with Autism," World Professional Association for Transgender Health Biannual Conference.
18. March 2019: "Gender Trajectories in Child and Adolescent Development and Identity," Austin Riggs Grand Rounds.
19. Janssen, A., et. al., "Ethical Principles in Gender Affirming Care," AACAP Annual Conference, October 2019.

20. Janssen, A., "Gender Diversity and Gender Dysphoria in Youth," EPATH Conference, April 2019
21. Englander, E., Janssen A., et. al., "The Good, The Bad, and The Risky: Sexual Behaviors Online," AACAP Annual Conference, October 2020
22. Englander, E., Janssen, A., et. al., "Love in Quarantine," AACAP Annual Conference, October 2021
23. Janssen, A., Leibowitz, S., et. al., "The Evidence and Ethics for Transgender Youth Care: Updates on the International Standards of Care, 8th Edition," AACAP Annual Conference, October 2021
24. Turban, J., Janssen, A., et. al., "Transgender Youth: Understanding "Detransition," Nonlinear Gender Trajectories, and Dynamic Gender Identities." AACAP Annual Conference, October 2021

Books

1. Janssen, A., Leibowitz, S (editors), Affirmative Mental Health Care for Transgender and Gender Diverse Youth: A Clinical Casebook. Springer Publishing, 2018.

Book Chapters

1. Janssen, A., Shatkin, J., "Atypical and Adjunctive Agents," Pharmacotherapy for Child and Adolescent Psychiatric Disorders, 3rd Edition, Marcel Dekker, Inc, New York, 2012.
2. Janssen, A; Liaw, K: "Not by Convention: Working with People on the Sexual & Gender Continuum," book chapter in The Massachusetts General Hospital Textbook on Cultural Sensitivity and Diversity in Mental Health. Humana Press, New York, Editor R. Parekh, January 2014.
3. Janssen, A; Glaeser, E., Liaw, K: "Paving their own paths: What kids & teens can teach us about sexual and gender identity," book chapter in Cultural Sensitivity in Child and Adolescent Mental Health, MGH Psychiatry Academy Press, Editor R. Parekh, 2016
4. Janssen A., "Gender Identity," Textbook of Mental and Behavioral Disorders in Adolescence, February 2018.
5. Busa S., Wernick, J., & Janssen, A. (In Review) Gender Dysphoria in Childhood. Encyclopedia of Child and Adolescent Development. Wiley, 2018.
6. Janssen A., Busa S., "Gender Dysphoria in Childhood and Adolescence," Complex Disorders in Pediatric Psychiatry: A Clinician's Guide, Elsevier, Editors Driver D., Thomas, S., 2018.
7. Wernick J.A., Busa S.M., Janssen A., Liaw K.RL. "Not by Convention: Working with People on the Sexual and Gender Continuum." Book chapter in The Massachusetts General Hospital Textbook on Diversity and Cultural Sensitivity in Mental Health, editors Parekh R., Trinh NH. August, 2019.
8. Weis, R., Janssen, A., & Wernick, J. The implications of trauma for sexual and reproductive health in adolescence. In *Not Just a nightmare: Thinking beyond PTSD to help teens exposed to trauma.* 2019
9. Connors J., Irastorza, I., Janssen A., Kelly, B., "Child and Adolescent Medicine," The Equal Curriculum: The Student and Educator Guide to LGBTQ Health, editors Lehman J., et al. November 2019.

10. Janssen, A., et. al., "Gender and Sexual Diversity in Childhood and Adolescence," Dulcan's Textbook of Child and Adolescent Psychiatry, 3rd edition, editor Dulcan, M., (in press)
11. Busa S., Wernick J, Janssen, A., "Gender Dysphoria," The Encyclopedia of Child and Adolescent Development, DOI: 10.1002/9781119171492. Wiley, December 2020.

Invited Academic Seminars/Lectures

1. April 2006: "How to Talk to a Gay Medical Student" – presented at the National AAMC Meeting.
2. March 2011: "Kindling Inspiration: Two Model Curricula for Expanding the Role of Residents as Educators" – workshop presented at National AADPRT Meeting.
3. May 2011: Janssen, A., Shuster, A., "Sex Matters: Identity, Behavior and Development," Grand Rounds Presentation, NYU Department of Child and Adolescent Psychiatry.
4. March 2012: Janssen, A., Lothringer, L., "Gender Variance in Children and Adolescents," Grand Rounds Presentation, NYU Department of Child and Adolescent Psychiatry.
5. June 2012: Janssen, A., "Gender Variance in Childhood and Adolescence," Grand Rounds Presentation, Woodhull Department of Psychiatry
6. October 2012: "Advocating for the mental health of Lesbian, Gay, Bisexual and Transgender (LGBT) population: The Role of Psychiatric Organizations." Workshop for the American Psychiatric Association Institute of Psychiatric Services Annual Meeting.
7. March 2013: "Gender Variance in Childhood and Adolescence," Sexual Health Across the Lifespan: Practical Applications, Denver, CO.
8. October 18th, 2013: "Gender Variance in Childhood and Adolescence," Grand Rounds Presentation, NYU Department of Endocrinology.
9. October, 2014: GLMA Annual Conference: "Theory of Mind and Intolerance of Ambiguity: Two Case Studies of Transgender Individuals with High-Functioning ASD," Invited Presentation
10. October 2014: New York Transgender Health Conference: "Mental Health Assessment in Gender Variant Children," Invited Presentation.
11. November, 2014: Gender Spectrum East: "Affirmative Clinical Work with Gender-Expansive Children and Youth: Complex Situations."
12. October 2015: "Gender Dysphoria and Complex Psychiatric Co-Morbidity," LGBT Health Conference, Invited Speaker
13. October 2015: "Transgender Health Disparities: Challenges and Opportunities," Grand Rounds, Illinois Masonic Department of Medicine
14. November 2015: "Autism and Gender Variance," Gender Conference East, Invited Speaker
15. February 2016: "Working with Gender Variant Youth," New York State Office of Mental Health State Wide Grand Rounds, Invited Speaker
16. March, 2016: "Working with Gender Variant Youth," National Council for Behavioral Health Annual Meeting, Invited Speaker

17. March 2016: "Gender Variance Among Youth with Autism: A Retrospective Chart Review and Case Presentation," Working Group on Gender, Columbia University, Invited Speaker.
18. September, 2016: "Best Practices in Transgender Mental Health: Addressing Complex Issues for Gender Dysphoric and Non-Conforming Youth," DeWitt Wallace Institute for the History of Psychiatry, Weill Cornell.
19. October, 2016: "LGBTQ Youth Psychiatric Care," Midwest LGBTQ Health Symposim
20. October, 2016: "Gender Fluidity and Gender Identity Development," NYU Health Disparities Conference.
21. February, 2017: "Best Practices in Transgender Mental Health," Maimonides Grand Rounds
22. March, 2017: "Transgender Health: Challenges and Opportunities," Invited speaker, Center for Disease Control STD Prevention Science Series.
23. September 2017: "Autism and Gender Dysphoria," Grand Rounds, NYU Department of Neurology.
24. November 2017: "Consent and Assent in Transgender Adolescents," Gender Conference East.
25. November 2017: "Transgender Mental Health: Challenges and Opportunities," Grand Rounds, Lenox Hill Hospital.
26. April 2018: "Gender Trajectories in Childhood and Adolescent Development and Identity," Sex, Sexuality and Gender Conference, Harvard Medical School.
27. September 2019: "Social and Psychological Challenges of Gender Diverse Youth," Affirmative Mental Health Care for Gender Diverse Youth, University of Haifa.
28. October 2019: "Best Practices in Transgender Mental Health," Grand Rounds, Rush Department of Psychiatry.
29. February 2020: "The Overlap of Autism and Gender Dysphoria," Grand Rounds, Northwestern University Feinberg School of Medicine Department of Psychiatry
30. February 2020: "Gender Dysphoria and Autism," Grand Rounds, University of Illinois at Chicago Department of Psychiatry
31. September 2021: "Gender Diversity and Autism," Grand Rounds, Kaiser Permanente Department of Pediatrics
32. October 2021: Gender Dysphoria and Autism," Grand Rounds, Case Western Reserve University Department of Psychiatry.

Selected Invited Community Seminars/Lectures

1. April 2012: "Gender and Sexuality in Childhood and Adolescence," Commission on Race, Gender and Ethnicity, NYU Steinhardt Speakers Series.
2. February 2013: "Supporting Transgender Students in School," NYC Independent School LGBT Educators Panel, New York, NY.
3. June 2013: "LGBT Health," Presentation for Neuropsychology Department
4. August 2013: "Chronic Fatigue Syndrome: Etiology, Diagnosis and Management," invited presentation.
5. September 2013: Panelist, "LGBTQ Inclusive Sex Education."
6. April 2015: Transgender Children, BBC News, BBCTwo, invited expert

7. January 2016: Gender Dysphoria and Autism – Ackerman Podcast - http://ackerman.podbean.com/e/the-ackerman-podcast-22-gender-dysphoria-autism-with-aron-janssen-md/
8. February 2016: "Best Practices in Transgender Mental Health," APA District Branch Meeting, Invited Speaker.
9. May 2016: "Best Practices in Transgender Mental Health," Washington D.C., District Branch, APA, Invited Speaker
10. July 2016: "Transgender Youth," Union Square West
11. November 2017: "Understanding Gender: Raising Open, Accepting and Diverse Children," Heard in Rye, Conversations in Parenting.
12. January 2018: "The Emotional Life of Boys," Saint David's School Panel, Invited Speaker
13. June 2018: "Supporting Youth Engaged in Gender Affirming Care," NYU Child Study Center Workshop.
14. October 2018: "Medicine in Transition: Advances in Transgender Mental Health," NYCPS HIV Psychiatry and LGBT Committee Meeting.
15. October 2018: "Understanding Gender Fluidity in Kids," NYU Slope Pediatrics.
16. October, 2021: Issues of Ethical Importance: Health Care for Pediatric LGBTQ+ Patients, American Medical Association, Invited Talk

Major Research Interests

Gender and Sexual Identity Development
Member, Research Consortium for Gender Identity Development
Delirium: Assessment, Treatment and Management
Suicide Prevention

Research Studies

Study Title	IRB Study#	Dates
Suicide Attempts Identified in a Children's Hospital Before and During COVID-19	2021-4428	2/26/21-present
Lurie Children's Sex & Gender Development Program Clinical Measure Collection	2019-2898	2019-present
Adolescent Gender Identity Research Study (principal investigator) - unfunded	s15-00431	4/15-5/19
Co-Occurrence of Autism Spectrum Disorders and Gender Variance: Retrospective Chart Review (principal investigator) - unfunded	s14-01930	10/14-5/19
Expert Consensus on Social Transitioning Among Prepubertal Children Presenting with Transgender Identity and/or Gender Variance: A Delphi Procedure Study (principal investigator) - unfunded	s13-00576	3/16-5/19

Co-Occurrence of ADHD/Gender Dysphoria (principal investigator) - unfunded	s16-00001	1/16-5/19
PICU Early Mobility- unfunded	s16-02261	12/16-5/19
Metformin for Overweight and Obese Children and Adolescents with Bipolar Spectrum Disorders Treated with Second-Generation Antipsychotics – Funded by PCORI	s16-01571	8/16-5/19

Other

Grant Funding:
Zero Suicide Initiative, PI Aron Janssen, M.D.
Awarded by Cardinal Health Foundation, 9/2020
Total amount: $100,000

Catalyst Fund, PI Aron Janssen, M.D.
Suicide Prevention in Pediatric Primary Care
Total amount: $750,000

Selected Media Appearances:

Guest Expert on Gender Identity on Anderson, "When Your Husband Becomes Your Wife," Air Date February 8th, 2012
Guest Host, NYU About Our Kids on Sirius XM, 2011
NYU Doctor Radio: LGBT Health, September 2013
NYU Doctor Radio: LGBT Kids, November 2013
NYU Doctor Radio: LGBT Health, July 2014
NYU Doctor Radio: Gender Variance in Childhood, December 2014
BBC Two: Transgender Youth, April 2015
NYU Doctor Radio: Transgender Youth, June 2015
Fox-5 News: Trump's proposed military ban and Transgender Youth, July, 2017
Healthline.com: Mental Health Experts Call President's Tweets 'Devastating' for Trans Teens, July, 2017
Huffington Post: What the Military Ban Says to Our Transgender Youth: August, 2017
Metro: How to talk to your transgender kid about Trump, August 2017
NYU Doctor Radio: Transgender Youth, August 2017

EXHIBIT B

APPENDIX

American Academy of Child & Adolescent Psychiatry Policy Statement: Conversion Therapy (2018).

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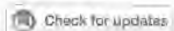

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Readiness assessments for gender-affirming surgical treatments: A systematic scoping review of historical practices and changing ethical considerations

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Transgender and gender diverse (TGD) are terms that refer to individuals whose gender identity differs from sex assigned at birth. TGD individuals may choose any variety of modifications to their gender expression including, but not limited to changing their name, clothing, or hairstyle, starting hormones, or undergoing surgery. Starting in the 1950s, surgeons and endocrinologists began treating what was then known as transsexualism with cross sex hormones and a variety of surgical procedures collectively known as sex reassignment surgery (SRS). Soon after, Harry Benjamin began work to develop standards of care that could be applied to these patients with some uniformity. These guidelines, published by the World Professional Association for Transgender Health (WPATH), are in their 8th iteration. Through each iteration there has been a requirement that patients requesting gender-affirming hormones (GAH) or gender-affirming surgery (GAS) undergo one or more detailed evaluations by a mental health provider through which they must obtain a "letter of readiness," placing mental health providers in the role of gatekeeper. WPATH specifies eligibility criteria for gender-affirming treatments and general guidelines for the content of letters, but does not include specific details about what must be included, leading to a lack of uniformity in how mental health providers approach performing evaluations and writing letters. This manuscript aims to review practices related to evaluations and letters of readiness for GAS in adults over time as the standards of care have evolved *via* a scoping review of the literature. We will place a particular emphasis on changing ethical considerations over time and the evolution of the model of care from gatekeeping to informed consent. To this end, we did an extensive review of the literature. We identified a trend across successive iterations of the guidelines in both reducing stigma against TGD

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individuals and shift in ethical considerations from "do no harm" to the core principle of patient autonomy. This has helped reduce barriers to care and connect more people who desire it to gender affirming care (GAC), but in these authors' opinions does not go far enough in reducing barriers.

KEYWORDS

gender-affirming surgery, standards of care, world professional association for transgender health, ethics, informed consent, transgender and gender diverse (TGD), mental health, scoping review

Introduction

Transgender and gender diverse (TGD) are terms that refer to any individual whose gender identity is different from their sex assigned at birth. Gender identity can be expressed through any combination of name, pronouns, hairstyle, clothing, and social role. Some TGD individuals wish to transition medically by taking gender-affirming hormones (GAH) and/or pursuing gender-affirming surgery (GAS) (1).[1] The medical community's comfort level with TGD individuals and, consequently, their willingness to provide a broad range of gender affirming care (GAC)[2] has changed significantly over time alongside an increasing understanding of what it means to be TGD and increasing cultural acceptance of LGBTQI people.

Historically physicians have placed significant barriers in the way of TGD people accessing the care that we now know to be lifesaving. Even today, patients wishing to receive GAC must navigate a system that sometimes requires multiple mental health evaluations for procedures, that is not required of cisgender individuals.

The medical and psychiatric communities have used a variety of terms over time to refer to TGD individuals. The first and second editions of DSM described TGD individuals using terms such as transvestism (TV) and transsexualism (TS), and often conflated gender identity with sexuality, by including them alongside diagnoses such as homosexuality and paraphilias. Both the DSM and the International Classification of Diseases (ICD) have continuously changed diagnostic terminology and criteria involving TGD individuals over time, from Gender Identity Disorder in DSM-IV to Gender Dysphoria in DSM-5 to Gender Incongruence in ICD-11.

In 1979, the Harry Benjamin International Gender Dysphoria Association[3], renamed the World Profession Association for Transgender Health (WPATH) in 2006, was the first to publish international guidelines for providing GAC to TGD individuals. The WPATH Standards of Care (SOC) are used by many insurance companies and surgeons to determine an individual's eligibility for GAC. Throughout each iteration, mental health providers are placed in the role of gatekeeper and tasked with conducting mental health evaluations and providing required letters of readiness for TGD individuals who request GAC (1). As part of this review, we will summarize the available literature examining the practical and ethical changes in conducting mental health readiness assessments and writing the associated letters.

While the WPATH guidelines specify eligibility criteria for GAC and a general guide for what information to include in a letter of readiness, there are no widely agreed upon standardized letter templates or semi-structured interviews, leading to a variety of practices in evaluation and letter writing for GAC (2). To our knowledge, this is the first scoping review to summarize the available research to date regarding the evolution of the mental health evaluation and process of writing letters of readiness for GAS. By summarizing trends in these evaluations over time, we aim to identify best practices and help further guide mental health professionals working in this field.

Methods

The review authors conducted a comprehensive search of the literature in collaboration with a research librarian (ABW)

1 Gender affirming surgery has historically been referred to as sexual reassignment surgery (SRS).

2 Gender affirming care is an umbrella term referring to any medical care a TGD individual might pursue that affirms their gender identity including primary care, mental health care, GAH or GAS.

Abbreviations: TGD, transgender and gender diverse; SRS, sex reassignment surgery; WPATH, World Professional Association for Transgender Health; SOC, standards of care; GAC, gender affirming care; GAS, gender-affirming surgery; GAH, gender-affirming hormones; TS, transsexualism; TV, transvestism; HBIGDA, Harry Benjamin International Gender Dysphoria Association; RLT, Real life test; MMPI, Minnesota Multiphasic Personality Inventory; FTM, female to male; MTF, male to female; LGBTQI, lesbian, gay, bisexual, transgender, queer, intersex; DSM, diagnostic and statistical manual of mental disorders; ICD, international classification of diseases.

3 The organization will be referred to as WPATH moving forward, even when referring to time periods before the name change.

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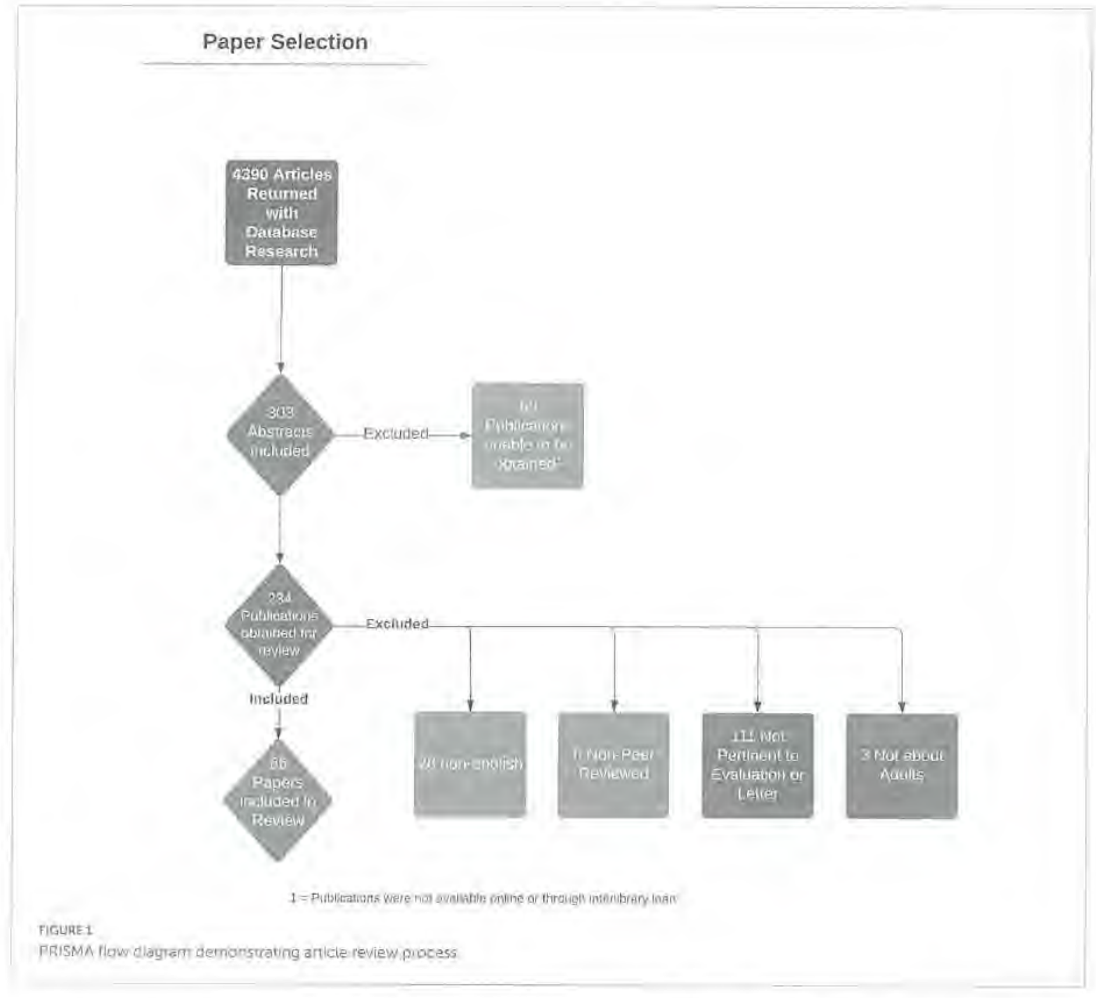

FIGURE 1
PRISMA flow diagram demonstrating article review process.

according to PRISMA guidelines. The search was comprised of database-specific controlled vocabulary and keyword terms for (1) mental health and (2) TGD-related surgeries. Searches were conducted on December 2, 2020 in MEDLINE (PubMed), the Cochrane Library Databases (Wiley), PsychINFO (EBSCOhost), CINAHL (EBSCOhost), Scopus (Elsevier), and Dissertations and Theses Global (ProQuest). All databases were searched from inception to present without the use of limits or filters. In total, 8,197 results underwent multi-pass deduplication in a citation management system (EndNote), and 4,411 unique entries were uploaded to an online screening software (Rayyan) for title/abstract screening by two independent reviewers. In total, 303 articles were included for full text screening (Figure 1), however, 69 of those articles were excluded as they were unable to be obtained online or through interlibrary loan. Both review authors conducted a full text screen of the remaining 234 articles. Articles were included in the final review if they specified criteria used for mental health screening/evaluation and/or letter writing for GAS, focused on TGD adults, were written in English, and were peer-reviewed publications. Any discrepancies were discussed between the two review authors TA and KK and a consensus was reached. A total of 86 articles met full inclusion criteria. Full documentation of all searches can be found in the Supplementary material.

Results

In total, 86 articles were included for review. Eleven articles were focused on ethical considerations while the remaining 75 articles focused on the mental health evaluation and process of writing letters of readiness for GAS. Version 8 of the SOC

was published in September of 2022 during the review process of this manuscript and is also included as a reference and point of discussion.

Prior to the publication of the standards of care

Fourteen articles were identified in the literature search as published prior to the development of the WPATH SOC version 1 in 1979. Prominent themes included classification, categorization, and diagnosis of TS. Few publications described the components of a mental health evaluation, and inclusion and exclusion criteria, for GAS. Many publications focused exclusively on transgender females, with a paucity of literature examining the experiences of transgender males during this timeframe.

Authors emphasized accurate diagnosis of TS, highlighting elements of the psychosocial history including early life cross-dressing, preference for play with the opposite gender toys and friends, and social estrangement around puberty (3). One author proposed the term gender dysphoria syndrome, which included the following criteria: a sense of inappropriateness in one's anatomically congruent sex role, that role reversal would lead to improvement in discomfort, homoerotic interest and heterosexual inhibition, an active desire for surgical intervention, and the patient taking on an active role in exploring their interest in sex reassignment (4). Many authors attempted to differentiate between the "true transsexual" and other diagnoses, including idiopathic TS; idiopathic, essential, or obligatory homosexuality; neuroticism; TV; schizophrenia; and intersex individuals (5, 6).

Money argued that the selection criteria for patients requesting GAS include a psychiatric evaluation to obtain collateral information to confirm the accuracy of the interview, work with the family to foster support of the individual, and proper management of any psychiatric comorbidities (5). Authors began to assemble a list of possible exclusion criteria for receiving GAS such as psychosis, unstable mental health, ambivalence, and secondary gain (e.g., getting out of the military), lack of triggering major life events or crises, lack of sufficient distress in therapy, presence of marital bonds (given the illegality of same-sex marriage during this period), and if natal genitals were used for pleasure (3–5, 7–13).

Others focused the role of the psychiatric evaluation on the social lives and roles of the patient. They believed the evaluation should include exploring the patient's motivation for change for at least 6–12 months (8), facilitating realistic expectations of treatment, managing family issues, providing support during social transition and post-operatively (13), and encouraging GAH and the "real-life test" (RLT). The RLT is a period in which a person must fully live in their affirmed gender identity, "testing" if it is right for them. In 1970, Green recommended that a primary goal of treatment was that, "the male patient must be able to pass in society as a socially acceptable woman in appearance and to conduct the normal affairs of the day without arousing undue suspicion" (14). Benjamin also noted concern that "too masculine" features may be a contraindication to surgery so as to not make an "acceptable woman" (7). Some publications recommended at least 1–2 years of a RLT (3, 7, 11, 15), while others recommended at least 5 years of RLT prior to considering GAS (12). Emphasis was placed on verifying the accuracy of reported information from family or friends to ensure "authentic" motivation for GAS and rule out ambivalence or secondary gain (e.g., getting out of the military) (10).

Ell recommended evaluation to ensure the patient has "adequate intelligence" to understand realistic expectations of surgery and attempted to highlight the patient's autonomy in the decision to undergo GAS. He wrote, "That is your decision [to undergo surgery]. It's up to you to prove that you are a suitable candidate for surgery. It's not for me to offer it to you. If you decide to go ahead with your plans to pass in the opposite gender role, you do it on your own responsibility" (8). Notably, many authors conceptualized gender transition along a binary, with individuals transitioning from one end to the other.

In these earliest publications, one can start to see the beginning framework of modern-day requirements for accessing GAS, including ensuring an accurate diagnosis of gender incongruence; ruling out other possible causes of presentation such as psychosis; ensuring general mental stability; making sure that the patient has undergone at least some time of living in their affirmed gender; and that they are able to understand the consequences of the procedure.

Standards of care version 1 and 2

Changes to the standards of care

The first two versions of the WPATH SOC were written in 1979 and 1980, respectively and are substantially similar to one another. SOC version three was the first to be published in an academic journal in 1985 and changes from the first two versions were documented within this publication. The first two versions required that all recommendations for GAC be completed by licensed psychologists or psychiatrists. The first version recommended that patients requesting GAH and non-genital GAS, spend 3 and 6 months, respectively, living full time in their affirmed gender. These recommendations were rescinded in subsequent versions (16). Figure 2 reviews changes to the recommendations for GAC within the WPATH SOC over time.

Results review

Five articles published between 1979 and 1980 were included in this review. Again, emphasis was placed on proper diagnosis,

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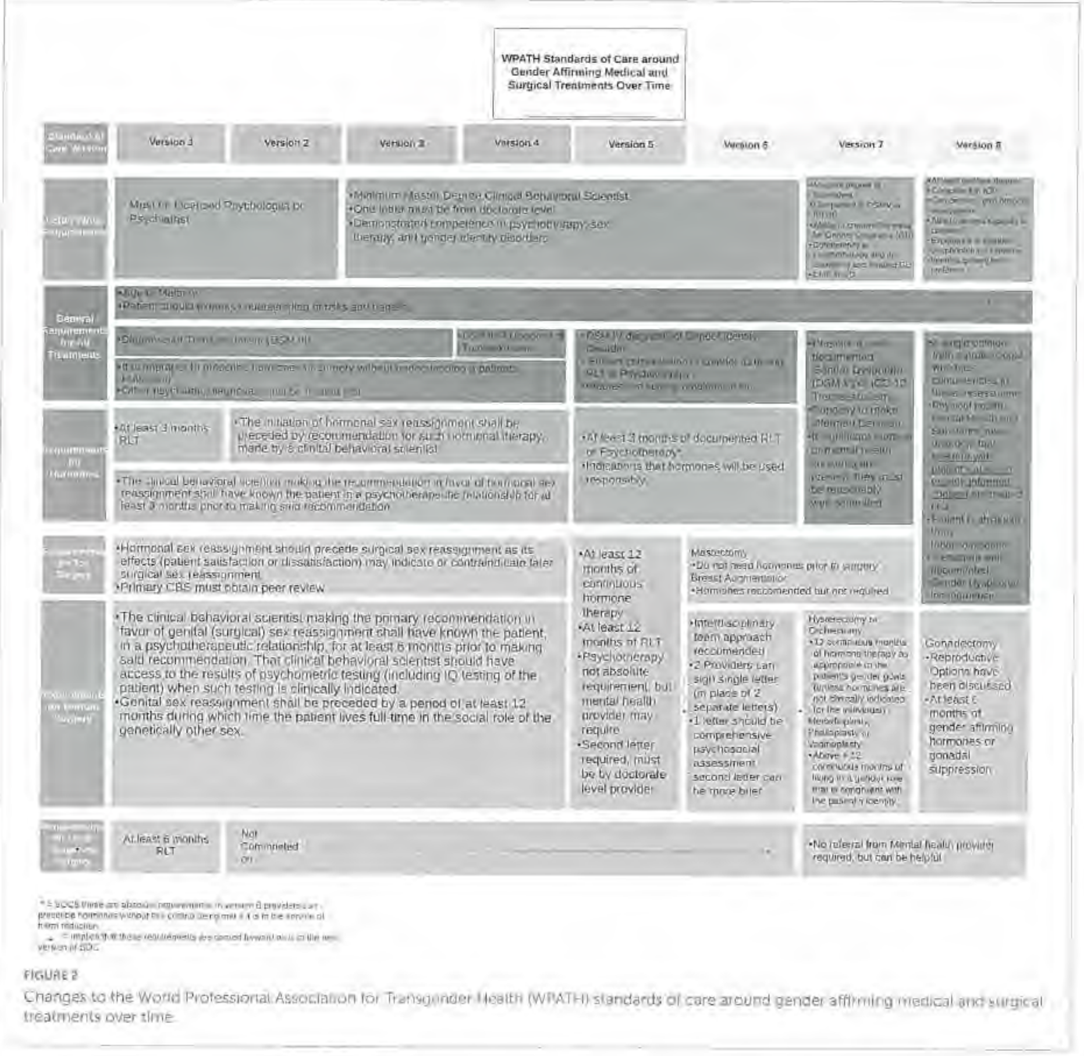

FIGURE 2
Changes to the World Professional Association for Transgender Health (WPATH) standards of care around gender affirming medical and surgical treatments over time.

classification and consistency of gender identity over time (17, 18).

Wise and Meyer explored the concept of a continuum between TV and TS, describing that those who experienced gender dysphoria often requested GAS, displayed evidence of strong cross-dressing desires with arousal, history of cross-gender roles, and absence of manic-depressive or psychotic illnesses (19). Requirements for GAS at the Johns Hopkins Gender Clinic included at least 2 years of cross-dressing, working in the opposite gender role, and undergoing treatment with GAH and psychotherapy (19). Bernstein identified factors correlated with negative GAS outcomes including presence of psychosis, drug abuse, frequent suicide attempts, criminality, unstable relationships, and low intelligence level (18). Lothstein stressed the importance of correct diagnosis, "since life stressors may lead some transvestites to clinically present as transsexuals desiring SRS" (20). Levine reviewed the diagnostic process employed by Case Western Reserve University Gender Identity Clinic which involved initial interview by a social worker to collect psychometric testing, followed by two independent psychiatric interviews to obtain the developmental gender history, understand treatment goals, and evaluate for underlying co-morbid mental health diagnoses, with a final multidisciplinary conference to integrate the various evaluations and develop a treatment plan (21).

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Standards of care version 3

Changes to the standards of care

Version 3 broadened the definition of the clinician thereby broadening the scope of providers who could write recommendation letters for GAC. Whereas prior SOC required letters from licensed psychologists or psychiatrists, version 3 allowed initial evaluations from providers with at least a Master's degree in behavioral science, and when required, a second evaluation from any licensed provider with at least a doctoral degree. Version 3 recommended that all evaluators demonstrate competence in "gender identity matters" and must know the patient, "in a psychotherapeutic relationship," for at least 6 months (16). Version 3 relied on the definition of TS in DSM-III, which specified the sense of discomfort with one's anatomic sex be "continuous (not limited to a period of stress) for at least 2 years" and be independently verified by a source other than the patient through collateral or through a longitudinal relationship with the mental health provider (16). Recommendation of GAS specifically required at least 6–12 months of RLT, for non-genital and genital GAS, respectively (16)."

Results review

Nine articles were published during the timeframe that the SOC version 3 were active (1981–1990). Themes in these publications included increasing focus on selection criteria for GAS and emphasis on the RLT, which was used to ensure proper diagnosis of gender dysphoria. Recommendations for the duration of the RLT ranged anywhere between 1 and 3 years (22, 23).

Proposed components of the mental health evaluation for GAS included a detailed assessment of the duration, intensity, and stability of the gender dysphoria, identification of underlying psychiatric diagnoses and suicidal ideation, a mental status examination to rule out psychosis, and an assessment of intelligence (e.g., IQ) to comment on the individual's "capacity and competence" to consent to GAC. The Minnesota Multiphasic Personality Inventory (MMPI), Weschler Adult Intelligence Scale (WAIS), and Lindgren-Pauly Body Image Scale were also used during assessments (24).

Authors developed more specific inclusion and exclusion criteria for undergoing GAS with inclusion criteria including age 21 or older, not legally married, no pending litigation, evidence of gender dysphoria, completion of 1 year of psychotherapy, between 1 and 2 years RLT with ability to "pass convincingly" and "perform successfully" in the opposite gender role, at least 6 months on GAH (if medically tolerable), reasonably stable mental health (including absence of psychosis, depression, alcoholism and intellectual disability), good financial standing with psychotherapy fees (25), and a prediction that GAS would improve personal and social functioning (26–29). A 1987 survey of European psychiatrists identified their most common requirements as completion of a RLT of 1–2 years, psychiatric observation, mental stability, no psychosis, and 1 year of GAH (27).

Standards of care version 4

Changes to the standards of care

World Professional Association for Transgender Health SOC version four was published in 1990. Between version three and version four, DSM-III-R was published in 1987. Version four relied on the DSM-III-R diagnostic criteria for TS as opposed to the DSM-III criteria in version three. The DSM-III-R criteria for TS included a "persistent discomfort and sense of inappropriateness about one's assigned sex," "persistent preoccupation for at least 2 years with getting rid of one's primary and secondary sex characteristics and acquiring the sex characteristics of the other sex," and that the individual had reached puberty (30). Notable changes from the DSM-III criteria include specifying a time duration for the discomfort (2 years) and designating that individuals must have reached puberty.

Results review

Six articles were published between 1990 and 1998 while version four was active. Earlier trends continued including emphasizing proper diagnosis of gender dysphoria (31, 32), however, a new trend emerged toward implementing more comprehensive evaluations, with an emphasis on decision making, a key element of informed consent.

Bockting and Coleman, in a move representative of other publications of this era, advocated for a more comprehensive approach to the mental health evaluation and treatment of gender dysphoria. Their treatment model was comprised of five main components: a mental health assessment consisting of psychological testing and clinical interviews with the individual, couple, and/or family; a physical examination; management of comorbid disorders with pharmacotherapy and/or psychotherapy; facilitation of identity formation and sexual identity management through individual and group therapy; and aftercare consisting of individual, couple, and/or family therapy with the option of a gender identity consolidation support group. Psychoeducation was a main thread throughout the treatment model and a variety of treatment "subtasks" such as understanding decision making, sexual functioning and sexual identity exploration, social support, and family of origin intimacy were identified as important. The authors advocated for "a clear separation of gender identity, social sex role, and sexual orientation which allows a wide spectrum of sexual identities and prevents limiting access to GAS to those who conform to a heterosexist paradigm of mental health" (33).

This process can be compared with the Italian SOC for GAS which recommend a multidisciplinary assessment

consisting of a psychosocial evaluation and informed consent discussion around treatment options, procedures, and risks. Requirements included 6 months of psychotherapy prior to initiating GAH, 1 year of a RLT prior to GAS, and provision of a court order approving GAS, which could not be granted any sooner than 2 years after starting the process of gender transition. Follow-up was recommended at 6, 12, and 24 months post-GAS to ensure psychosocial adjustment to the affirmed gender role (34).

Other authors continued to refine inclusion and exclusion criteria for GAS by surveying the actual practices of health centers. Inclusion criteria included those who had life-long cross gender identification with inability to live in their sex assigned at birth; a 1–2 years RLT (a nearly universal requirement in the survey); and ability to pass "effortlessly and convincingly in society"; completed 1 year of GAH; maintained a stable job; were unmarried or divorced; demonstrated good coping skills and social-emotional stability; had a good support system; and were able to maintain a relationship with a psychotherapist. Exclusion criteria included age under 21 years old, recent death of a parent (35), unstable gender identity, unstable psychosocial circumstances, unstable psychiatric illness (such as schizophrenia, suicide attempts, substance abuse, intellectual disability, organic brain disorder, AIDS), incompatible marital status, criminal history/activity or physical/medical disability (36).

The survey indicated some programs were more lenient around considering individuals with bipolar affective disorder, the ability to pass successfully, and issues around family support. Only three clinics used sexual orientation as a factor in decision for GAS, marking a significant change in the literature from prior decades. Overall, the authors found that 74% of the clinics surveyed did not adhere to WPATH SOC, instead adopting more conservative policies (36).

Standards of care version 5

Changes to the standards of care

Published in 1998, version five defined the responsibilities of the mental health professional which included diagnosing the gender disorder, diagnosing and treating co-morbid psychiatric conditions, counseling around GAC, providing psychotherapy, evaluating eligibility and readiness criteria for GAC, and collaborating with medical and surgical colleagues by writing letters of recommendation for GAC (Figure 3). Eligibility and readiness criteria were more explicitly described in this version to refer to the specific objective and subjective criteria, respectively, that the patient must meet before proceeding to the next step of their gender transition. The seven elements to include in a letter of readiness were more explicitly listed within this version as well including: the patient's identifying characteristics, gender, sexual orientation, any other psychological diagnoses, duration and nature of the treatment with the letter writer, whether the author is part of a gender team, whether eligibility criteria have been met, the patient's ability to follow the SOC and an offer of collaboration. Version five removes the requirement that patients undertake psychotherapy to be eligible for GAC (37).

Results review

Five articles were published between 1998 and 2001 while version five was active. Two of these articles were summaries of the SOC (37, 38). Themes in these publications included continued attempts to develop comprehensive treatment models for GAS.

Ma reviewed the role of the social worker in a multidisciplinary gender clinic in Hong Kong. Psychosocial assessment for GAS included evaluation of performance in affirmed social roles, adaptation to the affirmed gender role during the 1-year RLT and understanding the patient's identified gender role and the response to the new gender role culturally and interpersonally within the individual's support network and family unit. She noted five contraindications to GAS: a history of psychosis, sociopathy, severe depression, organic brain dysfunction or "defective intelligence," success in parental or marital roles, "successful functioning in heterosexual intercourse," ability to function in the pretransition gender role, and homosexual or TV history with genital pleasure. She proposed a social work practice model for patients who apply for GAS with categorization of TGD individuals into "better-adjusted" and "poorly-adjusted" with different intervention goals and methods for each. For those who were "better-adjusted," treatment focused on psychoeducation, building coping tools, and mobilization into a peer counselor role, while treatment goals for those who were "poorly-adjusted" focused on building support and resources (39).

Damodaran and Kennedy reviewed the assessment and treatment model used by the Monash gender dysphoria clinic in Melbourne, Australia for patients requesting GAS. All referrals for GAS were assessed independently by two psychiatrists to determine proper diagnosis of gender dysphoria, followed by endocrinology and psychology consultation to develop a comprehensive treatment plan. Requirements included RLT of minimum 18 months and GAH (40).

Miach reviewed the utility of using the Minnesota Multiphasic Personality Inventory-2 (MMPI-2), a revision of the MMPI which was standardized using a more heterogeneous population, in a gender clinic to assess stability of psychopathology prior to GAS, which was only performed on patients aged 21–55 years old. The authors concluded that while the TGD group had a significantly lower level of psychopathology than the control group, they believed that the MMPI-2 was a useful test in assessing readiness for GAC (41).

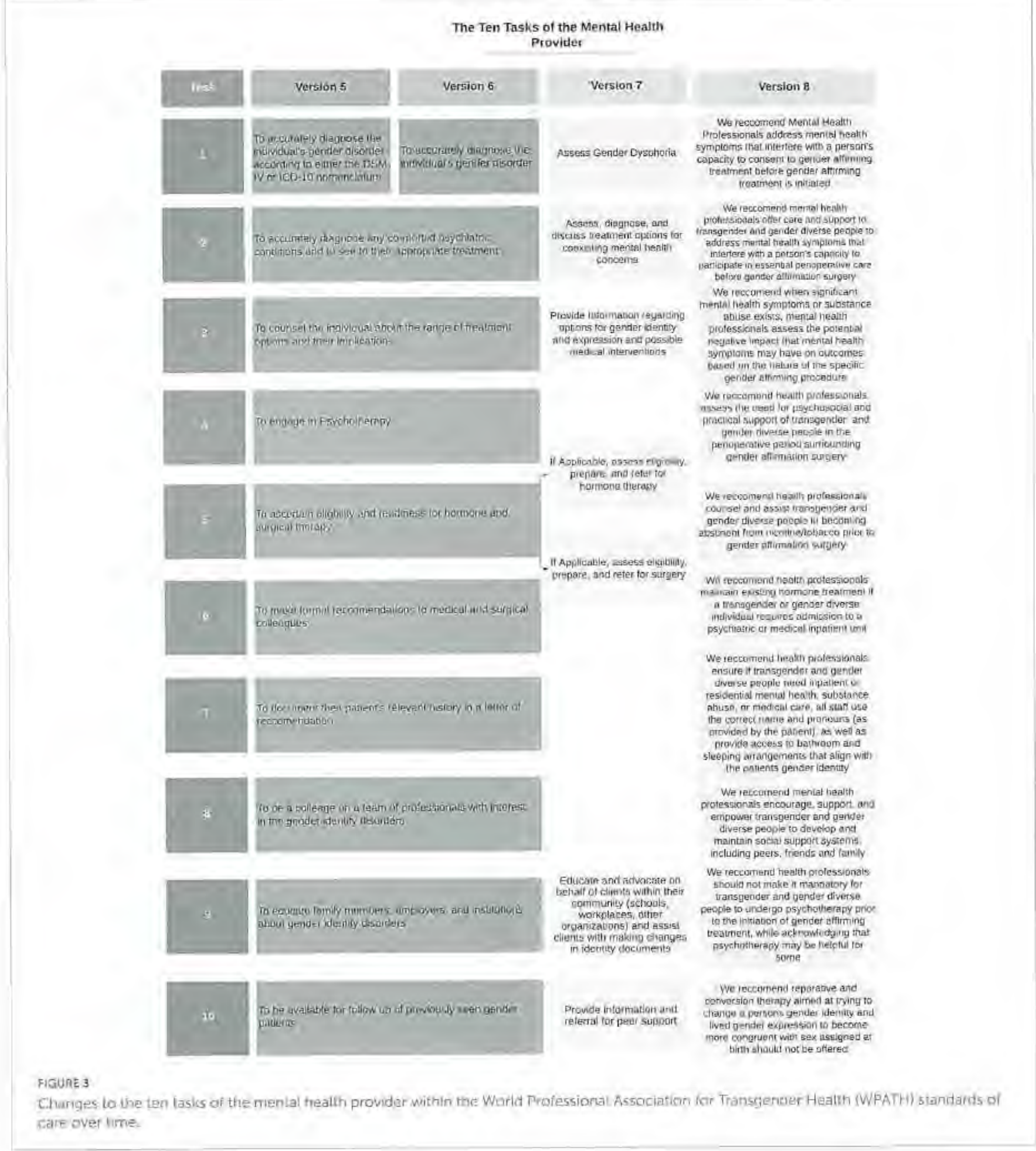

FIGURE 3
Changes to the ten tasks of the mental health provider within the World Professional Association for Transgender Health (WPATH) standards of care over time.

Standards of care version 6

Changes to the standards of care

Published in 2001, version six of the WPATH SOC did not include significant changes to the 10 tasks of the mental health professional (Figure 3) or in the general recommendations for content of the letters of readiness. An important change in the eligibility criteria for GAH allowed providers to prescribe hormones even if patients had not undergone RLT or psychotherapy if it was for harm reduction purposes (i.e., to prevent patient from buying black market hormones). A notable change in version six separated the eligibility and readiness criteria for top (breast augmentation or mastectomy) and bottom (any gender-affirming surgical

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alteration of genitalia or reproductive organs) surgery allowing some patients, particularly individuals assigned female at birth (AFAB), to receive a mastectomy without having been on GAH or completing a 12 month RLT (42, 43).

Results review

Thirteen articles were published between 2001 and 2012. One is a systematic review of evidence for factors that are associated with regret and suicide, and predictive factors of a good psychological and social functioning outcome after GAC. De Cuypere and Vercruysse note that less than one percent of patients regret having GAS or commit suicide, making detection of negative predictive factors in a study nearly impossible. They identified a wide array of positive predictive factors including age at time of request, sex of partner, premorbid social or psychiatric functioning, adequacy of social support system, level of satisfaction with secondary sexual characteristics, and surgical outcomes. Many of these predictive factors were later disproved. They also noted that there were not enough studies to determine whether following the WPATH guidelines was a positive predictive factor. In the end they noted that the evidence for all established evaluation regimens (i.e., RLT, age cut-off, psychotherapy, etc.) was at best indeterminate. They recommended that changes to WPATH criteria should redirect focus from gender identity to psychopathology, differential diagnosis, and psychotherapy for severe personality disorders (44).

The literature at this time supports two opposing approaches to requests for GAC, those advocating for a set of strictly enforced eligibility and readiness criteria associated with very thorough evaluations and those who advocate for a more flexible approach. Common approaches to the evaluation for GAC include: taking a detailed social history including current relationships, support systems, income, and social functioning; a sexual development history meant to understand when and how the patient began to identify as TGD and how their transition has affected their life; an evaluation of their coping skills, "psychic functions" and general mental well-being; and a focus on assessing the "correct diagnosis" of gender identity disorder (44–56). The use of a multidisciplinary team was also commonly recommended (44, 47, 48, 51, 54–56).

Those that advocated for a stricter interpretation of the eligibility and readiness criteria emphasized the importance of the RLT (45, 49, 51, 53, 55, 56). One clinic in the UK required a RLT lasting 2 years prior to starting GAH, twice as long as recommended by the SOC (49). The prevailing view continued to approach gender as a binary phenomenon, rather than as a spectrum of experiences. As a result, treatment recommendations emphasized helping the patient to "pass" in their chosen gender role and did not endorse patients receiving less than the full spectrum of treatment to transition fully from one sex to the other. Several authors indicated that they required some amount of psychotherapy before recommending GAC (46, 47, 51, 52, 55, 56). One author described requirements in Turkey, which unlike the US has the requirements enshrined in law and defines an important role for the courts in granting permission for GAC (51). In general, these authors supported the gatekeeping role of the mental health provider as a mechanism to prevent cases of regret.

Among groups supporting a flexible interpretation of the SOC, there was a much stronger emphasis on the supportive role of the mental health provider in the gender transition process (44–46, 48, 52, 53). This role included creating a supportive environment for the patient, asking and using the correct pronouns, and helping to guide them through what may be a difficult transition both socially and physically. They emphasized the importance of the psychosocial evaluation including the patient's connections to others in the TGD community, their social functioning, substance use, and psychiatric history/psychological functioning. While informed consent was mentioned as part of the evaluation, the process was not thoroughly explored and largely focused on patients' awareness that GAS is an irreversible procedure which removes healthy tissue (53). One author suggested that a "consumer handbook outlining such rights and responsibilities" related to GAS be made available, but they made no further comment on the informed consent process (44). There was no further guidance as to the contents of letters of readiness for GAC.

The lack of emphasis on informed consent by both groups of authors mirrors the discussion of informed consent within the SOC, which up through version six, had a relatively narrow definition and role specifically related to risks and benefits of surgery. As far back as version one, the SOC states "hormonal and surgical sex reassignment are procedures which must be requested by, and performed only with the agreement of, the patient having informed consent…[these procedures] may be conducted or administered only after the patient applicant has received full and complete explanations, preferably in writing, in words understood by the patient applicant, of all risks inherent in the requested procedures (16). " This reflects the dominant concerns of surgeons at the time that they were removing or damaging healthy tissue, which was unethical, and as such wanted to make sure that patients understood the irreversibility of the procedures. It was not until version 7 that there is a change in the discussion of informed consent.

Standards of care version 7

Changes to the standards of care

Standards of care version seven was published in 2013. Publication of version seven coincided with the publication of DSM-5, in which the diagnosis required to receive GAC shifted from Gender Identity Disorder to Gender Dysphoria, in an effort to de-pathologize TGD patients. Version seven highlights that these are *guidelines* meant to be flexible to account for

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different practices in different places. Compared to version six, a significantly expanded section on the "Tasks of the Mental Health Provider" was added, offering some instructions on what to include in the assessment of the patient for GAS. For the first time the SOC expand on what it means to obtain informed consent and describe a process where the mental health provider is expected to guide a conversation around gender identity and how different treatments and procedures might affect TGD individuals psychologically, socially, and physically. Other recommendations include "at a minimum, assessment of gender identity and gender dysphoria, history and development of gender dysphoric feelings, the impact of stigma attached to gender non-conformity on mental health, and the availability of support from family, friends, and peers." There is also a change to the recommended content of the letters: switching from "The initial and evolving gender, sexual, and other psychiatric diagnoses" to "Results of the client's psychosocial assessment, including any diagnoses", indicating a shift in the focus away from diagnosis toward the psychosocial assessment. Version 7 also adds two new tasks for the mental health provider including "Educate and advocate on behalf of clients within their community (schools, workplaces, other organizations) and assist clients with making changes in identity documents" and "Provide information and referral for peer support"(2).

There were also significant changes to eligibility criteria for GAC. For GAH, version seven eliminates entirely the requirement for a RLT and psychotherapy and adds requirements for "persistent well documented gender dysphoria" and "reasonably well controlled" medical or mental health concerns. Notably, the SOC do not define the meaning of "reasonably well controlled," leaving providers to interpret this on their own. Version seven delineates separate requirements for top and bottom surgeries. The criteria for both feminizing and masculinizing top surgeries are identical to each other and identical to those laid out for GAH. Version seven explicitly states that GAH is not required prior to top surgery, although GAH is still recommended prior to gender-affirming breast augmentation. Criteria for bottom surgery are more explicitly defined, namely internal (i.e., hysterectomy, orchiectomy) vs. external (i.e., metoidioplasty, phalloplasty, and vaginoplasty). For internal surgeries, criteria are the same as for top surgery with the addition of a required 12 months of GAH. For external surgeries the criteria are the same as for internal, with the addition of required 12 months of living in the patient's affirmed gender identity (2, 52).

Results review

Twenty-three articles were published while version 7 of the SOC have been active. Themes include identifying the role of psychometric testing in GAC evaluations, expanding the discussion around informed consent for GAC, and revising the requirements for letter writers.

A systematic review evaluated the accuracy of psychometric tests in those requesting GAC, identifying only two published manuscripts that met their inclusion criteria, both of which were of poor quality; this led them to question the utility of psychometric tests in in TGD patients (57). Keo-Meir and Fitzgerald provided a detailed narrative review of psychometric and neurocognitive exams in the TGD population and concluded that psychometric testing should not be done unless there is a question about the capacity of the patient to provide informed consent (58). The only other manuscripts that include a mention of psychological testing describe processes in Iran and China, both of which require extensive psychological testing prior to approval for GAC (59, 60). These two manuscripts, in addition to an ethnographic study of the evaluation process in Turkey (61), are also the only ones that indicate a requirement for psychotherapy prior to approval for treatment. The three international manuscripts described above plus three manuscripts from the US (62–64) are the only ones to include consideration of a RLT, with authors outside the US preferring a long RLT and US authors considering RLT as part of the informed consent process for GAS, and not required at all prior to the initiation of GAH.

Many authors describe the process of informed consent for GAC (1, 58, 60, 62–76). In China, a signature indicating informed consent from the patient's family is required in addition to that of the patient (60). Many authors emphasize evaluating for and addressing social determinants of health including housing status, income, transportation, trauma history, etc. (1, 58, 60, 67, 69–71, 75–77). Deutsch advocated for the psychosocial evaluation being the most important aspect of the evaluation and suggests that one of the letters required for bottom surgery be replaced by a functional assessment (i.e., ADLs/iADLs), which could be repeated as needed or removed entirely for high functioning patients (69).

Practice patterns and opinions on who should write letters of readiness and how many letters should be required vary widely. Many letters that surgeons receive are cursory, and short and non-personal letters correlate with poor surgical outcomes (1). Several authors advocate for eliminating the second letter entirely, for at least some procedures, as it is a barrier to care (68, 69, 74). Some support removing the requirement that both letter writers be therapists or psychiatrists, and even suggesting the second letter be written by a urologist (72) or a social worker who has performed a detailed social assessment (69, 75). The evaluation in Turkey requires a report written by an extensive multidisciplinary team and submitted to a court for approval (61). Surveys of providers indicate that the SOC are not uniformly implemented leading to huge disparities based on the providers knowledge level and personal beliefs (77, 78). Additional recommendations include that providers spend significant time discussing the SOC and diagnosis of gender dysphoria with the patients prior to providing a letter to prepare them for the stigma such a diagnosis may confer

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(65, 66), and dropping gender dysphoria entirely in favor the ICD-11 diagnosis of gender incongruence, as it may be less stigmatizing (71).

The Mount Sinai Gender Clinic describes an integrated multidisciplinary model where a patient will see a primary care doctor, endocrinologist, social worker, psychiatrist, and obtain any necessary lab work in a single visit, significantly reducing barriers to care. The criteria in this model focus on informed consent, the social determinants of health, being physically ready for surgery, and putting measurable goals on psychiatric stability, while deemphasizing the gender dysphoria diagnosis. Their study showed that people who received their evaluation over a 2-year period were more likely to meet their in-house criteria than they were to meet criteria as set forth in WPATH SOC. The Mount Sinai criteria allowed for significantly decreased barriers to care, allowing more people to progress through desired GAC in a timely fashion (75).

Standards of care version 8

Changes to the standards of care

Standards of care version 8, published in September 2022, includes major updates to the guidelines around GAS. This version explicitly highlights the importance of informed decision making, patient autonomy, and harm reduction models of care, as well as emphasizing the flexibility of the guidelines which the authors note can be modified by the healthcare provider in consultation with the TGD individual.

Version 8 lays out the roles of the assessor which are to identify the presence of gender incongruence and any co-existing mental health concerns, provide information on GAC, support the TGD individual in their decision-making, and to assess for capacity to consent to GAC. The authors emphasize the collaborative nature of this decision-making process between the assessor and the TGD individual, as well as recommending TGD care occur in a multidisciplinary team model when possible.

Version 8 recommends that providers who assess TGD individuals for GAC hold at least a Master's level degree and have sufficient knowledge in diagnosing gender incongruence and distinguishing it from other diagnoses which may present similarly. These changes allow for non-mental health providers to be the main assessors for GAC.

Version 8 recommends reducing the number of evaluations prior to GAS to a single evaluation in an effort to reduce barriers to care for the TGD population. Notably, the authors have removed the recommendations around content of the letter of readiness for GAC. The guidelines note that the complexity of the assessment process may differ from patient to patient, based on the type of GAC requested and the specific characteristics of the patient. Version eight directly states that psychometric testing and psychotherapy are not requirements to pursue GAC. While evaluations should continue to identify co-existing mental health diagnoses, version 8 highlights that the presence of a mental health diagnosis should not prevent access to GAC unless the mental health symptoms directly interfere with capacity to provide informed consent for treatment or interfere with receiving treatment. Version 8 recommends that perioperative matters, such as travel requirements, presence of stable, safe housing, hygiene/healthy living, any activity restrictions, and aftercare optimization, be discussed by the surgeon prior to GAS. In terms of eligibility criteria, the authors recommend a reduced duration of GAH from 12 months (from version 7) to 6 months (in version 8) prior to pursuing GAS involving reproductive organs (79).

Ethical discussions

Results review

A total of eleven articles explored ethical considerations of conducting mental health evaluations and writing letters of readiness for GAS, including a comparison of the ethical principles prioritized within the "gatekeeping" model vs. the informed consent model for GAC and the differential treatment of TGD individuals compared to cisgender individuals seeking similar surgical procedures.

Many authors compare the informed consent model of care for TGD individuals to the WPATH SOC model. In the informed consent model, the role of the health practitioner is to provide TGD patients with information about risks, side effects, benefits, and possible consequences of undergoing GAC, and to obtain informed consent from the patient (80). Cavanaugh et al. argue that the informed consent model is more patient-centered and elevates the ethical principle of autonomy above non-maleficence, the principle often prioritized in the "gatekeeping" model (81). They write, "Through a discussion of risks and benefits of possible treatment options with the patient. . .clinicians work to assist patients in making decisions. This approach recognizes that patients are the only ones who are best positioned, in the context of their lived experience, to assess and judge beneficence (i.e., the potential improvement in their welfare that might be achieved), and it also affords prescribing clinicians a better and fuller sense of how a particular patient balances principles of non-maleficence and beneficence." Authors note that mental health providers can be particularly helpful in situations where an individual desires additional mental health treatment, which some argue should remain optional, or when an individual's capacity is in question (81). Additional ethical considerations include balancing the respect for the dignity of persons, responsible caring, integrity in relationships, and responsibility to society (82). Other authors argue for a more systematic approach to ethical issues, including consulting the literature and/or experts in the

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field of TGD mental health for support in making decisions around GAC (74).

Hale criticizes the WPATH SOC noting that these guidelines create a barrier between patient and mental health provider in establishing trust and a therapeutic relationship, overly pathologize TGD individuals, and unnecessarily impose financial costs to the TGD individual. As a "gatekeeper," the mental health provider is placed in the position of either granting or denying GAC and must weigh the competing ethical principles of beneficence, non-maleficence, and autonomy. He argues that mental health providers are not surrogate decision makers and that framing requests for GAS as a "phenomenon of incapacity" is "reflective of the overall incapacitating effects of society at large toward the TGD community" (83). This reflects the broader approach to determining capacity utilized in other medical contexts, namely that patients have capacity until proven otherwise (84). Additionally, due to the gatekeeping dynamic between patient and clinician, many TGD patients may not mention concerns or fears surrounding GAS out of concern they will be denied services, thereby limiting the quality and utility of the informed consent discussion. Ashley proposes changes to the informed consent model, specifically that the informed consent process should include not only information about whether to go through with a procedure, but how to go through the procedure including relevant information about timeline, side effects, need for perioperative support, and treatment plan (85). Gruenweld argues for a bottom-up, TGD-led provision of GAC instead of focusing solely on alleviating gender dysphoria through a top-down, medical expert approach *via* such systems like the WPATH SOC (86).

MacKinnon et al. conducted an institutional ethnographic study of both TGD individuals undergoing mental health evaluations for GAC and mental health providers to better understand the process of conducting such evaluations (87). They found that providers cited three concerns with the evaluation: determining the authenticity of an individual's TGD identity, determining if the individual has the capacity to consent to treatment, and determining the readiness of the individual to undergo treatment. TGD individuals cited concerns around presenting enough distress to be diagnosed with gender dysphoria (a SOC requirement) versus too much distress, and risk being diagnosed with an uncontrolled mental health condition therefore being ineligible for GAC. The authors conclude, "although they are designed to optimize and universalize care… psychosocial readiness assessments actually create a medically risky and arguably unethical situation in which trans people experiencing mental health issues have to decide what is more important – transitioning at the potential expense of care for their mental health or disclosing significant mental health issues at the expense of being rendered not ready to transition (which in turn may produce or exacerbate mental distress)" (87).

With regards to writing letters of readiness for GAS, authors comment on the differential treatment of TGD compared to cisgender individuals. Bouman argues that requiring two letters for gender-affirming orchiectomy or hysterectomy is unethical given that orchiectomy and hysterectomy for chronic scrotal pain and dysfunctional uterine bleeding, respectively, do not require any mental health evaluation. Requiring a second letter may cause delays in treatment, increase financial costs, and may be invasive to the patient who must undergo two detailed evaluations, while allowing for diffusion of responsibility for the mental health provider (88).

Discussion

Changing standards

Starting in the 1950's with the first successful gender affirming procedure in the US on Christine Jorgenson, TGD people in the US started seeking surgical treatment of what was then called TS. The medical community's understanding of TGD people, their mental health, and the role of the mental health provider in their medical and surgical transition has progressed and evolved since this time. Prior to the first iteration of what would later be known as WPATH's SOC, patients were mostly evaluated within a system that viewed gender and sexual minorities as deviants and thereby largely limited access to GAC. We can also see this reflected in the changes to DSM and ICD diagnostic criteria between 1980 and today which demonstrates a trend from pathologizing identity and conflating sexual and gender identity toward pathologizing the distress experienced due to the discordant identity, and finally removing the relevant diagnosis from the chapter of Mental and Behavioral Disorders altogether in the ICD and instead into a new chapter titled "conditions related to sexual health (69)." These changes have clearly yielded positive benefits for TGD individuals by reducing stigma and improving access to care, but significant problems remain. Requiring TGD people to have a diagnosis at all to obtain care, no matter the terminology used, is pathologizing. The practice of requiring a diagnosis continues to put mental health and other medical providers in the position of gatekeeping, continuing the vestigial historical focus on "confirming" a person's gender identity, rather than trusting that TGD people understand their identities better than providers do. Version 8 of the SOC put a much heavier emphasis on shared decision making and informed consent, but continue to maintain the requirement of a diagnosis (79). Many insurance companies and other health care payers require the diagnosis to justify paying for GAC, but providers should continue to advocate for removing such labels as a gatekeeping mechanism for GAC.

With each version of the SOC, guidelines for GAC become more specific, with more explanation of the reasoning

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behind each recommendation; more flexible requirements, a broadening of the definition of mental health provider, and elimination of the requirement that at least one letter be written by a doctoral level provider. There has been a notable shift in the conceptualization of gender identity, away from a strict gender binary, with individuals transitioning fully from one end to the other, to gender identity and transition as a spectrum of experiences. Over time the SOC became more flexible by removing requirements for psychotherapy, narrowing requirement for the RLT to only those pursuing bottom surgery, eliminating requirements for a mental health evaluation prior to initiating GAH, and eliminating requirements for GAH prior to top surgery. Version 8 of the SOC was even more explicit about removing requirements for psychotherapy and psychometric testing prior to receiving GAC (79).

Despite these positive changes, those wishing to access GAC still face significant challenges. Access to providers knowledgeable about GAC remains limited, especially in more rural areas, therefore requiring evaluations and letters of readiness for GAC continues to significantly limit access to treatment. By requiring letters of readiness for GAC, adult TGD individuals are not afforded the same level of autonomy present in almost any other medical context, where capacity to provide informed consent is automatically established (84). The WPATH SOC continue to perpetuate differential treatment of TGD individuals by requiring extensive, and often invasive, evaluations for procedures that their cisgender peers are able to access without such evaluations (88). The WPATH guidelines apply a one-size-fits-all approach to an extremely heterogeneous community who have varying levels of needs based on a variety of factors including but not limited to age, socioeconomic status, race, natal sex, and geographic location (90). It should be noted, however, that the version 8 of the SOC does acknowledge that different patients may require evaluations of varying complexity based on the procedure they are requesting as well as a variety of psychosocial factors, although it remains vague about exactly what those different evaluations should entail (79). We propose that future work be directed toward three primary goals: conducting research to determine the utility of letters of readiness; to better understand factors that impact GAS outcomes; and to develop easily accessible and understandable guides to conducting readiness evaluations and writing letters. These aims will help to further our goals of advocating for this vastly underserved population by further removing barriers to life-saving GAC.

Changing ethics

Early iterations of the SOC were strict, placing the mental health provider within a gatekeeper role, tasked with distinguishing the "true transsexual" that would benefit from GAS from those who would not, which in effect elevated the ethical principal of non-maleficence above autonomy. This created a barrier to forming a therapeutic alliance between the patient and mental health provider as there was little motivation for patients to give any information outside of the expected gender narrative (50, 65). Mistrust flowed both ways leading to longer and more involved evaluations then than what is required today, with many providers requiring patients to undergo extensive psychological testing and psychotherapy, provide extensive collateral, and undergo lengthy RLTs, with some focusing on a patient's ability to "pass" within the desire gender role, before agreeing to write a letter (11, 15, 19, 49, 57, 58).

As understanding around the experiences of TGD individuals has evolved over time, the emphasis has shifted from the reliance on non-maleficence toward elevating patient autonomy as the guiding principle of care. Evaluations within this informed consent model focus much more on the patient's ability to understand the treatment, its aftercare, and its potential effect on their lives. Informed consent evaluations also shift focus toward other psychosocial factors that will contribute to successful surgical outcomes, for example, housing, transportation, a support system, and treatment of any underlying mental health symptoms. While there is still a lack of consistency in current evaluations and the SOC are enforced unevenly (77), the use of the informed consent model by some providers has reduced barriers for some patients. Many authors now agree that psychological or neuropsychological testing should not be used when evaluating for surgical readiness unless there is a concern about the patient's ability to provide informed consent such as in the case of a neurocognitive or developmental disorder (58). Also important to note here is that while there is a general shift in the focus of the literature from that of gatekeeping toward one of informed consent, neither the informed consent model nor the WPATH SOC more broadly are evenly applied by providers, leading to continued barriers for many patients (77, 78).

Within the literature, there is support for further reducing barriers to care by widening the definition of who can conduct evaluations, write letters, or facilitate the informed consent discussion for GAC. Recommending that the physician providing the GAC be the one to conduct the informed consent evaluation would bring GAC practices more in line with practices in place within the broader medical community. It is very rare for mental health providers to be the gatekeepers for medical or surgical procedures, except for transplant surgery, where mental health providers may have a clearer role given the prominence of substance use disorders and the very limited resource of organs. However, even within transplant psychiatry, a negative psychiatric evaluation would not necessarily preclude the patient from receiving the transplant, but instead may be used to guide a treatment plan to improve chances of a successful recovery post-operatively. We then should consider what it means to embrace patient autonomy as our guiding

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principle, especially with more than 40 years of evidence of the positive effects around GAC behind us. Future guidelines should focus on making sure that TGD individuals are good surgical candidates, not based on their gender identity, but instead on a more holistic understanding of the factors that lead to good and bad gender-affirming surgical outcomes, along the lines of those proposed by Mt. Sinai's gender clinic for vaginoplasty (75). Additionally, the physicians providing the GAC should in most cases be the ones to obtain informed consent, while retaining the ability to request a mental health evaluation if specific concerns related to mental health arise. This would both allow mental health providers to adopt a supportive consultant role rather than that of gatekeeper, as well as provide more individualized rather than one-size-fits-all care to patients.

Version 8 of the SOC go a long way toward changing the ethical focus of evaluations toward one of shared decision making and informed consent by removing the requirement of a second letter and the requirement that the letter be written by a mental health provider. This will, in theory, lower barriers to care by allowing other providers (as long as they have at least a master's degree) to write letters for surgery (79). In practice, however, this change is likely to only affect a small portion of the patient population. This is because, as noted in the section below in more detail, insurance companies already do not adhere closely to the SOC (91) and are unlikely to quickly adopt the new guidelines if at all. Further, it is possible that many surgeons will require that the letter of readiness be written by a mental health provider, especially if the patient has any previous mental health problems. While changes to SOC 8 are a step in the direction we propose in this manuscript, it is important to remember that the primary decision makers of who can access GAC in the US are insurance companies with surgeons, primary care providers, and mental health providers as secondary decision makers; this leaves patients with much less real-world autonomy than the SOC state they should have in the process. While insurance companies hold this effective decision-making power in all of US healthcare, it could be at least partially addressed by developing clear, evidence based guidelines for which patients might require a more in-depth evaluation in the first place. Screening out patients that have little or no mental health or social barriers to care would directly reduce those patients' barriers to receiving GAC, while freeing up mental health and other providers to provide evaluation, resources, and support to those patients who will actually benefit from these services.

Letter writing

There are few published guides for writing letters of readiness for GAC. The WPATH SOC provide vague guidelines as to the information to include within the letter itself, which, in addition to a lack of consistency in implementation of the SOC, lead to a huge variety in current practices around letter writing and limit their usefulness to surgical providers (1). There is much debate within the literature about how many letters should be required and who should be able to write them. Guidelines from China, Turkey, and Iran recommend much stricter processes requiring input from a wider variety of specialists to comment on a patient's readiness (59–61). Within the US, the few recent recommendations include having a frank discussion with patients about the gender dysphoria diagnosis and allowing them to have input into the content of the letter itself (65, 66, 70, 71, 75). The heterogeneity of current practices around letter writing demonstrates a reality in which many providers do not uniformly operate within the informed consent model, and do not even uniformly adhere to the SOC as written. This heterogeneity in practice by providers also extends to requirements by insurance companies in the US. The lack of clear guidelines about what should go into a letter, especially across different insurance providers, can lead to increased barriers to care due to insurance denials for incorrectly written letters. While direct data examining insurance denials for incorrectly written letters is not available, we can see this indirect effects in the fact that while 90% of insurance providers in the US provide coverage for GAC, only 5–10% of TGD patients had received bottom surgery even though about 50% of TGD patients have reported wanting it (91). Version 8 of the SOC reduce some of the letter writing requirements as discussed above, but they still do not give clear instructions on exactly how to write a letter of readiness or perform an evaluation (79). Given the lack of uniformity and limited benefit of such letters to surgical providers, these authors propose that future research be conducted into the need for letters of readiness for GAC, ways to ensure the content of such letters are evidence-based to improve outcomes of GAC, and improve education to providers by creating an easily accessible and free semi-structured interview with letter template.

Limitations

The reviewed articles included opinion manuscripts, published SOC, and proposed models for how to design and operate GAC clinics, however, this narrative review is limited by a lack of peer reviewed clinical trials that assess the evidence for the GAC practices described here. As a result, it is challenging to comment on the effectiveness of various interventions over time.

Conclusion

The WPATH SOC have evolved significantly over time with regards to their treatment of TGD individuals. Review of the literature shows a clear progression of practices from paternalistic gatekeeping toward increasing emphasis on patient autonomy and informed consent. Mental health evaluations, still required by SOC version eight are almost entirely unique as a requirement for GAS, apart from some

bariatric and transplant surgeries. Individuals who wish to pursue GAC are required to get approval for treatments that their cisgender peers may pursue without such evaluations. While there may be some benefits from these evaluations in helping to optimize a patient socially, emotionally, and psychologically for GAC, the increased stigma and burden placed on patients by having a blanket requirement for such evaluations leads us to seriously question the readiness evaluation requirements in SOC version 8, despite a reduction in the requirements compared to previous SOC. This burden is made worse by limited access to providers knowledgeable and competent in conducting GAC evaluations, writing letters of readiness, and a lack of consistency in the application and interpretations of the SOC by both providers and insurance companies. Other barriers to care created by multiple letter requirements include the often-prohibitive cost of getting multiple evaluations and the delay in receiving their medical or surgical treatments due to extensive wait times to see a mental health provider. This barrier will in theory be ameliorated by updates to SOC in version 8, but multiple letters are likely to at least be required by insurance companies for some time. Overall, the shift from gate keeping to informed consent has been a net positive for patients by reducing barriers to care and improving patient autonomy, but the mental health evaluation is still an unnecessary barrier for many people. Further research is necessary to develop a standardized evaluation and letter template for providers to access, as well as further study into who can most benefit from an evaluation in the first place.

Data availability statement

The original contributions presented in this study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

TA and KK contributed to the conception and design of the study under the guidance of RL and AJ, reviewed and analyzed the literature, and wrote the manuscript. AW organized the literature search and wrote the "Methods" section. RL and AJ assisted in review and revision of the completed manuscript. All authors approved of the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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CHAPTER 6 Adolescents

Historical context and changes since previous Standards of Care

Specialized health care for transgender adolescents began in the 1980s when a few specialized gender clinics for youth were developed around the world that served relatively small numbers of children and adolescents. In more recent years, there has been a sharp increase in the number of adolescents requesting gender care (Arnoldussen et al., 2019; Kaltiala, Bergman et al., 2020). Since then, new clinics have been founded, but clinical services in many places have not kept pace with the increasing number of youth seeking care. Hence, there are often long waitlists for services, and barriers to care exist for many transgender youth around the world (Tollit et al., 2018).

Until recently, there was limited information regarding the prevalence of gender diversity among adolescents. Studies from high school samples indicate much higher rates than earlier thought, with reports of up to 1.2% of participants identifying as transgender (Clark et al., 2014) and up to 2.7% or more (e.g., 7–9%) experiencing some level of self-reported gender diversity (Eisenberg et al., 2017; Kidd et al., 2021; Wang et al., 2020). These studies suggest gender diversity in youth should no longer be viewed as rare. Additionally, a pattern of uneven ratios by assigned sex has been reported in gender clinics, with adolescents assigned female at birth (AFAB) initiating care 2.5–7.1 times more frequently as compared to adolescents who are assigned male at birth (AMAB) (Aitken et al., 2015; Arnoldussen et al., 2019; Bauer et al., 2021; de Graaf, Carmichael et al., 2018; Kaltiala et al., 2015; Kaltiala, Bergman et al., 2020).

A specific World Professional Association for Transgender Health's (WPATH) Standards of Care section dedicated to the needs of children and adolescents was first included in the 1998 WPATH Standards of Care, 5th version (Levine et al., 1998). Youth aged 16 or older were deemed potentially eligible for gender-affirming medical care, but only in select cases. The subsequent 6th (Meyer et al., 2005) and 7th (Coleman et al., 2012) versions divided medical-affirming treatment for adolescents into three categories and presented eligibility criteria regarding age/puberty stage—namely fully reversible puberty delaying blockers as soon as puberty had started; partially reversible hormone therapy (testosterone, estrogen) for adolescents at the age of majority, which was age 16 in certain European countries; and irreversible surgeries at age 18 or older, except for chest "masculinizing" mastectomy, which had an age minimum of 16 years. Additional eligibility criteria for gender-related medical care included a persistent, long (childhood) history of gender "non-conformity"/dysphoria, emerging or intensifying at the onset of puberty; absence or management of psychological, medical, or social problems that interfere with treatment; provision of support for commencing the intervention by the parents/caregivers; and provision of informed consent. A chapter dedicated to transgender and gender diverse (TGD) adolescents, distinct from the child chapter, has been created for this 8th edition of the Standards of Care given 1) the exponential growth in adolescent referral rates; 2) the increased number of studies specific to adolescent gender diversity-related care; and 3) the unique developmental and gender-affirming care issues of this age group.

Non-specific terms for gender-related care are avoided (e.g., gender-affirming model, gender exploratory model) as these terms do not represent unified practices, but instead heterogenous care practices that are defined differently in various settings.

Adolescence overview

Adolescence is a developmental period characterized by relatively rapid physical and psychological maturation, bridging childhood and adulthood (Sanders, 2013). Multiple developmental processes occur simultaneously, including pubertal-signaled changes. Cognitive, emotional, and social systems mature, and physical changes associated with puberty progress. These processes do not all begin and end at the same time for a given individual, nor do they occur at the same age for all persons. Therefore, the lower and upper borders of adolescence are imprecise and cannot be defined exclusively by age. For example, physical pubertal changes may

begin in late childhood and executive control neural systems continue to develop well into the mid-20s (Ferguson et al., 2021). There is a lack of uniformity in how countries and governments define the age of majority (i.e., legal decision-making status; Dick et al., 2014). While many specify the age of majority as 18 years of age, in some countries it is as young as 15 years (e.g., Indonesia and Myanmar), and in others as high as 21 years (e.g., the U.S. state of Mississippi and Singapore).

For clarity, this chapter applies to adolescents from the start of puberty until the legal age of majority (in most cases 18 years), however there are developmental elements of this chapter, including the importance of parental/caregiver involvement, that are often relevant for the care of transitional-aged young adults and should be considered appropriately.

Cognitive development in adolescence is often characterized by gains in abstract thinking, complex reasoning, and metacognition (i.e., a young person's ability to think about their own feelings in relation to how others perceive them; Sanders, 2013). The ability to reason hypothetical situations enables a young person to conceptualize implications regarding a particular decision. However, adolescence is also often associated with increased risk-taking behaviors. Along with these notable changes, adolescence is often characterized by individuation from parents and the development of increased personal autonomy. There is often a heightened focus on peer relationships, which can be both positive and detrimental (Gardner & Steinberg, 2005). Adolescents often experience a sense of urgency that stems from hypersensitivity to reward, and their sense of timing has been shown to be different from that of older individuals (Van Leijenhorst et al., 2010). Social-emotional development typically advances during adolescence, although there is a great variability among young people in terms of the level of maturity applied to inter- and intra-personal communication and insight (Grootens-Wiegers et al., 2017). For TGD adolescents making decisions about gender-affirming treatments—decisions that may have lifelong consequences—it is critical to understand how all these aspects of development may impact decision-making for a given young person within their specific cultural context.

Gender identity development in adolescence

Our understanding of gender identity development in adolescence is continuing to evolve. When providing clinical care to gender diverse young people and their families, it is important to know what is and is not known about gender identity during development (Berenbaum, 2018). When considering treatments, families may have questions regarding the development of their adolescent's gender identity, and whether or not their adolescent's declared gender will remain the same over time. For some adolescents, a declared gender identity that differs from the assigned sex at birth comes as no surprise to their parents/caregivers as their history of gender diverse expression dates back to childhood (Leibowitz & de Vries, 2016). For others, the declaration does not happen until the emergence of pubertal changes or even well into adolescence (McCallion et al., 2021; Sorbara et al., 2020).

Historically, social learning and cognitive developmental research on gender development was conducted primarily with youth who were not gender diverse in identity or expression and was carried out under the assumption that sex correlated with a specific gender; therefore, little attention was given to gender identity development. In addition to biological factors influencing gender development, this research demonstrated psychological and social factors also play a role (Perry & Pauletti, 2011). While there has been less focus on gender identity development in TGD youth, there is ample reason to suppose, apart from biological factors, psychosocial factors are also involved (Steensma, Kreukels et al., 2013). For some youth, gender identity development appears fixed and is often expressed from a young age, while for others there may be a developmental process that contributes to gender identity development over time.

Neuroimaging studies, genetic studies, and other hormone studies in intersex individuals demonstrate a biological contribution to the development of gender identity for some

individuals whose gender identity does not match their assigned sex at birth (Steensma, Kreukels et al., 2013). As families often have questions about this very issue, it is important to note it is not possible to distinguish between those for whom gender identity may seem fixed from birth and those for whom gender identity development appears to be a developmental process. Since it is impossible to definitively delineate the contribution of various factors contributing to gender identity development for any given young person, a comprehensive clinical approach is important and necessary (see Statement 3). Future research would shed more light on gender identity development if conducted over long periods of time with diverse cohort groups. Conceptualization of gender identity by shifting from dichotomous (e.g., binary) categorization of male and female to a dimensional gender spectrum along a continuum (APA, 2013) would also be necessary.

Adolescence may be a critical period for the development of gender identity for gender diverse young people (Steensma, Kreukels et al., 2013). Dutch longitudinal clinical follow-up studies of adolescents with childhood gender dysphoria who received puberty suppression, gender-affirming hormones, or both, found that none of the youth in adulthood regretted the decisions they had taken in adolescence (Cohen-Kettenis & van Goozen, 1997; de Vries et al., 2014). These findings suggest adolescents who were comprehensively assessed and determined emotionally mature enough to make treatment decisions regarding gender- affirming medical care presented with stability of gender identity over the time period when the studies were conducted.

When extrapolating findings from the longer-term longitudinal Dutch cohort studies to present-day gender diverse adolescents seeking care, it is critical to consider the societal changes that have occurred over time in relation to TGD people. Given the increase in visibility of TGD identities, it is important to understand how increased awareness may impact gender development in different ways (Kornienko et al., 2016). One trend identified is that more young people are presenting to gender clinics with nonbinary identities (Twist & de Graaf, 2019). Another phenomenon occurring in clinical practice is the increased number of adolescents seeking care who have not seemingly experienced, expressed (or experienced and expressed) gender diversity during their childhood years. One researcher attempted to study and describe a specific form of later-presenting gender diversity experience (Littman, 2018). However, the findings of the study must be considered within the context of significant methodological challenges, including 1) the study surveyed parents and not youth perspectives; and 2) recruitment included parents from community settings in which treatments for gender dysphoria are viewed with scepticism and are criticized. However, these findings have not been replicated. For a select subgroup of young people, susceptibility to social influence impacting gender may be an important differential to consider (Kornienko et al., 2016). However, caution must be taken to avoid assuming these phenomena occur prematurely in an individual adolescent while relying on information from datasets that may have been ascertained with potential sampling bias (Bauer et al., 2022; WPATH, 2018). It is important to consider the benefits that social connectedness may have for youth who are linked with supportive people (Tuzun et al., 2022)(see Statement 4).

Given the emerging nature of knowledge regarding adolescent gender identity development, an individualized approach to clinical care is considered both ethical and necessary. As is the case in all areas of medicine, each study has methodological limitations, and conclusions drawn from research cannot and should not be universally applied to all adolescents. This is also true when grappling with common parental questions regarding the stability versus instability of a particular young person's gender identity development. While future research will help advance scientific understanding of gender identity development, there may always be some gaps. Furthermore, given the ethics of self-determination in care, these gaps should not leave the TGD adolescent without important and necessary care.

Research evidence of gender-affirming medical treatment for transgender adolescents

A key challenge in adolescent transgender care is the quality of evidence evaluating the effectiveness of medically necessary gender-affirming medical

and surgical treatments (GAMSTs) (see medically necessary statement in the Global chapter, Statement 2.1), over time. Given the lifelong implications of medical treatment and the young age at which treatments may be started, adolescents, their parents, and care providers should be informed about the nature of the evidence base. It seems reasonable that decisions to move forward with medical and surgical treatments should be made carefully. Despite the slowly growing body of evidence supporting the effectiveness of early medical intervention, the number of studies is still low, and there are few outcome studies that follow youth into adulthood. Therefore, a systematic review regarding outcomes of treatment in adolescents is not possible. A short narrative review is provided instead.

At the time of this chapter's writing, there were several longer-term longitudinal cohort follow-up studies reporting positive results of early (i.e., adolescent) medical treatment; for a significant period of time, many of these studies were conducted through one Dutch clinic (e.g., Cohen-Kettenis & van Goozen, 1997; de Vries, Steensma et al., 2011; de Vries et al., 2014; Smith et al., 2001, 2005). The findings demonstrated the resolution of gender dysphoria is associated with improved psychological functioning and body image satisfaction. Most of these studies followed a pre-post methodological design and compared baseline psychological functioning with outcomes after the provision of medical gender-affirming treatments. Different studies evaluated individual aspects or combinations of treatment interventions and included 1) gender-affirming hormones and surgeries (Cohen-Kettenis & van Goozen, 1997; Smith et al., 2001, 2005); 2) puberty suppression (de Vries, Steensma et al., 2011); and 3) puberty suppression, affirming hormones, and surgeries (de Vries et al., 2014). The 2014 long-term follow-up study is the only study that followed youth from early adolescence (pretreatment, mean age of 13.6) through young adulthood (posttreatment, mean age of 20.7). This was the first study to show gender-affirming treatment enabled transgender adolescents to make age-appropriate developmental transitions while living as their affirmed gender with satisfactory objective and subjective outcomes in adulthood (de Vries et al., 2014). While the study employed a small (n = 55), select, and socially supported sample, the results were convincing. Of note, the participants were part of the Dutch clinic known for employing a multidisciplinary approach, including provision of comprehensive, ongoing assessment and management of gender dysphoria, and support aimed at emotional well-being.

Several more recently published longitudinal studies followed and evaluated participants at different stages of their gender-affirming treatments. In these studies, some participants may not have started gender-affirming medical treatments, some had been treated with puberty suppression, while still others had started gender-affirming hormones or had even undergone gender-affirming surgery (GAS) (Achille et al., 2020; Allen et al., 2019; Becker-Hebly et al., 2021; Carmichael et al., 2021; Costa et al., 2015; Kuper et al., 2020, Tordoff et al., 2022). Given the heterogeneity of treatments and methods, this type of design makes interpreting outcomes more challenging. Nonetheless, when compared with baseline assessments, the data consistently demonstrate improved or stable psychological functioning, body image, and treatment satisfaction varying from three months to up to two years from the initiation of treatment.

Cross-sectional studies provide another design for evaluating the effects of gender-affirming treatments. One such study compared psychological functioning in transgender adolescents at baseline and while undergoing puberty suppression with that of cisgender high school peers at two different time points. At baseline, the transgender youth demonstrated lower psychological functioning compared with cisgender peers, whereas when undergoing puberty suppression, they demonstrated better functioning than their peers (van der Miesen et al., 2020). Grannis et al. (2021) demonstrated transgender males who started testosterone had lower internalizing mental health symptoms (depression and anxiety) compared with those who had not started testosterone treatment.

Four additional studies followed different outcome designs. In a retrospective chart study, Kaltiala, Heino et al. (2020) reported transgender

adolescents with few or no mental health challenges prior to commencing gender-affirming hormones generally did well during the treatment. However, adolescents with more mental health challenges at baseline continued to experience the manifestations of those mental health challenges over the course of gender-affirming medical treatment. Nieder et al. (2021) studied satisfaction with care as an outcome measure and demonstrated transgender adolescents were more satisfied the further they progressed with the treatments they initially started. Hisle-Gorman et al. (2021) compared health care utilization pre- and post-initiation of gender-affirming pharmaceuticals as indicators of the severity of mental health conditions among 3,754 TGD adolescents in a large health care data set. Somewhat contrary to the authors' hypothesis of improved mental health, mental health care use did not significantly change, and psychotropic medication prescriptions increased. In a large non-probability sample of transgender-identified adults, Turban et al. (2022) found those who reported access to gender-affirming hormones in adolescence had lower odds of past-year suicidality compared with transgender people accessing gender- affirming hormones in adulthood.

Providers may consider the possibility an adolescent may regret gender-affirming decisions made during adolescence, and a young person will want to stop treatment and return to living in the birth-assigned gender role in the future. Two Dutch studies report low rates of adolescents (1.9% and 3.5%) choosing to stop puberty suppression (Brik et al., 2019; Wiepjes et al., 2018). Again, these studies were conducted in clinics that follow a protocol that includes a comprehensive assessment before the gender-affirming medical treatment is started. At present, no clinical cohort studies have reported on profiles of adolescents who regret their initial decision or detransition after irreversible affirming treatment. Recent research indicate there are adolescents who detransition, but do not regret initiating treatment as they experienced the start of treatment as a part of understanding their gender-related care needs (Turban, 2018). However, this may not be the predominant perspective of people who detransition (Littman, 2021; Vandenbussche, 2021). Some adolescents may regret the steps they have taken (Dyer, 2020). Therefore, it is important to present the full range of possible outcomes when assisting transgender adolescents. Providers may discuss this topic in a collaborative and trusting manner (i.e., as a "potential future experience and consideration") with the adolescent and their parents/caregivers before gender-affirming medical treatments are started. Also, providers should be prepared to support adolescents who detransition. In an internet convenience sample survey of 237 self-identified detransitioners with a mean age of 25.02 years, which consisted of over 90% of birth assigned females, 25% had medically transitioned before age 18 and 14% detransitioned before age 18 (Vandenbussche, 2021). Although an internet convenience sample is subject to selection of respondents, this study suggests detransitioning may occur in young transgender adolescents and health care professionals should be aware of this. Many of them expressed difficulties finding help during their detransition process and reported their detransition was an isolating experience during which they did not receive either sufficient or appropriate support (Vandenbussche, 2021).

To conclude, although the existing samples reported on relatively small groups of youth (e.g., n = 22-101 per study) and the time to follow-up varied across studies (6 months–7 years), this emerging evidence base indicates a general improvement in the lives of transgender adolescents who, following careful assessment, receive medically necessary gender-affirming medical treatment. Further, rates of reported regret during the study monitoring periods are low. Taken as a whole, the data show early medical intervention—as part of broader combined assessment and treatment approaches focused on gender dysphoria and general well-being—can be effective and helpful for many transgender adolescents seeking these treatments.

Ethical and human rights perspectives

Medical ethics and human rights perspectives were also considered while formulating the

Statements of Recommendations

6.1- We recommend health care professionals working with gender diverse adolescents:
6.1.a- Are licensed by their statutory body and hold a postgraduate degree or its equivalent in a clinical field relevant to this role granted by a nationally accredited statutory institution.
6.1.b- Receive theoretical and evidenced-based training and develop expertise in general child, adolescent, and family mental health across the developmental spectrum.
6.1.c- Receive training and have expertise in gender identity development, gender diversity in children and adolescents, have the ability to assess capacity to assent/consent, and possess general knowledge of gender diversity across the life span.
6.1.d- Receive training and develop expertise in autism spectrum disorders and other neurodevelopmental presentations or collaborate with a developmental disability expert when working with autistic/neurodivergent gender diverse adolescents.
6.1.e- Continue engaging in professional development in all areas relevant to gender diverse children, adolescents, and families.
6.2- We recommend health care professionals working with gender diverse adolescents facilitate the exploration and expression of gender openly and respectfully so that no one particular identity is favored.
6.3- We recommend health care professionals working with gender diverse adolescents undertake a comprehensive biopsychosocial assessment of adolescents who present with gender identity-related concerns and seek medical/surgical transition-related care, and that this be accomplished in a collaborative and supportive manner.
6.4- We recommend health care professionals work with families, schools, and other relevant settings to promote acceptance of gender diverse expressions of behavior and identities of the adolescent.
6.5- We recommend against offering reparative and conversion therapy aimed at trying to change a person's gender and lived gender expression to become more congruent with the sex assigned at birth.
6.6- We suggest health care professionals provide transgender and gender diverse adolescents with health education on chest binding and genital tucking, including a review of the benefits and risks.
6.7- We recommend providers consider prescribing menstrual suppression agents for adolescents experiencing gender incongruence who may not desire testosterone therapy, who desire but have not yet begun testosterone therapy, or in conjunction with testosterone therapy for breakthrough bleeding.
6.8- We recommend health care professionals maintain an ongoing relationship with the gender diverse and transgender adolescent and any relevant caregivers to support the adolescent in their decision-making throughout the duration of puberty suppression treatment, hormonal treatment, and gender- related surgery until the transition is made to adult care.
6.9- We recommend health care professionals involve relevant disciplines, including mental health and medical professionals, to reach a decision about whether puberty suppression, hormone initiation, or gender-related surgery for gender diverse and transgender adolescents are appropriate and remain indicated throughout the course of treatment until the transition is made to adult care.
6.10- We recommend health care professionals working with transgender and gender diverse adolescents requesting gender-affirming medical or surgical treatments inform them, prior to initiating treatment, of the reproductive effects including the potential loss of fertility and available options to preserve fertility within the context of the youth's stage of pubertal development.
6.11- We recommend when gender-affirming medical or surgical treatments are indicated for adolescents, health care professionals working with transgender and gender diverse adolescents involve parent(s)/guardian(s) in the assessment and treatment process, unless their involvement is determined to be harmful to the adolescent or not feasible.

The following recommendations are made regarding the requirements for gender-affirming medical and surgical treatment (All of them must be met):
6.12- We recommend health care professionals assessing transgender and gender diverse adolescents only recommend gender-affirming medical or surgical treatments requested by the patient when:
6.12.a- The adolescent meets the diagnostic criteria of gender incongruence as per the ICD-11 in situations where a diagnosis is necessary to access health care. In countries that have not implemented the latest ICD, other taxonomies may be used although efforts should be undertaken to utilize the latest ICD as soon as practicable.
6.12.b- The experience of gender diversity/incongruence is marked and sustained over time.
6.12.c- The adolescent demonstrates the emotional and cognitive maturity required to provide informed consent/assent for the treatment.
6.12.d- The adolescent's mental health concerns (if any) that may interfere with diagnostic clarity, capacity to consent, and gender-affirming medical treatments have been addressed.
6.12.e- The adolescent has been informed of the reproductive effects, including the potential loss of fertility and the available options to preserve fertility, and these have been discussed in the context of the adolescent's stage of pubertal development.
6.12.f- The adolescent has reached Tanner stage 2 of puberty for pubertal suppression to be initiated.
6.12.g- The adolescent had at least 12 months of gender-affirming hormone therapy or longer, if required, to achieve the desired surgical result for gender-affirming procedures, including breast augmentation, orchiectomy, vaginoplasty, hysterectomy, phalloplasty, metoidioplasty, and facial surgery as part of gender-affirming treatment unless hormone therapy is either not desired or is medically contraindicated.

adolescent SOC statements. For example, allowing irreversible puberty to progress in adolescents who experience gender incongruence is not a neutral act given that it may have immediate and lifelong harmful effects for the transgender young person (Giordano, 2009; Giordano & Holm, 2020; Kreukels & Cohen-Kettenis, 2011). From a human rights perspective, considering gender diversity as a normal and expected variation within the broader diversity of the human experience, it is an adolescent's right to participate in their own decision-making

process about their health and lives, including access to gender health services (Amnesty International, 2020).

Short summary of statements and unique issues in adolescence

These guidelines are designed to account for what is known and what is not known about gender identity development in adolescence, the evidence for gender-affirming care in adolescence, and the unique aspects that distinguish adolescence from other developmental stages.

Identity exploration: A defining feature of adolescence is the solidifying of aspects of identity, including gender identity. Statement 6.2 addresses identity exploration in the context of gender identity development. Statement 6.12.b accounts for the length of time needed for a young person to experience a gender diverse identity, express a gender diverse identity, or both, so as to make a meaningful decision regarding gender-affirming care.

Consent and decision-making: In adolescence, consent and decision-making require assessment of the individual's emotional, cognitive, and psychosocial development. Statement 6.12.c directly addresses emotional and cognitive maturity and describes the necessary components of the evaluation process used to assess decision-making capacity.

Caregivers/parent involvement: Adolescents are typically dependent on their caregivers/parents for guidance in numerous ways. This is also true as the young person navigates through the process of deciding about treatment options. Statement 6.11 addresses the importance of involving caregivers/parents and discusses the role they play in the assessment and treatment. No set of guidelines can account for every set of individual circumstances on a global scale.

Statement 6.1

We recommend health care professionals working with gender diverse adolescents:

a. **Are licensed by their statutory body and hold a postgraduate degree or its equivalent in a clinical field relevant to this role granted by a nationally accredited statutory institution.**
b. **Receive theoretical and evidenced-based training and develop expertise in general child, adolescent, and family mental health across the developmental spectrum.**
c. **Receive training and have expertise in gender identity development, gender diversity in children and adolescents, have the ability to assess capacity to assent/consent, and possess general knowledge of gender diversity across the life span.**
d. **Receive training and develop expertise in autism spectrum disorders and other neurodevelopmental presentations or collaborate with a developmental disability expert when working with autistic/neurodivergent gender diverse adolescents.**
e. **Continue engaging in professional development in all areas relevant to gender diverse children, adolescents, and families.**

When assessing and supporting TGD adolescents and their families, care providers/health care professionals (HCPs) need both general as well as gender-specific knowledge and training. Providers who are trained to work with adolescents and families play an important role in navigating aspects of adolescent development and family dynamics when caring for youth and families (Adelson et al., 2012; American Psychological Association, 2015; Hembree et al., 2017). Other chapters in these standards of care describe these criteria for professionals who provide gender care in more detail (see Chapter 5—Assessment for Adults; Chapter 7—Children; or Chapter 13—Surgery and Postoperative Care). Professionals working with adolescents should understand what is and is not known regarding adolescent gender identity development, and how this knowledge base differs from what applies to adults and prepubertal children. Among HCPs, the mental health professional (MHP) has the most appropriate training and dedicated clinical time to conduct an assessment and elucidate treatment priorities and goals when working with transgender youth, including those seeking gender-affirming medical/surgical care. Understanding and managing the dynamics of family members who may share differing perspectives regarding the history and needs of the

young person is an important competency that MHPs are often most prepared to address.

When access to professionals trained in child and adolescent development is not possible, HCPs should make a commitment to obtain training in the areas of family dynamics and adolescent development, including gender identity development. Similarly, considering autistic/neurodivergent transgender youth represent a substantial minority subpopulation of youth served in gender clinics globally, it is important HCPs seek additional training in the field of autism and understand the unique elements of care autistic gender diverse youth may require (Strang, Meagher et al., 2018). If these qualifications are not possible, then consultation and collaboration with a provider who specializes in autism and neurodiversity is advised.

Statement 6.2

We recommend health care professionals working with gender diverse adolescents facilitate the exploration and expression of gender openly and respectfully so that no one particular identity is favored.

Adolescence is a developmental period that involves physical and psychological changes characterized by individuation and the transition to independence from caregivers (Berenbaum et al., 2015; Steinberg, 2009). It is a period during which young people may explore different aspects of identity, including gender identity.

Adolescents differ regarding the degree to which they explore and commit to aspects of their identity (Meeus et al., 2012). For some adolescents, the pace to achieving consolidation of identity is fast, while for others it is slower. For some adolescents, physical, emotional, and psychological development occur over the same general timeline, while for others, there are certain gaps between these aspects of development. Similarly, there is variation in the timeline for gender identity development (Arnoldussen et al., 2020; Katz-Wise et al., 2017). For some young people, gender identity development is a clear process that starts in early childhood, while for others pubertal changes contribute to a person's experience of themselves as a particular gender (Steensma, Kreukels et al., 2013), and for many others a process may begin well after pubertal changes are completed. Given these variations, there is no one particular pace, process, or outcome that can be predicted for an individual adolescent seeking gender-affirming care.

Therefore, HCPs working with adolescents should promote supportive environments that simultaneously respect an adolescent's affirmed gender identity and also allows the adolescent to openly explore gender needs, including social, medical, and physical gender-affirming interventions should they change or evolve over time.

Statement 6.3

We recommend health care professionals working with gender diverse adolescents undertake a comprehensive biopsychosocial assessment of adolescents who present with gender identity-related concerns and seek medical/surgical transition-related care, and that this be accomplished in a collaborative and supportive manner.

Given the many ways identity may unfold during adolescence, we recommend using a comprehensive biopsychosocial assessment to guide treatment decisions and optimize outcomes. This assessment should aim to understand the adolescent's strengths, vulnerabilities, diagnostic profile, and unique needs to individualize their care. As mentioned in Statement 6.1, MHPs have the most appropriate training, experience, and dedicated clinical time required to obtain the information discussed here. The assessment process should be approached collaboratively with the adolescent and their caregiver(s), both separately and together, as described in more detail in Statement 6.11. An assessment should occur prior to any medically necessary medical or surgical intervention under consideration (e.g., puberty blocking medication, gender-affirming hormones, surgeries). See medically necessary statement in Chapter 2—Global Applicability, Statement 2.1; see also Chapter 12—Hormone Therapy and Chapter 13—Surgery and Postoperative Care.

Youth may experience many different gender identity trajectories. Sociocultural definitions and experiences of gender continue to evolve over time, and youth are increasingly presenting with a range of identities and ways of describing their experiences and gender-related needs (Twist & de

Graaf, 2019). For example, some youth will realize they are transgender or more broadly gender diverse and pursue steps to present accordingly. For some youth, obtaining gender-affirming medical treatment is important while for others these steps may not be necessary. For example, a process of exploration over time might not result in the young person self-affirming or embodying a different gender in relation to their assigned sex at birth and would not involve the use of medical interventions (Arnoldussen et al., 2019).

The most robust longitudinal evidence supporting the benefits of gender-affirming medical and surgical treatments in adolescence was obtained in a clinical setting that incorporated a detailed comprehensive diagnostic assessment process over time into its delivery of care protocol (de Vries & Cohen-Kettenis, 2012; de Vries et al., 2014). Given this research and the ongoing evolution of gender diverse experiences in society, a comprehensive diagnostic biopsychosocial assessment during adolescence is both evidence-based and preserves the integrity of the decision-making process. In the absence of a full diagnostic profile, other mental health entities that need to be prioritized and treated may not be detected. There are no studies of the long-term outcomes of gender-related medical treatments for youth who have not undergone a comprehensive assessment. Treatment in this context (e.g., with limited or no assessment) has no empirical support and therefore carries the risk that the decision to start gender-affirming medical interventions may not be in the long-term best interest of the young person at that time.

As delivery of health care and access to specialists varies globally, designing a particular assessment process to adapt existing resources is often necessary. In some cases, a more extended assessment process may be useful, such as for youth with more complex presentations (e.g., complicating mental health histories (Leibowitz & de Vries, 2016)), co-occurring autism spectrum characteristics (Strang, Powers et al., 2018), and/or an absence of experienced childhood gender incongruence (Ristori & Steensma, 2016). Given the unique cultural, financial, and geographical factors that exist for specific populations, providers should design assessment models that are flexible and allow for appropriately timed care for as many young people as possible, so long as the assessment effectively obtains information about the adolescent's strengths, vulnerabilities, diagnostic profile, and individual needs. Psychometrically validated psychosocial and gender measures can also be used to provide additional information.

The multidisciplinary assessment for youth seeking gender-affirming medical/surgical interventions includes the following domains that correspond to the relevant statements:

- **Gender Identity Development:** Statements 6.12.a and 6.12.b elaborate on the factors associated with gender identity development within the specific cultural context when assessing TGD adolescents.
- **Social Development and Support; Intersectionality:** Statements 6.4 and 6.11 elaborate on the importance of assessing gender minority stress, family dynamics, and other aspects contributing to social development and intersectionality.
- **Diagnostic Assessment of Possible Co-Occurring Mental Health and/or Developmental Concerns:** Statement 6.12.d elaborates on the importance of understanding the relationship that exists, if at all, between any co-occurring mental health or developmental concerns and the young person's gender identity/gender diverse expression.
- **Capacity for Decision-Making:** Statement 6.12.c elaborates on the assessment of a young person's emotional maturity and the relevance when an adolescent is considering gender affirming-medical/surgical treatments.

Statement 6.4

We recommend health care professionals work with families, schools, and other relevant settings to promote acceptance of gender diverse expressions of behavior and identities of the adolescent.

Multiple studies and related expert consensus support the implementation of approaches that promote acceptance and affirmation of gender diverse youth across all settings, including families, schools, health care facilities, and all other organizations and communities with which they

interact (e.g., Pariseau et al., 2019; Russell et al., 2018; Simons et al., 2013; Toomey et al., 2010; Travers et al., 2012). Acceptance and affirmation are accomplished through a range of approaches, actions, and policies we recommend be enacted across the various relationships and settings in which a young person exists and functions. It is important for the family members and community members involved in the adolescent's life to work collaboratively in these efforts unless their involvement is considered harmful to the adolescent. Examples proposed by Pariseau et al. (2019) and others of acceptance and affirmation of gender diversity and contemplation and expression of identity that can be implemented by family, staff, and organizations include:

1. Actions that are supportive of youth drawn to engaging in gender-expansive (e.g., nonconforming) activities and interests;
2. Communications that are supportive when youth express their experiences about their gender and gender exploration;
3. Use of the youth's asserted name/pronouns;
4. Support for youth wearing clothing/uniforms, hairstyles, and items (e.g., jewelry, makeup) they feel affirm their gender;
5. Positive and supportive communication with youth about their gender and gender concerns;
6. Education about gender diversity issues for people in the young person's life (e.g., family members, health care providers, social support networks), as needed, including information about how to advocate for gender diverse youth in community, school, health care, and other settings;
7. Support for gender diverse youth to connect with communities of support (e.g., LGBTQ groups, events, friends);
8. Provision of opportunities to discuss, consider, and explore medical treatment options when indicated;
9. Antibullying policies that are enforced;
10. Inclusion of nonbinary experiences in daily life, reading materials, and curricula (e.g., books, health, and sex education classes, assigned essay topics that move beyond the binary, LGBTQ, and ally groups);
11. Gender inclusive facilities that the youth can readily access without segregation from nongender diverse peers (e.g., bathrooms, locker rooms).

We recommend HCPs work with parents, schools, and other organizations/groups to promote acceptance and affirmation of TGD identities and expressions, whether social or medical interventions are implemented or not as acceptance and affirmation are associated with fewer negative mental health and behavioral symptoms and more positive mental health and behavioral functioning (Day et al., 2015; de Vries et al., 2016; Greytak et al., 2013; Pariseau et al., 2019; Peng et al., 2019; Russell et al., 2018; Simons et al., 2013; Taliaferro et al., 2019; Toomey et al., 2010; Travers et al., 2012). Russell et al. (2018) found mental health improvement increases with more acceptance and affirmation across more settings (e.g., home, school, work, and friends). Rejection by family, peers, and school staff (e.g., intentionally using the name and pronoun the youth does not identify with, not acknowledging affirmed gender identity, bullying, harassment, verbal and physical abuse, poor relationships, rejection for being TGD, eviction) was strongly linked to negative outcomes, such as anxiety, depression, suicidal ideation, suicide attempts, and substance use (Grossman et al., 2005; Klein & Golub; 2016; Pariseau et al., 2019; Peng et al., 2019; Reisner, Greytak et al., 2015; Roberts et al., 2013). It is important to be aware that negative symptoms increase with increased levels of rejection and continue into adulthood (Roberts et al., 2013).

Neutral or indifferent responses to a youth's gender diversity and exploration (e.g., letting a child tell others their chosen name but not using the name, not telling family or friends when the youth wants them to disclose, not advocating for the child about rejecting behavior from school staff or peers, not engaging or participating in other support mechanisms (e.g., with psychotherapists and support groups) have also been found to have negative consequences, such as increased depressive symptoms (Pariseau et al., 2019). For these reasons, it is important not to ignore a youth's gender questioning or delay consideration of the youth's gender-related

care needs. There is particular value in professionals recognizing youth need individualized approaches, support, and consideration of needs around gender expression, identity, and embodiment over time and across domains and relationships. Youth may need help coping with the tension of tolerating others' processing/adjusting to an adolescent's identity exploration and changes (e.g., Kuper, Lindley et al., 2019). It is important professionals collaborate with parents and others as they process their concerns and feelings and educate themselves about gender diversity because such processes may not necessarily reflect rejection or neutrality but may rather represent efforts to develop attitudes and gather information that foster acceptance (e.g., Katz-Wise et al., 2017).

Statement 6.5

We recommend against offering reparative and conversion therapy aimed at trying to change a person's gender and lived gender expression to become more congruent with the sex assigned at birth.

Some health care providers, secular or religious organizations, and rejecting families may undertake efforts to thwart an adolescent's expression of gender diversity or assertion of a gender identity other than the expression and behavior that conforms to the sex assigned at birth. Such efforts at blocking reversible social expression or transition may include choosing not to use the youth's identified name and pronouns or restricting self-expression in clothing and hairstyles (Craig et al., 2017; Green et al., 2020). These disaffirming behaviors typically aim to reinforce views that a young person's gender identity/expression must match the gender associated with the sex assigned at birth or expectations based on the sex assigned at birth. Activities and approaches (sometimes referred to as "treatments") aimed at trying to change a person's gender identity and expression to become more congruent with the sex assigned at birth have been attempted, but these approaches have not resulted in changes in gender identity (Craig et al., 2017; Green et al., 2020). We recommend against such efforts because they have been found to be ineffective and are associated with increases in mental illness and poorer psychological functioning (Craig et al., 2017; Green et al., 2020; Turban, Beckwith et al., 2020).

Much of the research evaluating "conversion therapy" and "reparative therapy" has investigated the impact of efforts to change gender expression (masculinity or femininity) and has conflated sexual orientation with gender identity (APA, 2009; Burnes et al., 2016; Craig et al., 2017). Some of these efforts have targeted both gender identity and expression (AACAP, 2018). Conversion/reparative therapy has been linked to increased anxiety, depression, suicidal ideation, suicide attempts, and health care avoidance (Craig et al., 2017; Green et al., 2020; Turban, Beckwith et al., 2020). Although some of these studies have been criticized for their methodologies and conclusions (e.g., D'Angelo et al., 2020), this should not detract from the importance of emphasizing efforts undertaken a priori to change a person's identity are clinically and ethically unsound. We recommend against any type of conversion or attempts to change a person's gender identity because 1) both secular and religion-based efforts to change gender identity/expression have been associated with negative psychological functioning that endures into adulthood (Turban, Beckwith et al., 2020); and 2) larger ethical reasons exist that should underscore respect for gender diverse identities.

It is important to note potential factors driving a young person's gender-related experience and report of gender incongruence, when carried out in the context of supporting an adolescent with self-discovery, is not considered reparative therapy as long as there is no a priori goal to change or promote one particular gender identity or expression (AACAP, 2018; see Statement 6.2). To ensure these explorations are therapeutic, we recommend employing affirmative consideration and supportive tone in discussing what steps have been tried, considered, and planned for a youth's gender expression. These discussion topics may include what felt helpful or affirming, what felt unhelpful or distressing and why. We recommend employing affirmative responses to these steps and discussions, such as those identified in SOC-8 Statement 6.4.

Statement 6.6

We suggest health care professionals provide transgender and gender diverse adolescents with health education on chest binding and genital tucking, including review of the benefits and risks.

TGD youth may experience distress related to chest and genital anatomy. Practices such as chest binding, chest padding, genital tucking, and genital packing are reversible, nonmedical interventions that may help alleviate this distress (Callen-Lorde, 2020a, 2020b; Deutsch, 2016a; Olson-Kennedy, Rosenthal et al., 2018; Transcare BC, 2020). It is important to assess the degree of distress related to physical development or anatomy, educate youth about potential nonmedical interventions to address this distress, and discuss the safe use of these interventions.

Chest binding involves compression of the breast tissue to create a flatter appearance of the chest. Studies suggest that up to 87% of trans masculine patients report a history of binding (Jones, 2015; Peitzmeier, 2017). Binding methods may include the use of commercial binders, sports bras, layering of shirts, layering of sports bras, or the use of elastics or other bandages (Peitzmeier, 2017). Currently, most youth report learning about binding practices from online communities composed of peers (Julian, 2019). Providers can play an important role in ensuring youth receive accurate and reliable information about the potential benefits and risks of chest binding. Additionally, providers can counsel patients about safe binding practices and monitor for potential negative health effects. While there are potential negative physical impacts of binding, youth who bind report many benefits, including increased comfort, improved safety, and lower rates of misgendering (Julian, 2019). Common negative health impacts of chest binding in youth include back/chest pain, shortness of breath, and overheating (Julian, 2019). More serious negative health impacts such as skin infections, respiratory infections, and rib fractures are uncommon and have been associated with chest binding in adults (Peitzmeier, 2017). If binding is employed, youth should be advised to use only those methods considered safe for binding—such as binders specifically designed for the gender diverse population—to reduce the risk of serious negative health effects. Methods that are considered unsafe for binding include the use of duct tape, ace wraps, and plastic wrap as these can restrict blood flow, damage skin, and restrict breathing. If youth report negative health impacts from chest binding, these should ideally be addressed by a gender-affirming medical provider with experience working with TGD youth.

Genital tucking is the practice of positioning the penis and testes to reduce the outward appearance of a genital bulge. Methods of tucking include tucking the penis and testes between the legs or tucking the testes inside the inguinal canal and pulling the penis back between the legs. Typically, genitals are held in place by underwear or a gaff, a garment that can be made or purchased. Limited studies are available on the specific risks and benefits of tucking in adults, and none have been carried out in youth. Previous studies have reported tight undergarments are associated with decreased sperm concentration and motility. In addition, elevated scrotal temperatures can be associated with poor sperm characteristics, and genital tucking could theoretically affect spermatogenesis and fertility (Marsh, 2019) although there are no definitive studies evaluating these adverse outcomes. Further research is needed to determine the specific benefits and risks of tucking in youth.

Statement 6.7

We recommend providers consider prescribing menstrual suppression agents for adolescents experiencing gender incongruence who may not desire testosterone therapy, who desire but have not yet begun testosterone therapy, or in conjunction with testosterone therapy for breakthrough bleeding.

When discussing the available options of menstrual-suppressing medications with gender diverse youth, providers should engage in shared decision-making, use gender-inclusive language (e.g., asking patients which terms they utilize to refer to their menses, reproductive organs, and genitalia) and perform physical exams in a sensitive, gender-affirmative manner (Bonnington et al., 2020; Krempasky et al., 2020). There is no formal research evaluating how menstrual

suppression may impact gender incongruence and/or dysphoria. However, the use of menstrual suppression can be an initial intervention that allows for further exploration of gender-related goals of care, prioritization of other mental health care, or both, especially for those who experience a worsening of gender dysphoria from unwanted uterine bleeding (see Statement 6.12d; Mehringer & Dowshen, 2019). When testosterone is not used, menstrual suppression can be achieved via a progestin. To exclude any underlying menstrual disorders, it is important to obtain a detailed menstrual history and evaluation prior to implementing menstrual-suppressing therapy (Carswell & Roberts, 2017). As part of the discussion about menstrual-suppressing medications, the need for contraception and information regarding the effectiveness of menstrual-suppressing medications as methods of contraception also need to be addressed (Bonnington et al., 2020). A variety of menstrual suppression options, such as combined estrogen-progestin medications, oral progestins, depot and subdermal progestin, and intrauterine devices (IUDs), should be offered to allow for individualized treatment plans while properly considering availability, cost and insurance coverage, as well as contraindications and side effects (Kanj et al., 2019).

Progestin-only hormonal medication are options, especially in trans masculine or nonbinary youth who are not interested in estrogen-containing medical therapies as well as those at risk for thromboembolic events or who have other contraindications to estrogen therapy (Carswell & Roberts, 2017). Progestin-only hormonal medications include oral progestins, depo-medroxyprogesterone injection, etonogestrel implant, and levonorgestrel IUD (Schwartz et al., 2019). Progestin-only hormonal options vary in terms of efficacy in achieving menstrual suppression and have lower rates of achieving amenorrhea than combined oral contraception (Pradhan & Gomez-Lobo, 2019). A more detailed description of the relevant clinical studies is presented in Chapter 12—Hormone Therapy. HCPs should not make assumptions regarding the individual's preferred method of administration as some trans masculine youth may prefer vaginal rings or IUD implants (Akgul et al., 2019). Although hormonal medications require monitoring for potential mood lability, depressive effects, or both, the benefits and risks of untreated menstrual suppression in the setting of gender dysphoria should be evaluated on an individual basis. Some patients may opt for combined oral contraception that includes different combinations of ethinyl estradiol, with ranging doses, and different generations of progestins (Pradhan & Gomez-Lobo, 2019). Lower dose ethinyl estradiol components of combined oral contraceptive pills are associated with increased breakthrough uterine bleeding. Continuous combined oral contraceptives may be used to allow for continuous menstrual suppression and can be delivered as transdermal or vaginal rings.

The use of gonadotropin releasing hormone (GnRH) analogues may also result in menstrual suppression. However, it is recommended gender diverse youth meet the eligibility criteria (as outlined in Statement 6.12) before this medication is considered solely for this purpose (Carswell & Roberts, 2017; Pradhan & Gomez-Lobo, 2019). Finally, menstrual-suppression medications may be indicated as an adjunctive therapy for breakthrough uterine bleeding that may occur while on exogenous testosterone or as a bridging medication while awaiting menstrual suppression with testosterone therapy. When exogenous testosterone is employed as a gender-affirming hormone, menstrual suppression is typically achieved in the first six months of therapy (Ahmad & Leinung, 2017). However, it is vital adolescents be counseled ovulation and pregnancy can still occur in the setting of amenorrhea (Gomez et al., 2020; Kanj et al., 2019).

Statement 6.8

We recommend health care professionals maintain an ongoing relationship with the gender diverse and transgender adolescent and any relevant caregivers to support the adolescent in their decision-making throughout the duration of puberty suppression treatment, hormonal treatment, and gender-related surgery until the transition is made to adult care.

HCPs with expertise in child and adolescent development, as described in Statement 6.1, play an important role in the continuity of care for

young people over the course of their gender-related treatment needs. Supporting adolescents and their families necessitates approaching care using a developmental lens through which understanding a young person's evolving emotional maturity and care needs can take place over time. As gender-affirming treatment pathways differ based on the needs and experiences of individual TGD adolescents, decision-making for these treatments (puberty suppression, estrogens/androgens, gender-affirmation surgeries) can occur at different points in time within a span of several years. Longitudinal research demonstrating the benefits of pubertal suppression and gender-affirming hormone treatment (GAHT) was carried out in a setting where an ongoing clinical relationship between the adolescents/families and the multidisciplinary team was maintained (de Vries et al., 2014).

Clinical settings that offer longer appointment times provide space for adolescents and caregivers to share important psychosocial aspects of emotional well-being (e.g., family dynamics, school, romantic, and sexual experiences) that contextualize individualized gender-affirming treatment needs and decisions as described elsewhere in the chapter. An ongoing clinical relationship can take place across settings, whether that be within a multidisciplinary team or with providers in different locations who collaborate with one another. Given the wide variability in the ability to obtain access to specialized gender care centers, particularly for marginalized groups who experience disparities with access, it is important for the HCP to appreciate the existence of any barriers to care while maintaining flexibility when defining how an ongoing clinical relationship can take place in that specific context.

An ongoing clinical relationship that increases resilience in the youth and provides support to parents/caregivers who may have their own treatment needs may ultimately lead to increased parental acceptance—when needed—which is associated with better mental health outcomes in youth (Ryan, Huebner et al., 2009).

Statement 6.9

We recommend health care professionals involve relevant disciplines, including mental health and medical professionals, to reach a decision about whether puberty suppression, hormone initiation, or gender-related surgery for gender diverse and transgender adolescents are appropriate and remain indicated throughout the course of treatment until the transition is made to adult care.

TGD adolescents with gender dysphoria/gender incongruence who seek gender-affirming medical and surgical treatments benefit from the involvement of health care professionals (HCPs) from different disciplines. Providing care to TGD adolescents includes addressing 1) diagnostic considerations (see Statements 6.3, 6.12a, and 6.12b) conducted by a specialized gender HCP (as defined in Statement 6.1) whenever possible and necessary; and 2) treatment considerations when prescribing, managing, and monitoring medications for gender-affirming medical and surgical care, requiring the training of the relevant medical/surgical professional. The list of key disciplines includes but is not limited to adolescent medicine/primary care, endocrinology, psychology, psychiatry, speech/language pathology, social work, support staff, and the surgical team.

The evolving evidence has shown a clinical benefit for transgender youth who receive their gender-affirming treatments in multidisciplinary gender clinics (de Vries et al., 2014; Kuper et al., 2020; Tollit et al., 2019). Finally, adolescents seeking gender-affirming care in multidisciplinary clinics are presenting with significant complexity necessitating close collaboration between mental health, medical, and/or surgical professionals (McCallion et al., 2021; Sorbara et al., 2020; Tishelman et al., 2015).

As not all patients and families are in the position or in a location to access multidisciplinary care, the lack of available disciplines should not preclude a young person from accessing needed care in a timely manner. When disciplines are available, particularly in centers with existing multidisciplinary teams, disciplines, or both, it is recommended efforts be made to include the relevant providers when developing a gender care team. However, this does not mean all disciplines are necessary to provide care to a particular youth and family.

If written documentation or a letter is required to recommend gender-affirming medical and surgical treatment (GAMST) for an adolescent, only one letter of assessment from a member of the multidisciplinary team is needed. This letter needs to reflect the assessment and opinion from the team that involves both medical HCPs and MHPs (American Psychological Association, 2015; Hembree et al., 2017; Telfer et al., 2018). Further assessment results and written opinions may be requested when there is a specific clinical need or when team members are in different locations or choose to write their own summaries. For further information see Chapter 5—Assessment for Adults, Statement 5.5.

Statement 6.10

We recommend health care professionals working with transgender and gender diverse adolescents requesting gender-affirming medical or surgical treatments inform them, prior to the initiation of treatment, of the reproductive effects, including the potential loss of fertility and available options to preserve fertility within the context of the youth's stage of pubertal development.

While assessing adolescents seeking gender-affirming medical or surgical treatments, HCPs should discuss the specific ways in which the required treatment may affect reproductive capacity. Fertility issues and the specific preservation options are more thoroughly discussed in Chapter 12—Hormone Therapy and Chapter 16—Reproductive Health.

It is important HCPs understand what fertility preservation options exist so they can relay the information to adolescents. Parents are advised to be involved in this process and should also understand the pros and cons of the different options. HCPs should acknowledge adolescents and parents may have different views around reproductive capacity and may therefore come to different decisions (Quain et al., 2020), which is why HCPs can be helpful in guiding this process.

HCPs should specifically pay attention to the developmental and psychological aspects of fertility preservation and decision-making competency for the individual adolescent. While adolescents may think they have made up their minds concerning their reproductive capacity, the possibility their opinions about having biologically related children in the future might change over time needs to be discussed with an HCP who has sufficient experience, is knowledgeable about adolescent development, and has experience working with parents.

Addressing the long-term consequences on fertility of gender-affirming medical treatments and ensuring transgender adolescents have realistic expectations concerning fertility preservation options or adoption cannot not be addressed with a one-time discussion but should be part of an ongoing conversation. This conversation should occur not only before initiating any medical intervention (puberty suppression, hormones, or surgeries), but also during further treatment and during transition.

Currently, there are only preliminary results from retrospective studies evaluating transgender adults and the decisions they made when they were young regarding the consequences of medical-affirming treatment on reproductive capacity. It is important not to make assumptions about what future adult goals an adolescent may have. Research in childhood cancer survivors found participants who acknowledged missed opportunities for fertility preservation reported distress and regret surrounding potential infertility (Armuand et al., 2014; Ellis et al., 2016; Lehmann et al., 2017). Furthermore, individuals with cancer who did not prioritize having biological children before treatment have reported "changing their minds" in survivorship (Armuand et al., 2014).

Given the complexities of the different fertility preservation options and the challenges HCPs may experience discussing fertility with the adolescent and the family (Tishelman et al., 2019), a fertility consultation is an important consideration for every transgender adolescent who pursues medical-affirming treatments unless the local situation is such that a fertility consultation is not covered by insurance or public health care plans, is not available locally, or the individual circumstances make this unpreferable.

Statement 6.11

We recommend when gender-affirming medical or surgical treatments are indicated for adolescents, health care professionals working with transgender and gender diverse adolescents

involve parent(s)/guardian(s) in the assessment and treatment process, unless their involvement is determined to be harmful to the adolescent or not feasible.

When there is an indication an adolescent might benefit from a gender-affirming medical or surgical treatment, involving the parent(s) or primary caregiver(s) in the assessment process is recommended in almost all situations (Edwards-Leeper & Spack, 2012; Rafferty et al., 2018). Exceptions to this might include situations in which an adolescent is in foster care, child protective services, or both, and custody and parent involvement would be impossible, inappropriate, or harmful. Parent and family support of TGD youth is a primary predictor of youth well-being and is protective of the mental health of TGD youth (Gower, Rider, Coleman et al., 2018; Grossman et al., 2019; Lefevor et al., 2019; McConnell et al., 2015; Pariseau et al., 2019; Ryan, 2009; Ryan et al., 2010; Simons et al., 2013; Wilson et al., 2016). Therefore, including parent(s)/caregiver(s) in the assessment process to encourage and facilitate increased parental understanding and support of the adolescent may be one of the most helpful practices available.

Parent(s)/caregiver(s) may provide key information for the clinical team, such as the young person's gender and overall developmental, medical, and mental health history as well as insights into the young person's level of current support, general functioning, and well-being. Concordance or divergence of reports given by the adolescent and their parent(s)/caregiver(s) may be important information for the assessment team and can aid in designing and shaping individualized youth and family supports (De Los Reyes et al., 2019; Katz-Wise et al., 2017). Knowledge of the family context, including resilience factors and challenges, can help providers know where special supports would be needed during the medical treatment process. Engagement of parent(s)/caregiver(s) is also important for educating families about various treatment approaches, ongoing follow-up and care needs, and potential treatment complications. Through psychoeducation regarding clinical gender care options and participation in the assessment process, which may unfold over time, parent(s)/caregiver(s) may better understand their adolescent child's gender-related experience and needs (Andrzejewski et al., 2020; Katz-Wise et al., 2017).

Parent/caregiver concerns or questions regarding the stability of gender-related needs over time and implications of various gender-affirming interventions are common and should not be dismissed. It is appropriate for parent(s)/caregiver(s) to ask these questions, and there are cases in which the parent(s)/caregiver(s)' questions or concerns are particularly helpful in informing treatment decisions and plans. For example, a parent/caregiver report may provide critical context in situations in which a young person experiences very recent or sudden self-awareness of gender diversity and a corresponding gender treatment request, or when there is concern for possible excessive peer and social media influence on a young person's current self-gender concept. Contextualization of the parent/caregiver report is also critical, as the report of a young person's gender history as provided by parent(s)/caregiver(s) may or may not align with the young person's self-report. Importantly, gender histories may be unknown to parent(s)/caregiver(s) because gender may be internal experience for youth, not known by others unless it is discussed. For this reason, an adolescent's report of their gender history and experience is central to the assessment process.

Some parents may present with unsupportive or antagonistic beliefs about TGD identities, clinical gender care, or both (Clark et al., 2020). Such unsupportive perspectives are an important therapeutic target for families. Although challenging parent perspectives may in some cases seem rigid, providers should not assume this is the case. There are many examples of parent(s)/caregiver(s) who, over time with support and psychoeducation, have become increasingly accepting of their TGD child's gender diversity and care needs.

Helping youth and parent(s)/caregiver(s) work together on important gender care decisions is a primary goal. However, in some cases, parent(s)/caregiver(s) may be too rejecting of their adolescent child and their child's gender needs to be part of the clinical evaluation process. In these situations, youth may require the engagement of larger systems of advocacy and support to move

forward with the necessary support and care (Dubin et al., 2020).

Statement 6.12

We recommend health care professionals assessing transgender and gender diverse adolescents only recommend gender-affirming medical or surgical treatments requested by the patient when:

Statement 6.12.a

The adolescent meets the diagnostic criteria of gender incongruence as per the ICD-11 in situations where a diagnosis is necessary to access health care. In countries that have not implemented the latest ICD, other taxonomies may be used although efforts should be undertaken to utilize the latest ICD as soon as practicable.

When working with TGD adolescents, HCPs should realize while a classification may give access to care, pathologizing transgender identities may be experienced as stigmatizing (Beek et al., 2016). Assessments related to gender health and gender diversity have been criticized, and controversies exist around diagnostic systems (Drescher, 2016).

HCPs should assess the overall gender-related history and gender care-related needs of youth. Through this assessment process, HCPs may provide a diagnosis when it is required to get access to transgender-related care.

Gender incongruence and gender dysphoria are the two diagnostic terms used in the World Health Organization's International Classification of Diseases (ICD) and the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM), respectively. Of these two widely used classification systems, the DSM is for psychiatric classifications only and the ICD contains all diseases and conditions related to physical as well as mental health. The most recent versions of these two systems, the DSM-5 and the ICD-11, reflect a long history of reconceptualizing and de-psychopathologizing gender-related diagnoses (American Psychiatric Association, 2013; World Health Organization, 2019a). Compared with the earlier version, the DSM-5 replaced gender identity disorder with gender dysphoria, acknowledging the distress experienced by some people stemming from the incongruence between experienced gender identity and the sex assigned at birth. In the most recent revision, the DSM-5-TR, no changes in the diagnostic criteria for gender dysphoria are made. However, terminology was adapted into the most appropriate current language (e.g., birth-assigned gender instead of natal-gender and gender-affirming treatment instead of gender reassignment (American Psychiatric Association, 2022). Compared with the ICD 10th edition, the gender incongruence classification was moved from the Mental Health chapter to the Conditions Related to Sexual Health chapter in the ICD-11. When compared with the DSM-5 classification of gender dysphoria, one important reconceptualization is distress is not a required indicator of the ICD-11 classification of gender incongruence (WHO, 2019a). After all, when growing up in a supporting and accepting environment, the distress and impairment criterion, an inherent part of every mental health condition, may not be applicable (Drescher, 2012). As such, the ICD-11 classification of gender incongruence may better capture the fullness of gender diversity experiences and related clinical gender needs.

Criteria for the ICD-11 classification gender incongruence of adolescence or adulthood require a marked and persistent incongruence between an individual's experienced gender and the assigned sex, which often leads to a need to "transition" to live and be accepted as a person of the experienced gender. For some, this includes hormonal treatment, surgery, or other health care services to enable the individual's body to align as much as required, and to the extent possible, with the person's experienced gender. Relevant for adolescents is the indicator that a classification cannot be assigned "prior to the onset of puberty." Finally, it is noted "that gender variant behaviour and preferences alone are not a basis for assigning the classification" (WHO, ICD-11, 2019a).

Criteria for the DSM-5 and DSM-5-TR classification of gender dysphoria in adolescence and adulthood denote "a marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration' (criterion A, fulfilled when 2 of 6 subcriteria are manifest; DSM-5, APA, 2013; DSM 5-TR, APA, 2022).

Of note, although a gender-related classification is one of the requirements for receiving medical gender-affirming care, such a classification alone does not indicate a person needs medical-affirming care. The range of youth experiences of gender incongruence necessitates professionals provide a range of treatments or interventions based on the individual's needs. Counseling, gender exploration, mental health assessment and, when needed, treatment with MHPs trained in gender development may all be indicated with or without the implementation of medical-affirming care.

Statement 6.12.b

The experience of gender diversity/incongruence is marked and sustained over time.

Identity exploration and consolidation are experienced by many adolescents (Klimstra et al., 2010; Topolewska-Siedzik & Cieciuch, 2018). Identity exploration during adolescence may include a process of self-discovery around gender and gender identity (Steensma, Kreukels et al., 2013). Little is known about how processes that underlie consolidation of gender identity during adolescence (e.g., the process of commitment to specific identities) may impact a young person's experience(s) or needs over time.

Therefore, the level of reversibility of a gender-affirming medical intervention should be considered along with the sustained duration of a young person's experience of gender incongruence when initiating treatment. Given potential shifts in gender-related experiences and needs during adolescence, it is important to establish the young person has experienced several years of persistent gender diversity/incongruence prior to initiating less reversible treatments such as gender-affirming hormones or surgeries. Puberty suppression treatment, which provides more time for younger adolescents to engage their decision-making capacities, also raises important considerations (see Statement 6.12f and Chapter 12—Hormone Therapy) suggesting the importance of a sustained experience of gender incongruence/diversity prior to initiation. However, in this age group of younger adolescents, several years is not always practical nor necessary given the premise of the treatment as a means to buy time while avoiding distress from irreversible pubertal changes. For youth who have experienced a shorter duration of gender incongruence, social transition-related and/or other medical supports (e.g., menstrual suppression/androgen blocking) may also provide some relief as well as furnishing additional information to the clinical team regarding a young person's broad gender care needs (see Statements 6.4, 6.6, and 6.7).

Establishing evidence of persistent gender diversity/incongruence typically requires careful assessment with the young person over time (see Statement 6.3). Whenever possible and when appropriate, the assessment and discernment process should also include the parent(s)/caregiver(s) (see Statement 6.11). Evidence demonstrating gender diversity/incongruence sustained over time can be provided via history obtained directly from the adolescent and parents/caregivers when this information is not documented in the medical records.

The research literature on continuity versus discontinuity of gender-affirming medical care needs/requests is complex and somewhat difficult to interpret. A series of studies conducted over the last several decades, including some with methodological challenges (as noted by Temple Newhook et al., 2018; Winters et al., 2018) suggest the experience of gender incongruence is not consistent for all children as they progress into adolescence. For example, a subset of youth who experienced gender incongruence or who socially transitioned prior to puberty over time can show a reduction in or even full discontinuation of gender incongruence (de Vries et al., 2010; Olson et al., 2022; Ristori & Steensma, 2016; Singh et al., 2021; Wagner et al., 2021). However, there has been less research focused on rates of continuity and discontinuity of gender incongruence and gender-related needs in pubertal and adolescent populations. The data available regarding broad unselected gender-referred pubertal/adolescent cohorts (from the Amsterdam transgender clinic) suggest that, following extended assessments over time, a subset of adolescents with gender incongruence presenting for gender care elect not to pursue gender-affirming medical care

(Arnoldussen et al., 2019; de Vries, Steensma et al., 2011). Importantly, findings from studies of gender incongruent pubertal/adolescent cohorts, in which participants who have undergone comprehensive gender evaluation over time, have shown persistent gender incongruence and gender-related need and have received referrals for medical gender care, suggest low levels of regret regarding gender-related medical care decisions (de Vries et al., 2014; Wiepjes et al., 2018). Critically, these findings of low regret can only currently be applied to youth who have demonstrated sustained gender incongruence and gender-related needs over time as established through a comprehensive and iterative assessment (see Statement 6.3).

Statement 6.12.c

The adolescent demonstrates the emotional and cognitive maturity required to provide informed consent/assent for the treatment.

The process of informed consent includes communication between a patient and their provider regarding the patient's understanding of a potential intervention as well as, ultimately, the patient's decision whether to receive the intervention. In most settings, for minors, the legal guardian is integral to the informed consent process: if a treatment is to be given, the legal guardian (often the parent[s]/caregiver[s]) provides the informed consent to do so. In most settings, assent is a somewhat parallel process in which the minor and the provider communicate about the intervention and the provider assesses the level of understanding and intention.

A necessary step in the informed consent/assent process for considering gender-affirming medical care is a careful discussion with qualified HCPs trained to assess the emotional and cognitive maturity of adolescents. The reversible and irreversible effects of the treatment, as well as fertility preservation options (when applicable), and all potential risks and benefits of the intervention are important components of the discussion. These discussions are required when obtaining informed consent/assent. Assessment of cognitive and emotional maturity is important because it helps the care team understand the adolescent's capacity to be informed.

The skills necessary to assent/consent to any medical intervention or treatment include the ability to 1) comprehend the nature of the treatment; 2) reason about treatment options, including the risks and benefits; 3) appreciate the nature of the decision, including the long-term consequences; and 4) communicate choice (Grootens-Wiegers et al., 2017). In the case of gender- affirming medical treatments, a young person should be well-informed about what the treatment may and may not accomplish, typical timelines for changes to appear (e.g., with gender-affirming hormones), and any implications of stopping the treatment. Gender-diverse youth should fully understand the reversible, partially reversible, and irreversible aspects of a treatment, as well as the limits of what is known about certain treatments (e.g., the impact of pubertal suppression on brain development (Chen and Loshak, 2020)). Gender-diverse youth should also understand, although many gender-diverse youth begin gender- affirming medical care and experience that care as a good fit for them long-term, there is a subset of individuals who over time discover this care is not a fit for them (Wiepjes et al., 2018). Youth should know such shifts are sometimes connected to a change in gender needs over time, and in some cases, a shift in gender identity itself. Given this information, gender diverse youth must be able to reason thoughtfully about treatment options, considering the implications of the choices at hand. Furthermore, as a foundation for providing assent, the gender-diverse young person needs to be able to communicate their choice.

The skills needed to accomplish the tasks required for assent/consent may not emerge at specific ages per se (Grootens-Wiegers et al., 2017). There may be variability in these capacities related to developmental differences and mental health presentations (Shumer & Tishelman, 2015) and dependent on the opportunities a young person has had to practice these skills (Alderson, 2007). Further, assessment of emotional and cognitive maturity must be conducted separately for each gender-related treatment decision (Vrouenraets et al., 2021).

The following questions may be useful to consider in assessing a young person's emotional and

cognitive readiness to assent or consent to a specific gender-affirming treatment:

- Can the young person think carefully into the future and consider the implications of a partially or fully irreversible intervention?
- Does the young person have sufficient self-reflective capacity to consider the possibility that gender-related needs and priorities can develop over time, and gender-related priorities at a certain point in time might change?
- Has the young person, to some extent, thought through the implications of what they might do if their priorities around gender do change in the future?
- Is the young person able to understand and manage the day-to-day short- and long-term aspects of a specific medical treatment (e.g., medication adherence, administration, and necessary medical follow-ups)?

Assessment of emotional and cognitive maturity may be accomplished over time as the care team continues to engage in conversations about the treatment options and affords the young person the opportunity to practice thinking into the future and flexibly consider options and implications. For youth with neurodevelopmental and/or some types of mental health differences, skills for future thinking, planning, big picture thinking, and self-reflection may be less-well developed (Dubbelink & Geurts, 2017). In these cases, a more careful approach to consent and assent may be required, and this may include additional time and structured opportunities for the young person to practice the skills necessary for medical decision-making (Strang, Powers et al., 2018).

For unique situations in which an adolescent minor is consenting for their own treatment without parental permission (see Statement 6.11), extra care must be taken to support the adolescent's informed decision-making. This will typically require greater levels of engagement of and collaboration between the HCPs working with the adolescent to provide the young person appropriate cognitive and emotional support to consider options, weigh benefits and potential challenges/costs, and develop a plan for any needed (and potentially ongoing) supports associated with the treatment.

Statement 6.12.d

The adolescent's mental health concerns (if any) that may interfere with diagnostic clarity, capacity to consent, and/or gender-affirming medical treatments have been addressed.

Evidence indicates TGD adolescents are at increased risk of mental health challenges, often related to family/caregiver rejection, non-affirming community environments, and neurodiversity-related factors (e.g., de Vries et al., 2016; Pariseau et al., 2019; Ryan et al., 2010; Weinhardt et al., 2017). A young person's mental health challenges may impact their conceptualization of their gender development history and gender identity-related needs, the adolescent's capacity to consent, and the ability of the young person to engage in or receive medical treatment. Additionally, like cisgender youth, TGD youth may experience mental health concerns irrespective of the presence of gender dysphoria or gender incongruence. In particular, depression and self-harm may be of specific concern; many studies reveal depression scores and emotional and behavioral problems comparable to those reported in populations referred to mental health clinics (Leibowitz & de Vries, 2016). Higher rates of suicidal ideation, suicide attempts, and self-harm have also been reported (de Graaf et al., 2020). In addition, eating disorders occur more frequently than expected in non-referred populations (Khatchadourian et al., 2013; Ristori et al., 2019; Spack et al., 2012). Importantly, TGD adolescents show high rates of autism spectrum disorder/characteristics (Øien et al., 2018; van der Miesen et al., 2016; see also Statement 6.1d). Other neurodevelopmental presentations and/or mental health challenges may also be present, (e.g., ADHD, intellectual disability, and psychotic disorders (de Vries, Doreleijers et al., 2011; Meijer et al., 2018; Parkes & Hall, 2006).

Of note, many transgender adolescents are well-functioning and experience few if any mental health concerns. For example, socially transitioned pubertal adolescents who receive medical

gender- affirming treatment at specialized gender clinics may experience mental health outcomes equivalent to those of their cisgender peers (e.g., de Vries et al., 2014; van der Miesen et al., 2020). A provider's key task is to assess the direction of the relationships that exist between any mental health challenges and the young person's self-understanding of gender care needs and then prioritize accordingly.

Mental health difficulties may challenge the assessment and treatment of gender-related needs of TGD adolescents in various ways:

1. First, when a TGD adolescent is experiencing acute suicidality, self-harm, eating disorders, or other mental health crises that threaten physical health, safety must be prioritized. According to the local context and existing guidelines, appropriate care should seek to mitigate the threat or crisis so there is sufficient time and stabilization for thoughtful gender-related assessment and decision-making. For example, an actively suicidal adolescent may not be emotionally able to make an informed decision regarding gender-affirming medical/surgical treatment. If indicated, safety-related interventions should not preclude starting gender-affirming care.
2. Second, mental health can also complicate the assessment of gender development and gender identity-related needs. For example, it is critical to differentiate gender incongruence from specific mental health presentations, such as obsessions and compulsions, special interests in autism, rigid thinking, broader identity problems, parent/child interaction difficulties, severe developmental anxieties (e.g., fear of growing up and pubertal changes unrelated to gender identity), trauma, or psychotic thoughts. Mental health challenges that interfere with the clarity of identity development and gender-related decision-making should be prioritized and addressed.
3. Third, decision-making regarding gender-affirming medical treatments that have life-long consequences requires thoughtful, future-oriented thinking by the adolescent, with support from the parents/caregivers, as indicated (see Statement 6.11). To be able to make such an informed decision, an adolescent should be able to understand the issues, express a choice, appreciate and give careful thought regarding the wish for medical-affirming treatment (see Statement 6.12c). Neurodevelopmental differences, such as autistic features or autism spectrum disorder (see Statement 6.1d, e.g., communication differences; a preference for concrete or rigid thinking; differences in self-awareness, future thinking and planning), may challenge the assessment and decision-making process; neurodivergent youth may require extra support, structure, psychoeducation, and time built into the assessment process (Strang, Powers et al., 2018). Other mental health presentations that involve reduced communication and self-advocacy, difficulty engaging in assessment, memory and concentration difficulties, hopelessness, and difficulty engaging in future-oriented thinking may complicate assessment and decision-making. In such cases, extended time is often necessary before any decisions regarding medical-affirming treatment can be made.
4. Finally, while addressing mental health concerns is important during the course of medical treatment, it does not mean all mental health challenges can or should be resolved completely. However, it is important any mental health concerns are addressed sufficiently so that gender -affirming medical treatment can be provided optimally (e.g., medication adherence, attending follow-up medical appointments, and self-care, particularly during a postoperative course).

Statement 6.12.e

The adolescent has been informed of the reproductive effects, including the potential loss of fertility, and available options to preserve fertility, and these have been discussed in the context of the adolescent's stage of pubertal development.

For guidelines regarding the clinical approach, the scientific background, and the rationale, see Chapter 12—Hormone Therapy and Chapter 16—Reproductive Health.

Statement 6.12.f

The adolescent has reached Tanner stage 2 of puberty for pubertal suppression to be initiated.

The onset of puberty is a pivotal point for many gender diverse youth. For some, it creates an intensification of their gender incongruence, and for others, pubertal onset may lead to gender fluidity (e.g., a transition from binary to nonbinary gender identity) or even attenuation of a previously affirmed gender identity (Drummond et al., 2008; Steensma et al., 2011, Steensma, Kreukels et al., 2013; Wallien & Cohen-Kettenis, 2008). The use of puberty-blocking medications, such as GnRH analogues, is not recommended until children have achieved a minimum of Tanner stage 2 of puberty because the experience of physical puberty may be critical for further gender identity development for some TGD adolescents (Steensma et al., 2011). Therefore, puberty blockers should not be implemented in prepubertal gender diverse youth (Waal & Cohen-Kettenis, 2006). For some youth, GnRH agonists may be appropriate in late stages or in the post-pubertal period (e.g., Tanner stage 4 or 5), and this should be highly individualized. See Chapter 12—Hormone Therapy for a more comprehensive review of the use of GnRH agonists.

Variations in the timing of pubertal onset is due to multiple factors (e.g., sex assigned at birth, genetics, nutrition, etc.). Tanner staging refers to five stages of pubertal development ranging from prepubertal (Tanner stage 1) to post-pubertal, and adult sexual maturity (Tanner stage 5) (Marshall & Tanner, 1969, 1970). For assigned females at birth, pubertal onset (e.g., gonadarche) is defined by the occurrence of breast budding (Tanner stage 2), and for birth-assigned males, the achievement of a testicular volume of greater than or equal to 4 mL (Roberts & Kaiser, 2020). An experienced medical provider should be relied on to differentiate the onset of puberty from physical changes such as pubic hair and apocrine body odor due to sex steroids produced by the adrenal gland (e.g., adrenarche) as adrenarche does not warrant the use of puberty-blocking medications (Roberts & Kaiser, 2020). Educating parents and families about the difference between adrenarche and gonadarche helps families understand the timing during which shared decision-making about gender-affirming medical therapies should be undertaken with their multidisciplinary team.

The importance of addressing other risks and benefits of pubertal suppression, both hypothetical and actual, cannot be overstated. Evidence supports the existence of surgical implications for transgender girls who proceed with pubertal suppression (van de Grift et al., 2020). Longitudinal data exists to demonstrate improvement in romantic and sexual satisfaction for adolescents receiving puberty suppression, hormone treatment and surgery (Bungener et al., 2020). A study on surgical outcomes of laparoscopic intestinal vaginoplasty (performed because of limited genital tissue after the use of puberty blockers) in transgender women revealed that the majority experienced orgasm after surgery (84%), although a specific correlation between sexual pleasure outcomes and the timing of pubertal suppression initiation was not discussed in the study (Bouman, van der Sluis et al., 2016), nor does the study apply to those who would prefer a different surgical procedure. This underscores the importance of engaging in discussions with families about the future unknowns related to surgical and sexual health outcomes.

Statement 6.12.g

The adolescent had at least 12 months of gender-affirming hormone therapy or longer, if required, to achieve the desired surgical result for gender-affirming procedures, including breast augmentation, orchiectomy, vaginoplasty, hysterectomy, phalloplasty, metoidioplasty, and facial surgery as part of gender-affirming treatment unless hormone therapy is either not desired or is medically contraindicated.

GAHT leads to anatomical, physiological, and psychological changes. The onset of the anatomic effects (e.g., clitoral growth, breast growth, vaginal mucosal atrophy) may begin early after the initiation of therapy, and the peak effect is expected at 1–2 years (T'Sjoen et al., 2019). To

ensure sufficient time for psychological adaptations to the physical change during an important developmental time for the adolescent, 12 months of hormone treatment is suggested. Depending upon the surgical result required, a period of hormone treatment may need to be longer (e.g., sufficient clitoral virilization prior to metoidioplasty/phalloplasty, breast growth and skin expansion prior to breast augmentation, softening of skin and changes in facial fat distribution prior to facial GAS) (de Blok et al., 2021).

For individuals who are not taking hormones prior to surgical interventions, it is important surgeons review the impact of hormone therapy on the proposed surgery. In addition, for individuals undergoing gonadectomy who are not taking hormones, a plan for hormone replacement can be developed with their prescribing professional prior to surgery.

Consideration of ages for gender-affirming medical and surgical treatment for adolescents

Age has a strong, albeit imperfect, correlation with cognitive and psychosocial development and may be a useful objective marker for determining the potential timing of interventions (Ferguson et al., 2021). Higher (i.e., more advanced) ages may be required for treatments with greater irreversibility, complexity, or both. This approach allows for continued cognitive/emotional maturation that may be required for the adolescent to fully consider and consent to increasingly complex treatments (see Statement 6.12c).

A growing body of evidence indicates providing gender-affirming treatment for gender diverse youth who meet criteria leads to positive outcomes (Achille et al., 2020; de Vries et al., 2014; Kuper et al., 2020). There is, however, limited data on the optimal timing of gender-affirming interventions as well as the long-term physical, psychological, and neurodevelopmental outcomes in youth (Chen et al., 2020; Chew et al., 2018; Olson-Kennedy et al., 2016). Currently, the only existing longitudinal studies evaluating gender diverse youth and adult outcomes are based on a specific model (i.e., the Dutch approach) that involved a comprehensive initial assessment with follow-up. In this approach, pubertal suppression was considered at age 12, GAHT at age 16, and surgical interventions after age 18 with exceptions in some cases. It is not clear if deviations from this approach would lead to the same or different outcomes. Longitudinal studies are currently underway to better define outcomes as well as the safety and efficacy of gender-affirming treatments in youth (Olson-Kennedy, Garofalo et al., 2019; Olson-Kennedy, Rosenthal et al., 2019). While the long-term effects of gender-affirming treatments initiated in adolescence are not fully known, the potential negative health consequences of delaying treatment should also be considered (de Vries et al., 2021). As the evidence base regarding outcomes of gender-affirming interventions in youth continues to grow, recommendations on the timing and readiness for these interventions may be updated.

Previous guidelines regarding gender-affirming treatment of adolescents recommended partially reversible GAHT could be initiated at approximately 16 years of age (Coleman et al., 2012; Hembree et al., 2009). More recent guidelines suggest there may be compelling reasons to initiate GAHT prior to the age of 16, although there are limited studies on youth who have initiated hormones prior to 14 years of age (Hembree et al., 2017). A compelling reason for earlier initiation of GAHT, for example, might be to avoid prolonged pubertal suppression, given potential bone health concerns and the psychosocial implications of delaying puberty as described in more detail in Chapter 12—Hormone Therapy (Klink, Caris et al., 2015; Schagen et al., 2020; Vlot et al., 2017; Zhu & Chan, 2017). Puberty is a time of significant brain and cognitive development. The potential neurodevelopmental impact of extended pubertal suppression in gender diverse youth has been specifically identified as an area in need of continued study (Chen et al., 2020). While GnRH analogs have been shown to be safe when used for the treatment of precocious puberty, there are concerns delaying exposure to sex hormones (endogenous or exogenous) at a time of peak bone mineralization may lead to decreased bone mineral density. The potential decrease in bone mineral density as well as the clinical significance of any decrease requires continued study (Klink, Caris et al., 2015; Lee, Finlayson et al.,

2020; Schagen et al., 2020). The potential negative psychosocial implications of not initiating puberty with peers may place additional stress on gender diverse youth, although this has not been explicitly studied. When considering the timing of initiation of gender-affirming hormones, providers should compare the potential physical and psychological benefits and risks of starting treatment with the potential risks and benefits of delaying treatment. This process can also help identify compelling factors that may warrant an individualized approach.

Studies carried out with trans masculine youth have demonstrated chest dysphoria is associated with higher rates of anxiety, depression, and distress and can lead to functional limitations, such as avoiding exercising or bathing (Mehringer et al., 2021; Olson-Kennedy, Warus et al., 2018; Sood et al., 2021). Testosterone unfortunately does little to alleviate this distress, although chest masculinization is an option for some individuals to address this distress long-term. Studies with youth who sought chest masculinization surgery to alleviate chest dysphoria demonstrated good surgical outcomes, satisfaction with results, and minimal regret during the study monitoring period (Marinkovic & Newfield, 2017; Olson-Kennedy, Warus et al., 2018). Chest masculinization surgery can be considered in minors when clinically and developmentally appropriate as determined by a multidisciplinary team experienced in adolescent and gender development (see relevant statements in this chapter). The duration or current use of testosterone therapy should not preclude surgery if otherwise indicated. The needs of some TGD youth may be met by chest masculinization surgery alone. Breast augmentation may be needed by trans feminine youth, although there is less data about this procedure in youth, possibly due to fewer individuals requesting this procedure (Boskey et al., 2019; James, 2016). GAHT, specifically estrogen, can help with development of breast tissue, and it is recommended youth have a minimum of 12 months of hormone therapy, or longer as is surgically indicated, prior to breast augmentation unless hormone therapy is not clinically indicated or is medically contraindicated.

Data are limited on the optimal timing for initiating other gender-affirming surgical treatments in adolescents. This is partly due to the limited access to these treatments, which varies in different geographical locations (Mahfouda et al., 2019). Data indicate rates of gender-affirming surgeries have increased since 2000, and there has been an increase in the number of TGD youth seeking vaginoplasty (Mahfouda et al., 2019; Milrod & Karasic, 2017). A 2017 study of 20 WPATH-affiliated surgeons in the US reported slightly more than half had performed vaginoplasty in minors (Milrod & Karasic, 2017). Limited data are available on the outcomes for youth undergoing vaginoplasty. Small studies have reported improved psychosocial functioning and decreased gender dysphoria in adolescents who have undergone vaginoplasty (Becker et al., 2018; Cohen-Kettenis & van Goozen, 1997; Smith et al.,2001). While the sample sizes are small, these studies suggest there may be a benefit for some adolescents to having these procedures performed before the age of 18. Factors that may support pursuing these procedures for youth under 18 years of age include the increased availability of support from family members, greater ease of managing postoperative care prior to transitioning to tasks of early adulthood (e.g., entering university or the workforce), and safety concerns in public spaces (i.e., to reduce transphobic violence) (Boskey et al., 2018; Boskey et al., 2019; Mahfouda et al., 2019). Given the complexity and irreversibility of these procedures, an assessment of the adolescent's ability to adhere to post-surgical care recommendations and to comprehend the long-term impacts of these procedures on reproductive and sexual function is crucial (Boskey et al., 2019). Given the complexity of phalloplasty, and current high rates of complications in comparison to other gender-affirming surgical treatments, it is not recommended this surgery be considered in youth under 18 at this time (see Chapter 13—Surgery and Postoperative Care).

Additional key factors that should be taken into consideration when discussing the timing of interventions with youth and families are addressed in detail in statements 6.12a-f. For a summary of the criteria/recommendations for medically necessary gender-affirming medical treatment in adolescents, see Appendix D.

Chapter 8
Gender Dysphoria and Autism Spectrum Disorders

Aron Janssen

Introduction

Sitting across from me in my office was a 13-year-old, here for a consultation while home from his residential treatment center with a request from his family on how best to understand and support his continued insistence that he be allowed to wear dresses and be referred to as a girl. Over the years of previous treatments, he's been diagnosed with many things—intellectual disability (IQ of 55), autism, and bipolar disorder—but none of these labels do anything to accurately describe this ebullient youngster who deftly differentiates between internal experience and external expectations of gender. In answering my request to draw a self-portrait, his response was "Should I draw it as I see myself or how others see me?" As the evaluation proceeded, it raised several important questions: How do we understand gender identity development in someone with intellectual disability and an autism spectrum disorder? How do we differentiate between symptoms of autism (including intense, restricted interests) and symptoms of gender dysphoria? How do we assess an individual's ability to understand the irreversible effects of medical and surgical interventions? Utilizing this patient's experience, we will review the literature into the overlap between autism and gender dysphoria and discuss the unique considerations when working with kids that experience both. Please note, for the sake of the case discussion, this patient used both "he/him" and "she/her" pronouns at various points during our work together. The pronouns used will reflect the patient's preference at the time.

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Brief Literature Review

Autism spectrum disorders (ASDs) are a set of neurodevelopmental disorders that are defined by deficits in two major domains. The first domain encompasses persistent deficits in social communication and interaction across multiple contexts. This could include difficulties in social-emotional reciprocity (i.e., difficulty with back and forth conversation), difficulties in nonverbal communication used for the purpose of social interaction (i.e., maintaining eye contact, using gestures, etc.), or difficulties in understanding complex social relationships. The second domain encompasses restricted and repetitive patterns of behavior, interests, or activities. This could include repetitive motor movements or speech (i.e., echolalia, frequent lining up of toys or rocking back and forth), an inflexible adherence to routines, interests that are highly fixated and abnormal in intensity or focus, or hyper- or hyporeactivity to sensory input [1]. Symptoms from both domains must be present in the early developmental period and must lead to significant impairments in functioning. The American Academy of Pediatrics recommends that all children should be screened for ASD during well doctor visits at 1.5 and 2 years of age. There are a number of available screening and diagnostic instruments and interviews available that have evidence-based support for their use in children suspected to have autism [2]. For children suspected to have an ASD, a further evaluation consisting of a parent/caregiver interview and an observational assessment should be employed to ensure the accuracy of the diagnosis.

Gender dysphoria, which has been described in depth earlier in this book, is defined primarily by a persistent incongruence between one's assigned sex at birth and expressed/experienced gender [1]. Over the last decade, there has been increased evidence to suggest an association between gender dysphoria, gender variance, and ASDs [3–6]. Current literature suggests a bidirectional relationship; that is, individuals presenting with gender dysphoria are more likely to have a co-occurring diagnosis of ASD, and individuals presenting with a diagnosis of ASD are more likely to have a co-occurring diagnosis of gender dysphoria. Current prevalence rates for ASD in the general population range from 0.3 to 1.16% [7], and individuals with ASDs are approximately seven times more likely to be gender variant than same aged peers [3, 5].

Gender dysphoria, gender variance, and ASDs are complex phenomena that are present among all populations of varying degrees of expression. Given their frequent overlap, researchers have sought to understand possible common shared etiologic mechanisms. Some have theorized a role for genetics, prenatal exposure to hormones, or even environmental toxins [8, 9], but these theories are speculative at best. Given the lack of research into the known mechanisms for social and gender identity development, we are left to use clinical observation to reflect on similarities and dissimilarities between those with autism, those with gender variance, and those with both.

Case reports on individuals with gender dysphoria and autism have pointed to unique presentations and treatment implications. Individuals with both gender

dysphoria and an ASD will commonly present with preoccupations that shape their life experiences, and this preoccupation may overlap with thinking about gender identity [10]. Furthermore, others have found that children with more profound intellectual disability, which frequently is present in children with ASDs, have more difficulty in establishing and articulating a gender identity that is consistent over time [11]. Jacobs et al. [12] discussed the role of impaired theory of mind and intolerance of ambiguity in shaping therapeutic interventions for individuals with both gender dysphoria and ASDs. These authors make a point to note that while there are unique elements to the individuals with autism and gender dysphoria, these unique elements should not be barriers to seeking out gender affirmative care.

In fact, the opposite is often the case. It is common for individuals with ASDs to have more difficulty in accessing transition-related care. Many practitioners are uncomfortable in assessing and/or working with individuals with both gender dysphoria and ASDs, and there is very limited pool of providers that have expertise (or even experience) with both. As such, individuals often face fragmented care with multiple different providers providing multiple different components to a treatment plan. However, for those of us lucky enough to work with this population, the rewards are self-evident, and there is a tremendous amount to learn by partnering with our patients to better understand their needs and experience.

Diagnosis and Assessment

JM was born to a biological mother with a history of schizophrenia and polysubstance abuse, and she was known to have used multiple substances during the pregnancy. JM was born on time, via vaginal delivery. He was born with typical male genitalia and had otherwise typical development. There was initial opiate withdrawal after birth; otherwise, the immediate postnatal period was unremarkable. JM was given up for adoption and placed with a foster family that later adopted him. His fine and gross motor skills were delayed, and he didn't say his first word until age 3 and didn't speak in full sentences until age 5. He would be noted to frequently flap his hands, rock back and forth, and would often do the same physical task over and over again. He was identified for early intervention and was diagnosed with autism and referred for intensive treatment.

Notably, by age 3, JM began demonstrating a clear preference for more typical feminine play. JM was preferentially drawn to dolls and his mother's clothes and shoes. While there was little demonstrated interest in socializing with other children, he was more attracted to the games played by the girls in his parents' social circles. As he got older, he began to play dress up, and his father recalled how JM's face would light up when he was allowed to wear a very specific pink tulle skirt. When the family asked about the significance of this preference, they were told that while some kids with autism are drawn to maps or trains or dinosaurs, JM was drawn to dresses.

By age 5, JM began to get aggressive. He would often appear to be internally preoccupied, and he would go days without more than an hour or 2 of sleep. He appeared in these periods to be even more drawn to dress up and to his mother's clothes and make up, and when these items were restricted from use, as was directed by his treatment providers, he would become increasingly agitated and would throw things around the house. And yet, when his mood was stabilized, and he was again sleeping through the night, he continued to have clear preference toward feminine attire and appearance. He would pee only from a sitting position and began to ask his parents when he would develop breasts. While he never made statements such as "I am a girl," he did discuss his belief that he would become a girl when he grew up.

Multiple evaluations and repeated neuropsychological testing was done, which consistently reinforced the intellectual disability, the autism, and the bipolar disorder. And at every step along the way, these were the reasons given for JM's longing for femininity. By the time he reached his teen years, JM has been living in a residential treatment facility for the past 2 years to manage his increasingly unsafe behaviors at home. While there, he began to assert requests to wear girls' clothing and go by a girls' name. His treatment center, working from the recommendations by his outpatient providers that this preference was a "restricted interest," disallowed him from accessing any feminine attire, and he was admonished when he requested to use a girls' name.

JM's parents, having seen a documentary about transgender children, wondered if they needed a different approach and brought him for an evaluation with a gender specialist. In this initial evaluation, it was clear that while JM certainly met criteria for ASD and for bipolar disorder, JM also had lifelong gender dysphoria and a female identity that had never been affirmed. During the initial meeting, JM was eager to tell his story and told me that he has always felt like a girl, that he hates "(his) twig," and wants to live full time as a girl. He told me in the initial meeting that he was sure of this, and his history was consistent. In every period of his life, in every mood state, JM was a child that consistently affirmed a female identity. However, his conception of gender was different than many of the kids I have seen. For example, JM reported that while he preferred a female name and attire, he did not mind he/him pronouns. He used he/him when referring to himself regardless of how he was presenting and which name he utilized. His experience of his gender was more about his own feeling and experience rather than how others saw him. He cared less about if he was perceived of as a girl than about whether he was allowed to wear what he wanted to wear and how he saw himself. So when I asked him to draw a picture of himself, of course I told him to draw it how he saw himself, which was as a princess in a ball gown with long, blonde hair.

Management

Given JM's clear gender dysphoria, we worked on a treatment plan to help JM manage the distress felt. First, the treatment center was educated on gender dysphoria and the role they can play in supporting JM in exploring identity rather than

restricting such developmentally appropriate tasks. Next, we worked with JM and family on social transition. Over a period of several months, JM transitioned to going by a girls' name full time, wearing girls' clothes (as she saw them), and she began to use she/her pronouns throughout the various contexts in her life.

There were unique challenges posed because of her co-occurring ASD. For example, JM could not understand why she couldn't wear a ball gown in every context and had a hard time understanding why others in her life had a hard time in using her new name and affirmed pronouns. She didn't appear to be particularly bothered by this but more perplexed. She had made the transition—why was it that not everyone seemed to notice? She needed help in constructing her narrative of her experience—how could she help others to understand her process, thereby helping herself to understand how others may think and react in certain situations. She had to learn about safety, bathroom use, and personal boundaries in a way that was at times much more explicit than others require.

Given JM's intellectual disability and ASD, one of the challenges in our work was establishing how to assess her capacity to make decisions that lead to irreversible and partially irreversible challenges. Given her limitations, this required more concrete examples of the risks, benefits, and alternatives through use of photos and videos to aid in discussions. We involved JM's parents in these discussions, and thankfully JM had parents that were supportive and appreciated the improvements that JM made with social transition and were eager to support JM in her decisions in her care.

As treatment progressed, and puberty began in earnest, she was able to articulate very clearly the increase in distress as a result of her changing body and a wish for puberty suppression. At 16, she has been living her life as a girl for over 2½ years and is about to start estrogen.

Clinical Pearls and Pitfalls

JM was lucky to have a supportive family that had the means and the resources to seek out a second opinion regarding gender identity development and was able to access care that was affirming. This process had a profound positive effect on her life. However, it is easy to imagine that if JM's parents were less supportive, or if they lived in an area without access to a gender specialist, JM would still be living in an environment in which she was punished for asserting her identity as a girl. Access to affirming and effective care is a chronic problem for children with gender variance and even more so for children with gender variance and an ASD. Working with JM was a privilege, and JM was excited to know that her experience would help others like her. In discussing the case, there were several main points to review: implications for assessment and diagnosis, assessing an individual's ability to give consent, unique treatment implications, and ensuring access to care.

Diagnostically, individuals with ASDs often have intense restricted interests. For example, one of my patients with autism is obsessed with laundry soap. She knows every possible type of laundry soap, wants only to talk about laundry soap, and at

any given time will have two to three different kinds of travel size laundry soap that she carries with her to smell and to show off. If given the opportunity, she will spend an entire conversation entirely dedicated to laundry soap. This obsessive interest though has developed over time. When she was younger, she was obsessed with hair and would play with her own hair so much that it would take an hour every night for her father to untangle it. Often this kind of restricted interests are used by those skeptical of gender dysphoria to dismiss a child's assertion of their own gender. For example, some might say: "My child wanted to be a horse when she was younger—we didn't allow her to identity as a horse then, so why when she says she now wants to be a boy would I allow that?" The reality is that there is a different developmental process for gender identity than for a child's normal imaginative process of trying on different personas and interests. And yet, for some children with ASDs, these interests are so intense they disallow for easy exploration of other more complex aspects of the self. This then begs the question—how do we understand if a transgender identity is authentic or a restricted interest? And does it matter?

One factor to look for is consistency of expression. For some individuals with ASD (particularly those who are nonverbal), it is difficult for them to easily communicate their needs and desires. As such, for some kids, these needs might be expressed like it was for JM with statements consistent with a transgender identity. For others, this may be frequent tantrums when forced to wear the clothes typical of their assigned sex at birth or a frequent repetitive play with more stereotypically masculine or feminine toys. For individuals with gender dysphoria, we would expect that as a child consolidates their gender identity, there would be a consistency across time and situations. For JM, this meant that she espoused a female identity when manic, when euthymic, and when depressed. She espoused it at home, at school, and in residential treatment. While the skeptics will use the horse example, I have yet to hear of a child that will consistently espouse an identity of that of a horse consistently over years with a worsening with puberty. As such, while identity development in more complex among children with ASDs, it does not mean that they cannot tell us what we need to know, if only we learn how to listen.

Another factor to help in the assessment is by examining the impact of various interventions on the individuals functioning and sense of self. For JM, many interventions were put into place over the years to attempt to in some way decondition the gender identity and expression. Most notably, JM had some behavioral difficulties at the residential treatment center, and their treatment plan included attempts to reduce more feminine expression. This was in context to time spent at home in which JM was allowed to dress as she wanted and was demonstrably more bright and cheerful during those times. Similarly, when the residential treatment center began to allow JM to assert her identity as a girl, use she/her pronouns, and dress in dresses, the behavioral difficulties diminished. She continued to struggle at times with her mood and her thought disorder persisted, but her overall functioning significantly improved with each step taken in her social transition.

Social transition represents a completely reversible intervention with very few risks. The risks involved are mostly situational and include potential exposure to

bias and violence, which is important for the clinician and the family to address however possible. When considering the reversible and potentially irreversible interventions such as puberty blockers, cross sex hormones, and surgery, it is important to assess an individual's capacity to consent to these treatments. For JM, she had significant intellectual impairments; however, she spent much of her time looking at information around transition and had a surprising degree of knowledge of the risks of the various interventions. This will not be the case for all individuals with ASDs. This places clinicians, families, and the patients themselves in a potential bind. How do we know how best to proceed when a patient lacks the means to communicate an understanding of the risks, benefits, and alternatives to a particular intervention?

In working with JM and her family, we are able to work collaboratively to discuss both in individual sessions and in family sessions all the various options, including hormones. We used verbal means and pictures online to review the various expected changes and the possible risks involved. For JM, despite her limitations, she was able to provide a clear assent, and her parents were able to provide consent for the various interventions. For most patients with psychiatric disorders, the capacity to consent is retained, even during active illness, and it is important to note that delayed access to transition-related care is correlated with worse outcomes for transgender individuals. While clearly the consent process is more complex with these individuals, it is possible nevertheless to engage patients in a shared decision-making process.

In treatment with individuals with both gender dysphoria and ASDs, it is important to take into account the unique considerations for each patient. For JM, the interventions around the gender dysphoria was one of the most straightforward pieces of the treatment plan. For others, it is much more complex. For example, some patients struggle with understanding the social cues that are associated with gender role. One patient I was working with could not understand why her transition went unnoticed, and we had to work for her to understand that since she had not changed anything about her appearance, pronoun, or name, it was difficult for others to know that she was not asserting herself as a woman. Another patient who struggled to communicate his needs spent several months in therapy having a difficult time engaging and only was able to engage in therapy after it was discovered that it was not the interpersonal aspect of the therapy that was uncomfortable (which had been the assumption) but instead the patient's discomfort about the sound of his voice. Discomfort in one's voice is a common occurrence in transgender individuals, but this individual patient had difficulties in social communication at baseline which made it difficult for him to express this in a way that felt safe.

Much of the treatment of gender dysphoria involves interacting with various systems—the healthcare system, the educational system, the family system, the legal system, and often individuals with ASDs need more assistance in advocating for their needs in these varied environments. Clinicians working with people with ASDs and gender dysphoria play an important role in this vital advocacy.

Conclusion

Individuals with ASDs are more likely to have gender dysphoria, and individuals with gender dysphoria are more likely to have an ASD. As more attention is given to this overlap, we will continue to discover the diverse ways in which gender is understood and expressed. Having a different view of gender development should not lead to disenfranchisement from treatment; however, having autism has historically been a barrier to accessing transition-related care. I would argue that individuals with autism can at times break down the artificiality of the rigidity of gender identity and expression more effectively than their non-autistic peers. When practitioners can learn to partner with their patients, we will recognize how much they can teach us about their experiences and, by extension, our own.

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SPECIAL SECTION: CLINICAL APPROACHES TO ADOLESCENTS WITH GENDER DYSPHORIA

The Complexities of Treatment Planning for Transgender Youth with Co-Occurring Severe Mental Illness: A Literature Review and Case Study

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Abstract
Gender variance and dysphoria are present across all classes, ethnicities, and experiences, including among those with severe and chronic mental illness. In these, our most vulnerable populations, adequate assessment and treatment of gender dysphoria often is overlooked despite evidence that appropriate treatment of gender dysphoria leads to improvement in psychological functioning (Smith, van Goozen, Kuiper, & Cohen-Kettenis, 2005). The World Professional Association for Transgender Health recommend in their Standards of Care that somatic and surgical treatments for gender dysphoria should be made available to those with medical or mental illness with the caveat that "[the illness] must be reasonably well-controlled (2011)." In this article, we will utilize case-based material to elucidate the challenges of treating gender dysphoria in the context of complex mental illness such as bipolar disorder, schizophrenia, and sexual trauma, and the pitfalls of defining "well-controlled" for the sake of treatment.

Keywords Transgender youth · Consent · Gender dysphoria · Mental health

Case Study

JB, who was assigned male at birth, was evaluated initially at age 13 at the request of his long-term psychiatrist for an evaluation of his gender identity and recommendations for his treatment plan. At the time of the initial consultation, JB was residing at a residential treatment center, where he had transferred after a prolonged hospitalization in the context of psychotic symptoms and ongoing difficulties with functioning secondary to his autism spectrum disorder (ASD) and developmental disabilities.

JB was born to a biological mother with an unclear past psychiatric history who used alcohol, methamphetamines, and other drugs during pregnancy and attempted suicide by ingestion of bleach in the first trimester. JB's biological mother did not have any prenatal care until the third trimester. JB was born with hypotonia and low birth weight. His adoptive parents were present at the delivery, and his early infancy was marked by an easy temperament and notable developmental delays in all areas. He qualified for early intervention, but it was noted that in addition to his global delays, he had limited interactivity with adults and by age 2 had not yet spoken a single word. He was diagnosed with ASD and referred for appropriate intervention.

Beginning as early as age 3, and continuing throughout his childhood, JB began to demonstrate clear preferences for more stereotypical female interests and play. His parents reported a preference for girls' clothes and hair and with his earliest speech made identity statements that pointed to an early identification of a female gender identity. Per his parents, he always gravitated toward dolls and anything pink and was avoidant of rough-and-tumble play. When given the opportunity, he would choose female characters and dress up as a girl, and when he did so, he would light up. Every Halloween was marked by dressing as a different Disney princess. His parents described that they never saw him as happy as when in his favorite princess dress. Per his father, he was not aware of any statements made about distress about his current body; however, he did report that JB would frequently ask about when he would develop breasts and when his penis would fall off.

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As JB progressed through his development, his psychiatric symptoms became more complex. He was initially assessed to have a mood disorder and ASD, and there was concern about the impact of fetal exposures on his development. He was quite impulsive, and he had frequent tantrums and dangerous behaviors that were difficult to safely manage at home. He would put things in the electrical sockets and would be quite emotionally labile, bursting into tears with the slightest provocation. He had periods of aggression and fixation on enacting violence toward his mother. He was described as having a degree of paranoia about his mother that was thought to be psychotic, and there was a blurred line between his fantasy play and overt auditory hallucinations. Importantly, throughout the various medication trials, and both when he had acute mood and psychotic symptoms and when these symptoms were in remission, his gender identity assertion remained consistent. He continued to express preference for the female gender and solidified his belief that he is a girl. Throughout his childhood, this was interpreted as a restricted or repetitive interest and conceptualized as a symptom of his ASD. As such, JB's parents were advised to discourage any stereotypically feminine behavior, and by the time of his initial gender evaluation, he had been "dressing in a masculine manner" as one of his components of his behavior plan at his residential treatment center. At home, however, beginning when JB was 11, despite the recommendations of his providers, his parents have allowed him to dress up however he wished when at home.

During the evaluation, JB was very articulate about his gender identity development. Despite having previously been tested as having a full scale IQ of 54, he was able to speak about his experience of gender with a surprising amount of nuance and demonstrable theory of mind. JB reported very clearly that he has always been a girl and has demonstrated improved mental health and cognitive progress when he has been able to dress in a way that aligned with his sense of self. He reported a clear desire to socially transition, has picked out a name, and read online about estrogen and about gender confirmation surgery, all of which he is hoping for. Notably, JB had frequent pronoun reversals, which is typical for youth with ASD, and while he identified clearly as a girl, he reported not having any preference for pronouns, and ultimately used male or female pronouns to mark periods of his life. At the time of the initial gender evaluation, he met full diagnostic criteria for ASD and intellectual disability with a rule-out for bipolar disorder with psychotic features. His gender dysphoria was clear and consistent across time and across varying periods of remission and recurrence of his mood and psychotic symptoms. As a part of his initial visit, JB requested assistance in being able to use his preferred name at his residential treatment center and dress like the other girls there. It is also important to note that despite being 13, JB had not yet entered puberty and had not reported any interest in or history of sexual encounters, fantasy, or masturbation.

After the initial evaluation, it was recommended that JB's treatment center be educated about gender dysphoria and the benefits of social transition. Subsequently, the treatment center successfully allowed JB to socially transition (and participate in shaping their new dress code policy), and JB began to use her female name and pronouns across all settings. Over the course of the next several years, she continued to be seen in our clinic for consultation, and while her psychiatric symptoms waxed and waned, her gender dysphoria did not. When she started puberty, she was referred for puberty suppression, and with the consent of her parents, she began estrogen at age 16. Her co-occurring psychiatric symptoms did not significantly change with the initiation of estrogen, though she described feeling much more comfortable in her body. She continues to require tremendous psychiatric support and residential treatment, but as a result of her treatment of her gender dysphoria, she was able to gain more confidence in her sense of self and was able to feel comfortable enough in her therapy to begin to explore her sexual identity and the complex interface with her past history of sexual abuse, which she had not told anyone until after her transition. She reported feeling newly confident in her sense of self and has described a desire for vaginoplasty when she turns 18. Of note, other elements of this case have been reported elsewhere (Janssen, 2018).

Literature Review

As identified through the case study above, gender dysphoria can co-occur with severe mental health issues; however, studying mental health issues in transgender youth is difficult, as the current literature is varied depending on method of the research and where the research is conducted (Fuss, Auer, & Briken, 2015). Gender dysphoria is present across all classes, ethnicities, and experiences, including those with severe mental illness, yet the research is lacking. The adult literature is consistent in the assertion that rates of psychiatric diagnoses in transgender adults vary greatly among studies, including rates of schizophrenia, mood, and anxiety disorders (Gijs, van der Putten-Bierman, & De Cuypere, 2014). The authors stress the importance that not all individuals who have gender dysphoria also have a co-occurring mental health diagnosis; however, it is important to address comorbidities if they do exist.

Literature that exists on the overall prevalence of gender dysphoria and co-occurring mental health issues, particularly among children and adolescents, has not provided a clear picture. A major difficulty in this literature is that there is no routine screening for gender identity in most non-specialty clinics. In general, studies of transgender youth include a high proportion of transgender youth seen in the mental health setting. In a recent study conducted in Finland assessing case files in a clinic for children applying for gender affirmative surgery, the number of referrals for mental health difficulties in gender

were high, indicating that 75% were seeking psychiatric services for reasons other than gender dysphoria (Kaltiala-Heino, Sumia, Tyolajarvi, & Lindberg, 2015). Despite this, many of these individuals did not meet criteria for a mental health disorder other than gender dysphoria. In contrast, we also know that having a diagnosis of gender dysphoria places children and adolescents at a higher risk for a variety of mental health concerns. In a study of gender dysphoric adolescents, 67.6% had no Axis I diagnosis, while 32.4% had at least one Axis I diagnosis and 15.2% had at least two diagnoses (de Vries, Doreleijers, Steensma, & Cohen-Kettenis, 2011). In one study, 56% of transgender boys and 47% of transgender girls met criteria for an additional diagnosis, compared to an 67% of the ADHD control group (Wallien, Swaab, & Cohen-Kettenis, 2007). While the majority of individuals in this study did not have an Axis I disorder, the proportion of individuals with a diagnosis was higher than the general adolescent population.

The literature varies in the range of percentages of individuals with co-occurring disorders. For example, the range for depressive symptoms ranges from 6 to 42% (Holt, Skagerberg, & Dunsford, 2016; Skagerberg, Parkinson, & Carmichael, 2013; Wallien et al., 2007), with suicide attempts ranging between 10 and 45% (Mustanski, Garofalo, & Emerson, 2010; Reisner et al., 2015). Self-injurious thoughts and behaviors are thought to range from 14 to 39% (Holt et al., 2016; Skagerberg et al., 2013). Anxiety disorders and disruptive behavior difficulties including ADHD are also prevalent (de Vries et al., 2011; Mustanski et al., 2010; Wallien et al., 2007). There are also high proportions of gender dysphoria and overlap with ASD (de Vries, Noens, Cohen-Kettenis, van Berckelaer-Onnes, & Doreleijers, 2010; Jacobs, Rachlin, Erickson-Schroth, & Janssen, 2014; Janssen, Huang, & Duncan, 2016; May, Pang, & Williams, 2016; Strang et al., 2014, 2016). Specifically, some studies have identified that restricted interests related to gender could be an indicator of the link between ASD and Gender Dysphoria (VanderLaan et al., 2015). Other studies have seen a higher representation of natal females presenting with both gender dysphoria, autism, and other developmental delays (Kaltiala-Heino et al., 2015).

When we compare transgender and cisgender youth, we see higher rates of mental health concerns for transgender youth across a variety of symptomology, including depression, anxiety, suicidal ideation and attempts, non-suicidal self-injurious behaviors, and higher rates of inpatient and outpatient psychological treatment (Reisner et al., 2015). There are a number of potential reasons that suggest the elevated rates of mental health concerns, including the social stress associated with a transgender or gender non-conforming identity. Transgender youth are exposed to high levels of discrimination and marginalization as well as poor access to care; however, not all gender non-conforming youth experience significant psychological distress. Most gender non-conforming youth report social exclusion, parental rejection, and high levels of discrimination, bullying, and violence (Bauer, Scheim, Pyne, Travers, & Hammond, 2015). Moreover, some researches demonstrate that the rate of psychopathology among transgender youth is comparable to that of cisgender youth and parental rejection may be a better predictor of psychological function in adulthood (Coker, Austin, & Schuster, 2010; Espelage, Aragon, & Birkett, 2008; Russell, Ryan, Toomey, Diaz, & Sanchez, 2011; Simon, Zsolt, Fogd, & Czobor, 2011).

Emerging literature suggests that social transition can be a protective factor for transgender youth. A recent longitudinal study assessed transgender youth between the ages of 9–14 matched to control subjects or siblings to determine depression and anxiety symptom differences. When matched to control subjects or siblings, transgender youth who have socially transitioned report no differences in depression and slightly higher levels of anxiety (Durwood, McLaughlin, & Olson, 2017) which is in significant contrast to youth who have not socially transitioned. In addition to the literature addressing social transition, there is also evidence that medical interventions have positive impacts on both gender dysphoria symptoms and global psychological functioning (Costa et al., 2015; de Vries et al., 2014; Smith, van Goozen, Kuiper, & Cohen-Kettenis, 2005). Studies have shown that children followed prospectively after being treated with gonadotropin-releasing hormone analogues (GNRHa) for gender dysphoria have comparable psychological adjustment when compared to cisgender controls (de Vries et al., 2014). Cohen-Kettenis, Schagen, Steensma, de Vries, and Delemarre-van de Waal (2011) conducted a longitudinal case study of an adolescent who had puberty suppression treatment at 13 years of age, testosterone treatment at 18 years of age, and gender-affirming surgeries at 20 and 22 years of age. Psychologically, this individual reported no regrets about the treatment protocol and was functioning well psychologically, intellectually, and socially. In addition to this case study, adolescents who used puberty suppression had decreased behavioral and emotional difficulties, though still experienced body dissatisfaction in a study of individuals who received puberty suppression between 2000 and 2008. Despite this, adolescents in this study experienced fewer depressive symptoms and overall improvement in general functioning. Feelings of anger, anxiety, and gender dysphoria remained the same (de Vries et al., 2014).

In addition to social transition and access to gender-affirming medical interventions, numerous recent studies indicate that social and parental support are protective against a variety of risk factors for gender non-conforming youth (Bauer et al., 2015; Darby-Mullins & Murdock, 2007; Davey, Bouman, Arcelus, & Meyer, 2014; Espelage et al., 2008; Friedman, Koeske, Silvestre, Korr, & Sites, 2006; Ryan, Huebner, Diaz, & Sanchez, 2009; Stanton et al., 2004). Although developmental research continues to demonstrate the impact of both social support and parenting have on children and adolescents, less is known about the mechanisms by which youth experiencing gender dysphoria benefit from supportive environments.

However, it is clear that there is a correlation between perceived support across settings and long-term psychological adjustment (Espelage et al., 2008).

In addition, a growing body of research suggests that these psychiatric problems may be the consequence of environmental factors related to poor psychological adjustment. (D'Augelli, Grossman, & Starks, 2006; de Vries et al., 2011; Simon et al., 2011). For example, research indicates that parental support is consistently protective against risk factors for psychological distress. While there are a variety of risk factors that are not feasible for targeted intervention, parental support is a modifiable factor associated with decreased anxiety, fewer post-traumatic stress symptoms, greater life satisfaction, reduced suicidal ideation, and fewer suicide attempts (Bauer et al., 2015; Bouris et al., 2010; Davey et al., 2014). Parental rejection during adolescence specifically is associated with substance use, increased sexual health risks, and poorer physical health outcomes (Ryan et al., 2009). However, the risks of enduring gender dysphoria without medical or psychosocial intervention are also significant. The development of unwanted sex characteristics and restricting of cross-gender role expression in youth experiencing gender dysphoria are associated with increased anxiety and depression (Byne et al., 2012; Drescher & Byne, 2012).

Gender dysphoria among children and adolescents necessitates gender affirmative services and interventions. As previously mentioned, The World Professional Association for Transgender Health (WPATH) recommends that medical interventions for gender dysphoria should be made available as long as any medical and mental illness is "reasonably well-controlled" (Coleman et al., 2011). Unfortunately, several ethical concerns restrict access to and complicate the provision of these services. Disparate legislation about children and adolescents' ability to consent and/or assent to medical interventions has contributed to long-standing difficulties among transgender youth accessing gender-affirming services (Giordano, 2014; Levin, 2017; Romero & Reingold, 2013). Although youth are entitled to sexual and reproductive healthcare in the USA, medical decision making is typically left to the parents or legal representatives due to a presumption of decisional incapacity (Romero & Reingold, 2013). Healthcare policies differ by state, and only some states designate that minors are capable of consenting to services related to sexually transmitted infections, pregnancy, and mental health disorders without parental consent or knowledge (Romero & Reingold, 2013). The capacity to provide informed consent in children and adolescents typically depends on subjective cognitive and developmental characteristics of the patient, rather than a particular age.

Patients are typically deemed capable of consenting to medical interventions when they can understand the information relevant to the treatment, consider choices in accordance with personal/family values, assess potential risks, and are able to communicate verbally or nonverbally with caregivers (Giordano, 2014). However, for youth seeking gender-affirming medical interventions, the number and type of interventions as well as the order in which these interventions take place vary from person to person. For some medical providers and parents, the complexity of gender-affirming medical services and informed consent variability complicates transgender adolescents' entitlement to health services that facilitate self-determination of gender identity (Romero & Reingold, 2013). Informed consent in the treatment of youth with gender dysphoria necessitates a standard of allowing children and adolescents to assent to treatment given a developmentally appropriate understanding of potential consequences of medical intervention (Cavanaugh, Hopwood, & Lambert, 2016).

One of the primary tasks of health professionals providing services to youth experiencing gender dysphoria is to evaluate the extent to which the patient and their family understand the short- and long-term consequences of gender-affirming medical interventions (Levine, 2017). Mental health professionals specifically conduct comprehensive evaluations to assess for concurrent mental health vulnerabilities, treatment adherence concerns, familial attitudes and beliefs about gender identity, and a reasonable capacity for informed consent (Byne et al., 2012). Difficulties with minors providing informed consent to gender-affirming medical interventions often reflects professional discomfort with uncertainty and family-specific cultural perspectives on gender diversity (Cavanaugh et al., 2016). In considering their own lived experience, minors experiencing gender dysphoria are responsible for considering how the knowledge provided by healthcare professionals about medical interventions aligns with their cultural and social contexts (Cavanaugh et al., 2016; Drescher & Byne, 2012; Levine, 2017; Romero & Reingold, 2013). However, healthcare professionals must balance patients' rights to autonomy and self-determination with clear evaluation of a minor's capacity to consider the potential risks and benefits of gender-affirming medical services. The movement toward facilitating informed consent from youth experiencing gender dysphoria does not preclude mental health treatment and acknowledges the possibility that some minors may be incapable of providing informed consent. However, many experts in the field argue that healthcare professionals providing gender-affirming medical interventions must assume that youth experiencing gender dysphoria are just as capable of providing informed consent as other minors consenting to sexual and reproductive health services (Giordano, 2008, 2014).

Conclusions

When thinking about the case of JB, it was clear that gender dysphoria was a primary concern along with a number of concerning psychiatric symptoms including ASD, intellectual disability, aggression, mood lability, and psychotic symptoms. The presentation was complex, yet nuanced assessment

allowed the patient to have a voice within treatment planning. JB was involved in all decisions made regarding treatment planning in our clinic. Some might worry that JB was not able to consent or assent to medical interventions; however, she was able to express a clear wish for treatment and understood to the best of her ability the risks and benefits of those choices. Through developmentally appropriate education and conversation, the team worked with JB and her family and valued her participation in the decision making process.

JB's persistent gender dysphoria symptoms were a significant factor in recommendations for medical interventions. The comprehensive evaluation over time with an expert in the field, paired with an extensive history provided by the parents, helped make the argument for the medical necessity of gender affirmative care. The primary clinician was able to elucidate a long-standing pattern of a gender identity that was different than JB's sex assigned at birth. The complex interaction between ASD and co-occurring gender dysphoria was important to consider in this case. Through the literature, we know there are high rates of comorbidity of ASD and Gender Dysphoria. Previous providers prematurely labeled the desire to be a girl as solely a restrictive and repetitive behavior, rather than considering the possibility that the child could have an ASD as well as question her gender identity. In addition, while her symptoms waxed and waned, JB continued to assert a female identity. We would expect JB's identity to waver with her symptoms and through the developmental process (as restrictive interests can change over time) if it was related to a repetitive and restricted interest, rather than a true female identity.

Parental and community support also played a significant role in working with JB. When JB's prior providers discouraged her parents from allowing her to dress up and play with dolls, her parents allowed her to. This support was protective toward her building a nuanced sense of self. Furthermore, her residential treatment facility successfully allowed JB to socially transition, which had clear benefits not only for JB, but also for the staff at the treatment center, who were able to see a much happier side of JB. Had these interventions and support not had been used, it is hard to know how JB's psychiatric symptoms might have been impacted. The literature suggests that parental support is a protective factor for these youth, and without support outcomes are worsened. We do not know whether JB would have been able to disclose her sexual trauma without this gender affirmative care.

In addition, it was clear that the psychiatric symptoms were independent of interventions related to transition. She understood to the best of her ability the risks and benefits of the medical services, and specifically asked for medical intervention as her gender dysphoria persisted. While it is unclear whether her psychiatric symptoms are "reasonably well controlled (WPATH, 2011)," the persistence of JB's gender dysphoria along with her strong desire and understanding of the medical interventions helped the team working with her understand the necessity of gender affirmative interventions. The role of medical and mental health professionals is not to arbitrate identity, but to work collaboratively with the patient and family to optimize outcomes, whatever they may be. For JB, this approach made all the difference.

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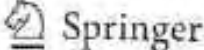

Chapter 3
Transgender Adolescents and the Gender-Affirming Interventions: Pubertal Suppression, Hormones, Surgery, and Other Pharmacological Interventions

Samantha M. Busa, Scott Leibowitz, and Aron Janssen

Introduction

I think I always just hoped that I would never get my period. I know I was in denial, but I still had this wish that perhaps it would skip me by.

Prior to the beginning stages of puberty, apart from the genitalia, there is little that separates the phenotypic appearance of boys and girls. Prior to this stage of development, it truly is the clothes, hair, and demeanor that identify the boy or girl. For youth with gender dysphoria that intensifies or presents at the onset of puberty and adolescence, it is a time for identity consolidation as well as potential anxiety. It is at this time that the body begins to develop the secondary sex characteristics that differentiate men from women, and just like the teen quoted above, it is a time in which transgender youth must confront change in their bodies that may not be welcome. In this chapter, we will review the physiology of puberty and the medical and surgical interventions available for youth with gender dysphoria. Of note, the use of the term *medical* is in reference to those interventions that require prescriptions and are not provided by psychiatrists. It is important to clarify that psychiatric interventions, even if not exogenous in nature (e.g., psychological interventions),

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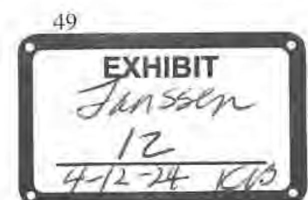

can also be considered *medical*; however, for the purposes of clarity, in this chapter, *medical* interventions refer to those interventions distinct from psychological or social interventions described in the previous chapter.

Pubertal Stages, Physical Changes, and Hormonal Changes

Puberty is a stage of life that can be both exciting and anxiety provoking for teens and parents alike and can be especially complicated for those who are gender nonconforming. It is referred to as the developmental stage in which secondary sexual characteristics appear, and children begin to confront changes in their body that differentiate men from women, physically and physiologically. For the youth experiencing gender dysphoria, this is compounded, as these changes may not be welcome and can introduce further confusion and frustration with their bodies. Changes in puberty are typically first noticed in birth-assigned females between 8 and 12 years of age and in birth-assigned males between 9 and 14 years of age, spanning a wide range of ages as well as maturity socially.

Physiologically, puberty begins when the hypothalamo-pituitary-gonadal axis is activated and there is pulsatile secretion of gonadotropin-releasing hormone (GnRH) by the hypothalamus. The secretion of GnRH stimulates the pituitary to release luteinizing hormone (LH) and follicle-stimulating hormone (FSH) by the pituitary, which in turn stimulates the ovaries and testicles to produce estrogens and androgens in both birth-assigned females and birth-assigned males, respectively. For birth-assigned females, FSH is responsible for developing follicles, which contain developing eggs, and also assists with the production of estrogen. For birth-assigned males, FSH stimulates the growth of seminiferous tubules ultimately leading to the production of sperm. LH is responsible for producing androgen male hormone in Leydig cells aiding growth of the seminiferous tubules. Birth-assigned females produce more estrogen and birth-assigned males produce more testosterone during this time. These hormones are increased within the bloodstream, triggering the physical and psychological changes that occur in puberty.

Physical changes are a consequence of the aforementioned physiological and hormonal changes occurring in the body. Adolescents of the two typical binary sexes experience *adrenarche*, the onset of androgen-dependent body changes, such as growth of axillary and pubic hair, body odor, and acne, and *pubarche*, the appearance of sexual hair. Birth-assigned females experience *thelarche*, the onset of breast development; *menarche*, the onset of menstruation; and weight changes. They also experience changes in their breasts. Both typical binary sexes also experience changes to their body shape, muscle content, and fat content. Birth-assigned males experience changes in their penis, scrotum, and an enlargement of testes. In addition, birth-assigned males will experience nocturnal emission, involuntary erection, and eventually will experience their first ejaculation. At this time, they are considered to be capable of procreation. Marshall and Tanner (1969, 1970) [1, 2] defined and mapped the stages of puberty as a means of a common language between

multidisciplinary health providers to describe the physiological, biological, and psychosocial changes that occur during puberty. Tables 3.1 and 3.2 delineate the Tanner stages defined and changes to the external genitalia, pubic hair, and height of individuals in each Tanner stage.

At the onset of Tanner stage II, youth with gender dysphoria begin to experience changes that begin to differentiate their bodies in to binary "categories" that may or may not be congruent with their own gender identity. By definition of those who meet criteria for gender dysphoria, these changes might cause significant distress, as the development of these secondary sex characteristics does not match their gender identity. The ramifications may be significant, as we know that transgender adolescents are at higher risk for a number of challenges at home, school, and socially. Puberty impacts *all* adolescents from the moment they wake up, to when they get dressed in the morning and go to school, until they go to bed at night, and so for these youth in particular it is important to understand the effect that puberty has on their emotional, social, and psychological development.

Table 3.1 Natal male tanner stages

Stage	External genitalia	Pubic hair	Growth
I	Prepubertal	Prepubertal	5–6 cm/year
II	Enlargement of the scrotum and testes; scrotum skin reddens and changes in texture	Sparse growth of slightly pigmented hair at the base of the penis	5–6 cm/year
III	Enlargement of the penis, length and then width; further growth of testes	Darker coarser curlier hair spreading over the pubic area	7–8 cm/year
IV	Increased penis size, growth and development of glans, scrotum and testes enlarge, scrotum skin darkens	Hair continues to look more adult-like, though has not spread to thighs	10 cm/year
V	Adult genitalia	Adult hair in quantity and type	No further increase after 17 years

Table 3.2 Natal female tanner stages

Stage	Breast development	Pubic hair	Growth
I	Prepubertal	Prepubertal	5–6 cm/year
II	Breast bud stage with elevation of breast and papilla; enlargement of areola	Sparse growth of slightly pigmented hair along the labia	7–8 cm/year
III	Further enlargement of breast and areola; no separation of contour	Darker coarser curlier hair spreading over the pubic area	8 cm/year
IV	Areola and papilla from a secondary mound above the level of the breast	Hair continues to look more adult-like, though has not spread to thighs	7 cm/year
V	Mature stage: projection of papilla only, related to recession of areola	Adult hair in quantity and type	No further increase after 16 years

Clinical Vignette

A 13-year-old transgender male (born with female anatomical features) reported that puberty had greatly impacted his view of himself and increased his anxiety socially. He stated, "I get dressed… sometimes I don't wear a binder in the mornings, it's so uncomfortable, I have to wriggle into it because it's tighter. I then have to adjust my breasts because they're fairly large, and if I'm not careful they look weird. I also have to periodically duck into a bathroom and readjust my binder to make sure that my chest looks 'natural' like a cis guys chest would look. I go through my daily routine and then I get on the bus, to go to school, the bus I take takes me very close to my previous school where everyone knew me as female. When that happens I'm always very worried someone will see me and be like 'oh that's deadname, that's her, that is a girl.'" This individual was interested in beginning a medical intervention and sought out help from me to work closely with his family to explore these medical options.

In the following section, we will review the types of interventions and the decision-making process that goes along with these interventions.

Medical Interventions

There are a number of medical interventions that are recommended for adolescents with gender dysphoria, which depend on how far advanced in puberty the adolescent has progressed according to current standards of care and clinical guidelines [3, 4]. These interventions are used to delay or reverse the physiological and visible changes that occur in puberty. We classify these types of interventions on the physical body as reversible, partially reversible, and irreversible.

Reversible interventions include the use of puberty suppression medications, which delay the development of secondary sex characteristics in order to buy time for a younger adolescent to mature into older adolescents who can then assent for more irreversible interventions such as hormones. The puberty-suppressing medications include gonadotropin-releasing hormone analogues (GNRHa), which are more widely used for children with precocious puberty. Other reversible medications that can be used to inhibit the effects of puberty in a pubertal adolescent include spironolactone, which has androgen-blocking properties for birth-assigned males, and oral contraceptive pills (OCP), which is used as menstrual suppression in birth-assigned females. All of the reversible interventions, if discontinued, will then allow the adolescent's body to resume the functioning that had been blocked or inhibited as a result of their use. Partially reversible interventions include the use of sex hormones, specifically testosterone for birth-assigned females and estrogen for birth-assigned males. These hormones lead to the development of secondary sex characteristics of the sex associated with the adolescent's gender identity regardless of the sex at birth. Finally, irreversible interventions include a number of different types of surgery, which will be described later in the chapter. We will examine the history, evidence base, indications, and ethical dilemmas related to each of these interventions.

Puberty Suppression

Medical treatment for gender dysphoria has a relatively short history of use within the medical community. The Amsterdam Gender Clinic in The Netherlands has been at the forefront of puberty suppression treatment in the context of gender dysphoria. This group of clinicians and researchers developed a protocol for the clinical management and treatment of gender dysphoria [5] in adolescents. This protocol recommended the use of GnRHa, a form of puberty suppression medication beginning at 12 years of age, as a means of (1) giving adolescents time to explore their gender, (2) determining whether or not more irreversible interventions would be appropriate for long-term gender transition needs, (3) temporarily ameliorating the distress of gender dysphoria by suppressing the development of irreversible secondary sex characteristics, and (4) preventing the need for more invasive procedures later on, should the adolescent ultimately decide to proceed with gender transition (e.g., without breast development, one need not go through top surgery, a mastectomy).

GnRHa mimic the action of the body's natural GnRH, shutting down the feedback loop in the hypothalamus and pituitary gland. GnRHa stop LH hormone secretion, ultimately preventing testosterone secretion for natal males and estrogen levels for natal females. GNRHa effectively shut down the HPG axis and decrease testosterone and estrogen levels. During treatment, pediatric endocrinologists should monitor adolescents. GNRHa come in the form of intramuscular injections or surgically placed implants. The use of GNRHa has some potential risks of use including impact on fertility and bone mass. There is also little data on the long-term impacts of prolonged use of these puberty-suppressing hormones.

The Amsterdam protocol recommended that pubertal suppression is initiated after the child enters Tanner stage II of development in order to understand how the young adolescent reacts to the changes brought on by puberty, considering the prospective literature at the time indicated that many children with gender dysphoria would ultimately not experience gender dysphoria in adolescence [6]. This protocol stressed the importance of a comprehensive assessment and noted that the potential and actual side effects to pubertal suppression do not outweigh the benefits of GNRHa treatment in appropriately screened youth. The protocol also recommended the use of gender-affirming sex hormones as early as 16 years of age, and finally surgery, if desired at 18 years of age.

Since this initial protocol was described, a number of studies have demonstrated that puberty suppression has a number of advantages when treating gender dysphoria of adolescence [7, 8]. The pause on pubertal progression that leads to the suffering associated with gender dysphoria allows for further gender identity exploration and evaluation in a multidisciplinary setting over time. Current research has continued to demonstrate the benefits of puberty suppression. Prospective data indicates that after being treated with GNRHa and subsequent sex hormone treatment for gender dysphoria, adolescents have comparable psychological adjustment when compared to cisgender adolescent controls [9]. Some adolescents feel that they are

able to be perceived as their true gender more effectively, ultimately leading to positive effects on psychosocial adjustment in young adulthood [10]. Cohen-Kettenis and colleagues [11] conducted a follow-up case study of an adolescent who had puberty suppression treatment at 13 years of age, testosterone treatment at 18 years of age, and finally sex reassignment surgery (also known as gender confirmation surgery) at 20 and 22 years of age. This follow-up evaluated psychological, medical, and physical side effects and long-term effects of puberty suppression. This individual reported no regrets about the treatment protocol and was functioning well psychologically, intellectually, and socially. The individual's metabolic and endocrine tests were all within normal limits, and there were no noted health difficulties. In addition to this case study, de Vries and colleagues [12] conducted a study of changes in adolescent behavioral and emotional health who received puberty suppression between 2000 and 2008. Results of this study indicated that adolescents treated with puberty suppression had decreased behavioral and emotional difficulties, though still experienced body dissatisfaction. Despite this, adolescents in this study experienced fewer depressive symptoms and overall improvement in general functioning. Feelings of anxiety and other mood symptoms (e.g., anger) remained the same however. Taken together, these studies indicate that the long-term psychological effects of puberty suppression may outweigh the negative potential side effects when treating gender dysphoria.

The criteria for use of hormone therapy have been defined by the WPATH [3] and the Endocrine Society Guidelines [4] and state that use of hormone-suppressing therapy is indicated when (1) there is a persistent and pervasive history of gender nonconformity or gender dysphoria; (2) the gender dysphoria emerged or worsened with the onset of puberty; (3) any co-occurring psychological, medical, or social difficulties that might interfere with treatment are addressed; and (4) the adolescent and family have given informed consent. These criteria can be assessed through a psychodiagnostic assessment with an expert in gender-affirming treatments. Expertise in gender development, as described by the 2017 Endocrine Society Guidelines [4], is defined thusly:

> "(1) training in child and adolescent developmental psychology and psychopathology, (2) competence in using the DSM and/or the ICD for diagnostic purposes, (3) the ability to make a distinction between GD/gender incongruence and conditions that have similar features (e.g., body dysmorphic disorder), (4) training in diagnosing psychiatric conditions, (5) the ability to undertake or refer for appropriate treatment, (6) the ability to psychosocially assess the person's understanding and social conditions that can impact gender-affirming hormone therapy, (7) a practice of regularly attending relevant professional meetings, and (8) knowledge of the criteria for puberty blocking and gender-affirming hormone treatment in adolescents."

Despite the fact that puberty blockers are generally considered reversible in nature, there are some concerns and potential risks that should be considered when considering GnRHa for an adolescent who meets criteria for gender dysphoria. The following risks have been described, but it is important to note that the long-term risks have not been fully demonstrated nor studied prospectively. Leibowitz and de Vries [13] summarize these hypothetical risks in a review article. They include the possibility of (1) disrupting the exploration of an individual's experience of the

gender of their birth-assigned sex; (2) impacting brain development and processes mediated by sex hormones that affect cognitive development and affect regulation, in particular for young people with co-occurring neurodevelopmental disorders; (3) impacting bone development and the effect on bone mineral density and fracture risk; (4) limiting genitalia growth, particularly relevant for birth-assigned males, which has implications in the future should the youth want to pursue genital surgery given the fact that sufficient penile tissue is necessary for the typical penile inversion procedure when creating a neovagina; and (5) affecting long-term metabolic processes that are still as of yet unknown.

It is important to note that current research is evaluating some of these potential risks. One fMRI study looked at executive functioning in adolescents with gender dysphoria treated with GnRHa and found no significant changes in a planning task [14]. Of note, none of the youth included in this study had any significant co-occurring neurodevelopmental disorders such as attention deficit hyperactivity disorder or autism spectrum disorder. Additionally, preliminary research on the effects of GnRHa on bone health indicates mild reduction in bone mineral density [15], but the implications on fracture risk were not studied. Anecdotally, it is described that when pubertal suppression is used to buy time to explore these issues, families may view the intervention as one step on a linear pathway for gender transition, without necessarily appreciating the exploration aspect that the premise of using pubertal suppression was originally based on. Therefore, parents may not feel the need to bring their adolescents in for continued exploration of gender in a mental health setting and then several years later may show up again with expectations to begin what they perceive to be the next step in treatment for their adolescents: cross-gender hormone therapy. Youth, parents, and families may have co-occurring psychiatric conditions that go untreated as a result, considering there may be a false attribution of these co-occurring symptoms as a *manifestation of* gender dysphoria instead of a *co-occurring condition* that may or may not exist regardless of the adolescent's gender dysphoria.

Ethical debates around pubertal suppression also exist in terms of timing of initiation of GnRHa, duration of treatment, and fertility implications. The original Amsterdam protocol recommended use of GnRHa begin at no less than age 12, but many youth will enter puberty at ages much younger than that. For those youth, waiting until age 12 (more relevant for the birth-assigned females on average) could mean that many of the benefits of pubertal suppression would be missed considering these youth may be well into the later stages of puberty by that time. However, given the unknowns of how long one can safely suppress puberty medically during a time when an adolescent *is physiologically supposed to be going through puberty*, suppressing puberty at 10 years of age could then introduce additional complex questions down the road regarding the timing of the initiation of hormone treatment considering one does not know how safe or unsafe it is to suppress hormones for an extended period of time, however that is defined. In addition to the medical unknowns, there is no data on psychological outcomes of waiting to initiate puberty at age 16 (whether it is the puberty of the patient's birth-assigned sex due to an unlikely reversal of feelings or whether it is due to the puberty of the patient's affirmed gender due to continued gender dysphoria). While fertility itself is not

impacted by the administration of GnRHa in the event that the GnRHa is discontinued (as the individual will continue to go through their natural puberty), should the adolescent wind up moving directly onto cross-sex hormone therapy, then this could very possibly render an adolescent unable to reproduce biologically since they never would go through their birth-assigned sex puberty sufficient enough to develop mature eggs or sperm. One additional logistical factor that is important to consider is whether or not GnRHa can be covered by insurance, as gender dysphoria is currently an off-label indication and the medication can be extremely expensive to obtain, if not covered [16]. In many situations, even if indicated, lack of access to these medications can prohibit their usage for an adolescent.

Therefore, ultimately multidisciplinary care is optimal when making individual decisions for specific youth, and in the event that a multidisciplinary team is not readily available to the mental health provider, seeking expert consultation on these issues from multidisciplinary gender clinic center providers would be prudent. As with all interventions addressing a health-related concern, weighing the risks and benefits of moving forward with the intervention versus not remains a complex yet important component of the risk-benefit analysis. Discussing the fertility implications, surgical implications, and hypothetical unknown effects with families is important. The purpose of describing these complexities is not to suggest universal withholding of these treatments but to help the provider appreciate the full degree of factors that need to be considered when assisting families and youth.

Reversible Androgen Blocking and Menstrual Suppression

In addition to GnRHa, there are other pharmacological interventions that can be used to suppress the effects of hormones released during puberty. These are discussed in more detail in Nahata, Chelvakumar, and Leibowitz [16]. They may be beneficial to use with adolescents who cannot access GnRHa for either lack of insurance coverage or parental consent reasons.

Spironolactone is an antiandrogen agent that can be used as an adjunctive therapy to GnRHa, cross-sex hormones, or as a stand-alone intervention. It is a potassium-sparing diuretic that also has antiandrogen properties, blocking the effects of testosterone on birth-assigned males. Hyperkalemia is a known side effect of these medications, so whoever is prescribing them would typically monitor potassium levels. When used in conjunction with estrogen in a transgender female adolescent, this medication may allow for lower doses of estrogen to be used in order to achieve similar degrees of feminization. Their effectiveness and safety have not been studied in adolescents with gender dysphoria; however anecdotally, they have been used clinically to help adolescents feel their gender dysphoria is being addressed medically [16].

Oral contraceptive pills can be used continuously in birth-assigned females to suppress menstruation, which can be a rather distressing monthly event for the birth-assigned female with gender dysphoria. There are many types of oral contraceptives that can be used to achieve menstrual suppression; however, they should be

prescribed by providers who are familiar with the differences and can monitor the effects safely. Data on the use of these medications for other indications (not gender dysphoria) with adolescents has demonstrated efficacy [17]; however, limited evidence is available on the psychological effectiveness of these medications in the transgender adolescent population [16]. The mental health professional may consider collaborating with a pediatrician or adolescent medicine specialist regarding the use of menstrual suppression to alleviate the distress that menses may have on the psychological well-being of the transgender male patient with gender dysphoria.

Gender-Affirming Sex Hormone Therapy

Gender-affirming sex hormone therapy to treat gender dysphoria includes testosterone for birth-assigned females and estrogen for birth-assigned males. The use of these hormones allows the individual to develop secondary sex characteristics that aligns with their core gender identity. The interventions also reduce endogenous hormone levels. This further affirms the individual's gender identity and is shown to have positive benefits for those who have gender dysphoria. The use of both estrogen and testosterone will potentially impact an individual's emotions as they are essentially going through a second puberty if GnRha were not used or if they are going through puberty for the first time in the event that GnRHa were used. The use of estrogen in birth-assigned males will cause the adolescent to slowly develop breasts, soften their hair, redistribute fat to potentially widen hips, and potentially feminize the face. Feminizing hormone therapy also includes the use of androgen-reducing medications described in the section above, as these medications decrease testosterone activity and help to minimize the dosage of estrogen needed. Testosterone used in birth-assigned females will lead to muscle mass increases, a deepening of the voice, and development of facial hair over time. Tables 3.3 and 3.4

Table 3.3 Estrogen effects and time course [3]

Effect	Onset	Maximum effect
Body fat redistribution	3–6 months	2–5 years
Decreased muscle mass	3–6 months	1–2 years
Softening of skin/decreased oiliness	3–6 months	Unknown
Decreased libido	1–3 months	1–2 years
Decreased spontaneous erections	1–3 months	3–6 months
Male sexual dysfunction	Variable	Variable
Breast growth	3–6 months	2–3 years
Decreased testicular volume	3–6 months	2–3 years
Decreased sperm production	Variable	Variable
Thinning and slowed growth of body and facial hair	6–12 months	More than 3 years
Male pattern baldness	No regrowth, loss stops 1–3 months	1–2 years

Table 3.4 Testosterone effects and time course [3]

Effect	Onset	Maximum effect
Skin oiliness/acne	1–6 months	1–2 years
Facial/body hair growth	3–6 months	3–5 years
Scalp hair loss	>12 months	Variable
Increased muscle mass/strength	6–12 months	2–5 years
Body fat redistribution	3–6 months	2–5 years
Cessation of menses	2–6 months	n/a
Clitoral enlargement	3–6 months	1–2 years
Vaginal atrophy	3–6 months	1–2 years
Deepened voice	3–12 months	1–2 years

show the expected onset of these changes for both estrogen and testosterone as well as the time to expected maximum effect.

The WPATH Standards of Care describe criteria related to treatment initiation. The standards require that individuals must be able to demonstrate capacity to consent to the medication and that any co-occurring psychological/mental health challenges are well controlled. Adolescents also must demonstrate persistent gender dysphoria. These criteria can be assessed through a psychodiagnostic assessment with an expert in gender development, as defined earlier in the chapter. In terms of age of initiation of this intervention, some prior guidelines recommend the use of gender-affirming hormones at 16 [18], though others recommend starting earlier in mid-adolescence [19]. The age requirement can be flexible, though it is recommended that when able, families should work together to support the adolescent seeking this type of intervention. The most recent recommendations from the Endocrine Society state that adolescents younger than the age of 16 should be eligible for gender-affirming hormones and strongly recommend an expert multidisciplinary team of medical and mental health professionals be involved throughout this treatment [4].

The definition of "well-controlled" as it relates to psychiatric co-occurring conditions is also not extremely well defined in the WPATH Standards of Care. Acute psychiatric conditions such as the presence of acute suicidal ideations, a recent psychiatric hospitalization, psychosis, mania, and/or a notable change in the functioning of the individual might be considered "uncontrolled." Long-standing depression and/or anxiety may very well be a manifestation of the gender dysphoria classification itself, and so therefore these issues could be alleviated with hormone treatment. A key task of the mental health provider is to determine the *relationship* between the gender dysphoria and any co-occurring mental health conditions so that the sequence and timeliness of the treatment intervention are appropriate. The cases in the rest of this casebook will serve to illustrate these complexities and guide the mental health provider when developing a treatment plan that is collaborative and affirming in nature with parents and the youth. On one hand, co-occurring psychiatric conditions could very well complicate the diagnostic picture, and therefore treatment of those conditions would be indicated to achieve a degree of "well-controlledness." On the other hand, needless delay of hormone treatment could perpetuate some of the psy-

chiatric symptoms of the co-occurring conditions, and therefore it is prudent to determine the relationship between the gender-related concerns and other issues when considering the hormone therapy.

In addition to considering the criteria that are recommended to start gender-affirming hormones, individuals and families also need to consider the medical risks of gender-affirming hormones. These are outlined in the WPATH Standards of Care [3] and the most recent Endocrine Society Guidelines [4]. Estrogen may lead to increased risk for venous thromboembolic disease, cardiovascular disease, changes in lipid levels, liver enzyme elevations, gallstones, type 2 diabetes, hypertension, and prolactinoma. Testosterone can have an increased risk of polycythemia, weight gain, worsening of lipid profiles, and elevations in liver enzymes. In addition to these medical risks studied in adults, there are limited long-term research on these treatments for adolescents. In addition, for individuals who are nonbinary in their gender identity, this decision-making process may become especially difficult (see chapter on nonbinary gender identities in adolescents for further discussion of these complexities). As with all medical interventions, treatment providers and families need to have informed meetings about the risks and benefits of these medications. Since these interventions are partially reversible, families will be involved in a collaborative decision-making process with multiple parties who may have differing priorities.

Surgery

Gender-confirming surgical procedures are often considered the last step in addressing symptoms of gender dysphoria; however, this is not always the case. For many, use of gender-affirming hormones may be sufficient to manage gender dysphoria; however, for many others, gender dysphoria will not resolve until one or more surgical interventions have been sought. In adolescents, the most common surgery that is becoming increasingly recommended worldwide before the age of 18 is top surgery, or a mastectomy, for transgender males or individuals who are transmasculine with gender dysphoria. Genital surgeries are typically reserved for when an individual is 18 years of age or older.

There are a number of studies identifying the benefits of these surgeries including sexual satisfaction (e.g., Klein and Gorzalka [20]), psychological outcomes (e.g., Gijs, van der Putten-Bierman, and De Cuypere [21]), etc. Despite this evidence, there are fewer studies that include adolescents, as recommendations in the past stated that individuals should to be at the age of majority in their respective country for surgeries with case-by-case exceptions [3]. Overall, methodological difficulties related to studying the impact of gender-confirming surgeries add additional complexity to decision-making as many of the studies are retrospective and some of the interventions (e.g., phalloplasty, the creation of a new penis) still have not yet been perfected to the point where a multitude of patients who would normally seek the intervention would do so considering its complication burden.

One difficulty in studying surgical interventions is directly related to the wide range of interventions available. Types of surgery include "top surgeries" and

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"bottom surgeries." The reason why these surgeries are referred to as "top surgery" and "bottom surgery" is because referring to the specific anatomical feature for an individual who is transgender (e.g., breast, instead of chest) can itself be very challenging to hear. Table 3.5 explains the different types of top and bottom surgeries. Top surgeries include surgeries that are related to the chest and include reconstructive chest surgery and breast augmentation. Bottom surgeries are used to alter genitals or internal reproductive organs.

Other types of surgeries are used to change cosmetic appearance (i.e., face, head, and neck procedures). An individual may choose to have one, none, or multiple surgeries to address their gender dysphoria and live a life that they would like to live. These interventions are complicated and costly, ranging from $5000 to $50,000 and beyond. Besides monetary considerations, there are a number of potential medical and health risks, both short and long term, that are associated with these interventions. Some or all of these costs may be covered through health insurance, as many insurance companies are starting to classify these surgeries as "medically necessary." It is also important to consider the cost of not having surgery, which could be high, as many transgender individuals may continue to experience negative ramifications in public and private situations without the surgical interventions.

In regard to criteria necessary to be eligible for surgical interventions, the WPATH [3] recommends that consent can be given at the age of majority depending on the country the individual resides. While this is the recommendation, there are exceptions to this rule, and at times, there are younger individuals who seek out this intervention. Regardless, one letter for chest surgery and two letters for genital surgery are required for these interventions. Letter writers must be well versed in the diagnosis of gender dysphoria, and best practices dictate that surgeons discuss the different techniques available to the patient, the advantages and disadvantages of each technique, the limitations of the techniques, and risks/complications associated with the techniques for that individual. Individual anatomy and health factors are often taken into account. This is known as the informed consent process in order

Table 3.5 Surgery types

Surgery type	Name of surgery	Use
Top	Breast augmentation	Used to increase size of breast
Top	Reconstructive chest surgery	Removal of breast tissue in order to create a male-contorted chest
Bottom	Orchiectomy	Removal of the testicles, which can also eliminate the need for testosterone blockers
Bottom	Penectomy	Removal of the penis
Bottom	Vaginoplasty	Creation of a vagina using the tissue of the shaft of the penis
Bottom	Metoidioplasty	Increase of clitoris or phallus length without the use of tissue grafts
Bottom	Phalloplasty	Creation of a penis and scrotoplasty is the creation of a scrotum

for the patient to have a realistic expectation of the outcomes of their surgery. Some recommendations state that individuals should live continuously in the gender role congruent with their gender identity and adolescent transgender male patients seeking chest surgery should wait until at least 1 year of testosterone treatment is completed according to the WPATH SOC [3]. Collaboration and communication with the surgeon, just as the mental health provider would do with the medical providers, ensure that the patients' unique needs are best addressed. This provides the surgeon with the opportunity to understand the adolescent's psychosocial factors when discussing potential interventions. This also provides the mental health provider with the opportunity to learn about the surgical procedures, pre-, peri-, and postoperative course, potential complications, and other necessary pieces of information about the procedure so that they can assist the patient and family through the process.

One evolving area of clinical practice and research is related to the adolescents with gender dysphoria whose core gender identity is gender nonbinary. Many of these adolescents are seeking chest surgery exclusively and do not want the masculinizing effects of testosterone. It is important to understand what the desires of the patient are and take these factors into account when making recommendations that involve anything that is irreversible. Overall, the guidelines are less clear and require more targeted research to evaluate risks and benefits.

Conclusion

The role of puberty suppression, gender-affirming hormones, and surgical interventions is extremely important in the evaluation, management, and treatment of transgender adolescents. While there is some emerging research, there is still a lack of full understanding of the impact of these interventions medically, psychologically, and psychosocially. de Vries and colleagues [9] conducted a longitudinal cohort study of 55 adolescents who met criteria for gender dysphoria assessed before the start of puberty-suppressing drugs, at the initiation of gender-affirming hormones, and 1 year after gender reassignment surgery. This study indicated improved psychological functioning over time, fewer behavioral and emotional problems after puberty suppression, and finally, gender dysphoria persisted until gender reassignment surgery. While there are some limitations to this study, medical interventions are demonstrated to have an important impact on mental health considerations for adolescents and their families, and further research and advocacy is needed.

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Chapter 12
Gender Dysphoria and Psychotic Spectrum Disorders

Aron Janssen and Brandon S. Ito

Introduction

This chapter highlights the experience of Amy, a 20-year-old transgender female with diagnoses of schizoaffective disorder, gender dysphoria, marijuana use disorder, and a history of cocaine abuse who was initially referred to an outpatient gender and sexuality mental health clinic at age 17 for an evaluation of gender and sexual identity issues. This case hopes to illustrate the developmental pathway of an adolescent with gender dysphoria and psychosis, to examine unique challenges in treating patients with both psychotic spectrum disorders and gender dysphoria, and to highlight the frequent traumas transgender individuals' face as a part of their gender identity.

Brief Literature Review

Gender affirmative care is effective in diminishing gender dysphoria (GD) for 80% of individuals, and 78% of individuals with GD that receive gender affirmative care had significant improvement in co-occurring psychiatric symptoms, including those of depression, anxiety, substance abuse, and suicidality [1]. And yet, the very

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domains that can improve with appropriate treatment of GD are also those that represent barriers to accessing that care. According to the World Professional Association of Transgender Health Standards of Care, Version 7, co-occurring psychiatric symptoms must be "reasonably well-controlled" to access gender-affirming hormones and surgery. For episodic illnesses, the concept of assessing for reasonably well-controlled symptoms is easier to define; however, for chronic psychotic disorders, this becomes a much more complex task.

Historically, until the mid-twentieth century, transgender individuals were assumed to be severely mentally disturbed in order to want to access care. The prevailing opinion of that time was that GD could exist only within the context of severe personality disorders or psychosis [2, 3]. Over time, more research and clinical experience pointed toward complex psychiatric symptoms being result of untreated GD as opposed to the cause. Alternatively, others have suggested that the reason for the increased psychiatric symptoms seen in transgender individuals as compared to the general population is related to the minority stress and increased exposure to trauma, bullying, and rejection as a result of their identity. That is, daily exposure to stigma and bias (be it covert or overt) has significant long-term impact on the psychosocial outcomes of a minority community. For transgender youth who face increased risk of violence and rejection, we would expect to see increased rates of psychopathology in this population.

Despite these advances in understanding the relationship between psychiatric symptoms and GD, individuals with psychotic spectrum symptoms and GD are still often thought to have the GD stem from the psychosis as opposed to the psychosis and GD co-occurring independently of one another. Recent research demonstrates that rates of psychosis among individuals with GD are no higher than in the general population [4]. And yet, much of the contemporary literature about the overlap between psychosis and GD discusses the need for extreme caution in allowing patients to access care. In a study from 2001 [5], the author cautioned that schizophrenic patients commonly present behind a mask of GD for surgery. Other studies, while less overtly biased, have excluded patients from enrollment when psychotic symptoms were present, making it difficult to draw conclusions about the specific needs for this population. Specific concerns raised include the potential impact of hormone treatment on psychotic symptoms, the capacity to provide consent among those with psychosis, the possibility of impulsive decision-making and/or regret, and the availability of safe, stable housing for recovery. Unfortunately, data on most of these concerns is sparse and limited only to case studies in the literature.

Specifically related to masculinizing hormones, there is literature to suggest that unmonitored, high-dose anabolic steroid use can lead to psychotic symptoms [6]. However, most of the participants studied used metabolites of testosterone, rather than testosterone itself. Additionally, systematic review of the impact of hormones on the mental health of individuals with GD do not demonstrate any elevated levels of psychosis among participants [7]. That said, it is difficult to draw conclusions from this research—the data on high-dose testosterone derivatives is not analogous to the use of testosterone in GD, and many individuals with active psychosis have historically been unable to access hormonal care, so the number of individuals with

chronic psychotic disorders in the systematic review is negligible. As for feminizing hormones, there is some evidence to suggest that estrogen is actually protective against psychosis in vulnerable individuals [8] and may explain why women have a later onset of initial symptoms of schizophrenia and why symptoms are exacerbated during low estrogen states. Again, we must be careful not to glean too much from this data, as systematic study of the impact of estrogen on individuals with both GD and psychosis has not been done.

However, more recent literature [9] has begun to compile case examples of the successful treatment of GD among the chronically psychotic population. These case studies have been able to demonstrate successful treatment with appropriate support.

In addition to the concern about the impact of gender-affirming care on the experience of psychiatric symptoms, there have also been concerns raised about the impact of psychiatric symptoms on the ability to follow through with the necessary steps for successful treatment, particularly for surgery. Historically, individuals with chronic psychotic symptoms have had their ability to consent to procedures underestimated by their medical providers. Many individuals with chronic psychotic symptoms are able to successfully navigate complex procedures and treatments with appropriate supports. However, there are occasional more complex structural barriers for individuals with psychosis that are independent of their mental illness that may impact ability to recovery from surgery. For example, many individuals with chronic psychotic symptoms lack stable housing and may have difficulty maintaining aftercare in a safe manner without support. In assessing all individuals for preparedness for surgery, but in particular those with chronic psychotic conditions, these potential structural barriers should be assessed and addressed as a part of the presurgical process.

Case Report

Amy began to identify as gay male at the age of 15 and struggled initially to come to terms with her sexuality. She found herself attracted emotionally and sexually exclusively to boys but found the label of gay didn't feel quite right. She had experienced some preferences for more stereotypically feminine interests and dress for a brief time in childhood but had never previously had thoughts about wishing she were or experiencing herself as a girl. Despite her discomfort with the label gay, and what it mean to her burgeoning gender identity, she nevertheless came out as gay to friends and family.

Her experience in coming out was met by conflict both at home and at school. At school in particular, she was constantly verbally assaulted by her classmates and was the victim of violence from peers. She became depressed at that time and began seeing both a psychologist and psychiatrist and treated with aripiprazole for a few months. Partly due to a rejection of her sexual orientation, she became estranged from her biological father whose parents had separated when she was a few months

old. Later that year, she also experienced her first sexual assault by a person she had met through a popular phone dating application. She initially told nobody about the assault and began to withdraw socially and began using drugs and alcohol during the weekends and occasionally while at school.

At the age of 16 years, Amy was psychiatrically hospitalized for the first time for depression and concurrent cocaine abuse for 2 weeks and discharged on escitalopram. Amy defined her gender identity as "androgynous" during this time, occasionally dressing publicly in woman's clothing, wearing makeup and long-haired wigs. She used both male and female gendered names among different social groups. As a result of ongoing bullying, Amy transferred to a specialized school for LGBTQ youth during her junior year of high school; however, that year there was a notable decline in her academics to the point where she was barely able to advance to her senior year. She was unable to maintain regular outpatient psychiatric follow-up but engaged in two outpatient substance abuse rehab programs at the insistence of her family.

As she began to come to terms with her gender identity as that of a woman, she also sought sex hormone treatment for the first time; however, she was told that she would not be eligible for hormone treatment through the clinic until she turned 18 years of age. She was then referred to the child and adolescent psychiatry gender and sexuality specialty clinic for further evaluation of gender identity issues.

Following her initial evaluation in the gender and sexuality clinic, Amy was instructed to go to the emergency room for a psychiatric evaluation due to her family's concerns about her recent odd behavior and safety. In the emergency room, it was noted that increasingly over the past few months, Amy began to voice that someone was "tapping" her phone, using her social security number, and she frequently worried about the safety of her family. This was accompanied by a dramatic change in dress, use of excessive makeup, and vague statements about needing to leave the family to join a secret society to obtain fame and fortune. Other symptoms included ideas of reference through the radio and television. Amy also endorsed feelings of depression, sleeping excessively, having little pleasure in activities, poor energy, poor concentration, and decreased appetite with a 20-pound weight loss over the past couple of months. While denying a decreased need for sleep or insomnia, the family had also noted that she had been spending money excessively and exchanging sex for money. Amy reported smoking two to three cigarettes daily, using marijuana daily, and drinking one to two days per week. She denied recent cocaine or stimulant use, and her urine toxicology was positive only for THC.

On exam, Amy was noted to be bizarrely dressed, wearing an unkempt blonde wig, dark sunglasses throughout the interview, "dramatic" eye makeup, excessive lipstick, and tight-fitting female clothing. She had a tangential thought process, with noted persecutory and grandiose delusions, and preoccupations about the secret society. Her mood was "scared," her affect was labile, and her insight and judgment were impaired. Her medical workup included routine psychiatric labs and a head CT, which were all within normal limits. Amy was admitted to the inpatient psychiatric unit and initially treated with risperidone, which was titrated up to 4 mg at bedtime with an improvement in paranoid ideation and psychotic symptoms. Amy

was discharged home with a diagnosis of schizophreniform disorder given the short duration of symptoms.

Amy was sent to the emergency room again a week later by her outpatient psychiatrist due to recurrent psychotic symptoms, mood lability, ideas of reference, and vocalizing a need to leave the family in order to join the secret society. When questioned about her plan to join the secret society, she stated that her plan was to begin walking aimlessly until she was "found" by them. Amy was again admitted to the inpatient psychiatric unit, and due to the ongoing mood lability and concern for bipolar illness, Amy was started on lithium and titrated up to 1200 mg. She remained in the hospital for 3 weeks, and risperidone was cross-taped to olanzapine, with significant improvement in both mood and psychotic symptoms. Amy was diagnosed with schizoaffective disorder and discharged home to family. She was seen in the emergency room once more the following week for ongoing delusions and plans to leave and join the secret society; however, she was evaluated and discharged back home.

Over the next couple of years, Amy was seen in outpatient treatment and treated with aripiprazole and escitalopram for her diagnosis of schizoaffective disorder and GD. She was seen in a combination of individual therapy in a dynamic, open-ended frame and medication management on a weekly basis. She continued to express her desire for estrogen, and given her history of GD, and the relative stability of her psychiatric symptoms, she was started on estrogen with careful monitoring from her entire treatment team. In many ways, she understood that her psychiatric treatment was a requirement for ongoing hormonal care and was motivated to attend her sessions to ensure she was able to access care.

Through her treatment, Amy maintained a strong and consistent gender identity. Amy maintained an intense desire and insistence to be a woman and consistently attended sessions with long hair, makeup, and female attire. She spoke frequently about her desire to have gender reassignment surgery and wanting to "have it off" in reference to her male genitalia. She was noticeably distressed during a session in which she did not have time to shave her face prior to arriving and endorsed high levels of discomfort and embarrassment about having male secondary sex characteristics. She also frequently made reference to her role as an older sister to her sibling and her role in the strong female lineage in the family. She spoke frequently about opening a "new chapter" following her gender reassignment surgery and talked with enthusiasm her ability to wear lower-cut shirts and skirts if she desired.

In the middle of the year with her current treatment provider, Amy began to report increasing depression, fatigue and hypersomnia, irritability, and anxiety. During this time, she was also noted to be consistently more distressed and tearful in session, along with an increase in the volume and veracity of delusional content. Her clinical picture at this time was complicated by concurrent marijuana use and suspected alprazolam abuse by the family. Due to concern for an episode of bipolar depression, along with ongoing side effects of sedation from aripiprazole, aripiprazole was cross-tapered to lurasidone with significant improvements in mood, sedation, and a decrease in delusional content to baseline levels.

Throughout the year, content of individual sessions frequently centered around feelings of being "stuck" in life, especially in terms of employment and romantic relationships. It was noted that since treatment at the beginning of the year, there had been little conversation about her gender reassignment surgery, which had been the initial stated goal at the beginning of the year. Following a discussion with both Amy and her family, a surgical consult was scheduled with improvements in her mood and future orientation.

During the latter part of the year, Amy endured a sexual assault resulting in a significant suicide attempt by overdose on her prescribed hormones and psychiatric medications. Following evaluation in the emergency room, she was admitted for a brief inpatient hospitalization and restarted on her medications.

Throughout treatment, Amy would frequently reminisce about her life as a gay male, commenting on how much she enjoyed her party lifestyle and popularity during those years. It was reflected back to Amy that this was also a time of greater acceptance of her gender identity, from her friends, her family, her romantic relationships, and to society in general. Amy's ongoing delusions were conceptualized as fantasy to escape the struggles of not only an individual with a mental illness but also being a transgender individual. By scheduling her surgical consult, Amy felt a needed sense of acceptance from her family of her gender identity as a female. Although she continued to endorse delusions throughout her treatment that varied in severity based upon mood symptoms and concurrent substance use, her stated gender identity remained constant throughout her treatment course. At this point, she is scheduled for her gender-affirming surgery under close watch from her family and her outpatient treatment team.

Notably, family members were involved throughout her treatment, with the primary family intervention being psychoeducation about GD and transgender issues along with the chronicity and stability of psychotic delusions. Amy's family was also very proactive in exploring community volunteer opportunities, supportive employment, and support groups through NAMI.

Case Discussion

Many studies have shown that transgender individuals face significant amounts of discrimination, harassment, violence, and family rejection. Members of the LGBT community, and especially transgender individuals, face a high degree of what is termed "minority stress." These factors play a tremendous role in the development and maintenance of psychopathology. Independent of this, GD is present across all societies, ethnicities, and backgrounds, and individuals with GD are not spared affliction with co-occurring psychiatric illnesses, including chronic psychotic illnesses such as schizophrenia and schizoaffective disorder. Unfortunately, the literature is limited on best approaches for individuals with both GD and psychotic illness, and, as a result, these individuals are often denied access to care.

For Amy, since her initial evaluation in the specialized gender service, she had come to understand herself as a woman and met full diagnostic criteria for GD. Diagnostically, prior to referring for either hormones or surgery, it was important to track Amy's symptoms of GD during her multiple emotional states. Due to the chronic nature of her psychotic illness, and her frequent experience of relapse of symptoms, there were multiple opportunities to assess her experience of her gender both during times of stability and times of overt psychosis. It is the consistent presence of GD across illness states that ultimately allowed her treatment providers to feel confident in connecting her to medical and surgical care for her GD. For Amy, when she was able to articulate clear understanding and insight into her psychotic symptoms, she experienced GD. When she was in the throes of psychosis and believed to the core of her being that she could wander the streets and be picked up by a secret society, she experienced GD. In many ways, her GD became the most consistent part of her experience, and regardless of illness state, she had a clear and consistent desire to medically and surgically transition and even in her most psychotic states could still clearly articulate the risks and benefits of the choices in her care.

As such, the challenge for the outpatient treatment providers was not if hormones or surgery would be appropriate but how to manage it safely. As it turns out, the hormones made no significant impact on her psychotic symptoms, but it did make her feel more whole and more comfortable in her body and her identity. Surprisingly, one of the biggest challenges was about the structural barriers to accessing care. As a part of her relapsing illness, Amy would often disappear from treatment and have difficulties in remembering follow-up visits. Some clinicians might interpret these missed appointments as possible unconscious ambivalence to treatment, and that was discussed as a possibility; however, it was clear with ongoing treatment that it was better explained as a primary failure in executive functioning due to her psychotic illness. Thus, the treatment team had to take a primary role in helping Amy to structure her weeks and put into place home-based resources to help her access the care she so desired and needed.

Conclusion

Amy has a chronic and severe mental illness that will persist throughout her life. She also happens to be a transgender woman with a tremendous number of strengths and a confidence in her sense of self and wishes for her future. Historically, her psychotic symptoms would have barred her from accessing gender-affirming care, and certainly they complicated her treatment course but often in ways that were unexpected. There was an appropriate balance of caution and advocacy for her care throughout, even though at times it was unclear if things were moving too quick or too slow. However, we found that if we used the basic ethical principles of autonomy, beneficence, non-malfeasance, and justice as a frame for treatment, it became much more straightforward on how to proceed.

Regarding autonomy, does an individual, even an individual who has a hard time differentiating reality from fantasy, have specific understanding about the risks, benefits, and alternatives of a medical intervention? Do they have capacity to consent to the specific interventions at hand? Is there wish for care consistent across disease states? If the answer is yes, regardless of psychotic symptoms, then they have a right to autonomy. Does gender-affirming care help the patient, fulfilling the ethical principle of beneficence? We know that accessing gender-affirming care improves quality of life and diminishes GD, and without evidence to the contrary, we can assume that it will also benefit those with psychotic symptoms. As for non-malfeasance, or the concept of doing no harm, we must build a more robust evidence base—there is no compelling evidence that estrogen or testosterone at usual treatment doses is any more dangerous to those with severe mental illness; however, there is also no compelling evidence that it is safe. There is simply no evidence either way. Which finally brings us to justice—the right to equal access of care. It is this ethical principle that has been most disregarded for individuals with severe psychotic illness. To be just in our care means to advocate for our patients who are unable to advocate for themselves and to get them access to care that is beneficial and necessary, even if it is at times controversial.

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Effects of gender affirming therapies in people with gender dysphoria: evaluation of the best available evidence

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1. Introduction

We prepared this report to fulfill a request from the Florida Agency for Health Care Administration. This report contains three documents: 1. Main document (this document) summarizing the methodology used and the findings, 2. Methods document, which provides a detailed description of the systematic methodology used to find, prioritize, appraise, and synthesize the evidence, and 3. Results document, which describes the evidence available, the estimates of the effects of gender affirming therapies, and the certainty (also known as quality) of the evidence.

This document is organized in four parts. First, we describe the credentials and expertise of the health research methodologists conducting this evidence evaluation. Second, we summarize the methodology used. Third, we summarize the main findings. Finally, we briefly discuss strengths and limitations of our process and of the evidence.

2. Credentials and expertise

Two experts in health research methodology, who specialize in evidence synthesis to support decision making, prepared this report. Their relevant credentials and expertise are described below.

Dr. Romina Brignardello-Petersen: Assistant Professor at the Department of Health Research Methods, Evidence, and Impact, at McMaster University. Dr. Brignardello-Petersen obtained a DDS degree (University of Chile) in 2007, an MSc degree in Clinical Epidemiology and Health Care Research (University of Toronto) in 2012, and MSc in Biostatistics (University of Chile) in 2015, and a PhD in Clinical Epidemiology and Health Care Research (University of Toronto) in 2016. Dr. Brignardello-Petersen has worked in evidence synthesis projects since 2010, and her research has focused on the methodology for the development of Systematic Reviews and Clinical Practice Guidelines since 2012. Through January 2022, she has published 122 peer reviewed scientific articles (24 as a first author and 9 as a senior author). Dr. Brignardello-Petersen has acted as a research methodologist for several groups and organizations, including the World Health Organization, the Pan-American Health Organization, the American Society of Hematologists, the American College of Rheumatology, and the Society for Evidence Based Gender Medicine, among others. Her research program has been awarded over $2M CAD from the Canadian Institutes for Health Research. Dr. Brignardello-Petersen has no lived experience as a person or family member of a person with gender dysphoria, and her research interests are not in this area.

Dr. Wojtek Wiercioch: Postdoctoral Research Fellow at the Department of Health Research Methods, Evidence, and Impact, at McMaster University. Dr. Wiercioch obtained an MSc degree (2014, McMaster University) and a PhD degree (2020, McMaster University) in Health Research Methodology. Dr. Wiercioch has worked in evidence syntheses projects since 2011, and his research focuses on evidence synthesis, guideline development methodology, and the guideline development process. Through April

2022, he has published 86 peer-reviewed scientific articles. Dr. Wiercioch has acted as a guideline methodologist for several groups and organizations, including the World Health Organization, the American Society of Hematologists, the Endocrine Society (of America), and the American Association for Thoracic Surgeons, among others. Dr. Wiercioch has no lived experience as a person or family member of a person with gender dysphoria, and his research interests are not in this area.

3. Methods

We conducted an overview of systematic reviews. We used a reproducible approach to search, select, prioritize, appraise, and synthesize the available evidence, following high methodological standards. We describe full details of the methodology in an accompanying document.

In brief, we searched for systematic reviews published in English language in Epistemonikos, OVID Medline, and grey literature sources, through April 30, 2022. We selected systematic reviews which included studies on young individuals with a diagnosis of gender dysphoria, who received puberty blockers, cross-sex hormones, or surgeries; and in which authors reported data regarding outcomes important to patients: gender dysphoria, depression, anxiety, quality of life, suicidal ideation, suicide, adverse effects, and complications. Systematic reviews could have included any type of primary study design.

The two reviewers screened all titles and abstracts, followed by full text of potentially relevant systematic reviews. We then prioritized the most useful systematic review providing evidence for each of the outcomes, using pre-established criteria that considered date of publication, applicability, availability of outcome data, methodological quality of the systematic review, and usefulness of the data synthesis conducted in the systematic review (see methods document for details).

After abstracting data from the systematic reviews, we synthesized the best available evidence for each of the outcomes, and assessed the certainty (also known as quality) of the evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. We conducted GRADE assessments using the information provided by the systematic review authors (risk of bias of primary studies, characteristics of included studies, results reported by the studies). We present the all the information about outcomes in GRADE summary of findings tables.

In addition, to evaluate the robustness of our conclusions, we systematically searched for and evaluated primary studies answering the questions of interest published after the authors of the included systematic reviews conducted their searches.

4. Results

We included 61 systematic reviews, from which 3 addressed the effects of puberty blockers, 22 addressed the effects of cross-sex hormones, 30 addressed the effects of surgeries, and 6 addressed the effects of more than one of these interventions. After our prioritization exercise, we included information from 2 systematic reviews on puberty blockers, 4 on cross-sex hormones, and 8 on surgeries.

4.1 Puberty blockers

For most outcomes (except suicidality), there is no evidence about the effect of puberty blockers compared to not using puberty blockers. In other words, no studies compared the outcomes between a group of people with gender dysphoria using puberty blockers and another group of people with gender dysphoria not using them. Therefore, it is unknown whether people with gender dysphoria who use puberty blockers experience more improvement in gender dysphoria, depression, anxiety, and quality of life than those with gender dysphoria who do not use them. There is very low certainty about the effects of puberty blockers on suicidal ideation.

The studies included in the systematic review reported outcomes among a group of people with gender dysphoria after receiving puberty blockers. Low certainty evidence suggests that after treatment with puberty blockers, people with gender dysphoria experience a slight increase in gender dysphoria, and an improvement in depression, and anxiety. Low certainty evidence also suggests that a moderate percentage of patients experience adverse effects. The findings must be interpreted considering that these studies did not have a comparison group, and that it is unknown if people with gender dysphoria that do not use puberty blockers experience similar or different outcomes.

4.2 Cross sex hormones

For almost all outcomes (except breast cancer) there is no evidence about the effect of cross sex hormones compared to not using cross sex hormones. In other words, no studies compared the outcomes between a group of people with gender dysphoria using cross sex hormones and another group of people with gender dysphoria not using them. Therefore, it is unknown whether people with gender dysphoria who use cross-sex hormones experience more improvement in gender dysphoria, depression, anxiety, quality of life, and suicidality than those with gender dysphoria who do not use cross-sex hormones. There is low certainty evidence suggesting that cross-sex hormones may not increase the risk of breast cancer.

The studies included in the systematic reviews reported changes in the outcomes among a group of patients with gender dysphoria after the use of cross-sex hormones. Low certainty evidence suggests that after treatment with cross-sex hormones, people with gender dysphoria experience an improvement in gender dysphoria, depression, anxiety, and suicidality. There is very low certainty evidence about the changes in quality of life. There is moderate certainty evidence suggesting a low prevalence of venous thromboembolism after treatment with cross-sex hormones. The findings must be interpreted considering that these studies did not have a comparison group, and that it is unknown if people with gender dysphoria that do not use cross-sex hormones experience similar or different outcomes.

4.3 Surgeries

There were no systematic reviews and studies reporting on gender dysphoria, depression, anxiety, and suicidality. Therefore, the effects of surgeries on these outcomes (when compared to a group of patients with gender dysphoria who do not undergo surgery), or the changes in these outcomes (improvements or deterioration) among patients who undergo any gender-affirming surgery is unknown. Because of the lack of comparative studies, it is also unknown whether people with gender dysphoria who undergo surgeries experience more improvement in quality of life or less regret than those with gender dysphoria who do not undergo any surgeries. There is low certainty evidence suggesting that a low percentage of participants experience regret, and very low certainty evidence about changes in quality of life after surgery.

In assigned females at birth, low certainty evidence suggests that a high percentage of people are satisfied after chest surgery. There is very low certainty evidence, however, about satisfaction after bottom surgery, and about complications after both chest and bottom surgery. In assigned males at birth, low certainty evidence suggests a high percentage of people satisfied and a low percentage of people experiencing regret after vaginoplasty. There is very low certainty, however, about satisfaction with chest surgery and complications and reoperations after bottom surgery.

4.4 Evidence published after the systematic reviews selected

We found 10 relevant studies that were published after the systematic reviews were conducted. This evidence was not sufficient to importantly change the conclusions previously made.

5. Discussion

5.1 Summary of the evidence

In this report, we systematically summarized the best available evidence regarding the effects of puberty blockers, cross-sex hormones, and surgeries in young people with gender dysphoria. We did not find evidence about the effect of these interventions on outcomes important to patients when compared to not receiving the intervention. We found low and very low certainty evidence suggesting improvements in gender dysphoria, depression, anxiety, and quality of life, as well as low rates of adverse events, after treatment with puberty blockers and cross-sex hormones.

5.2 Completeness and applicability

There are several gaps in the evidence regarding the effects of puberty blockers, cross-sex hormones, and surgeries in patients with gender dysphoria. Although we found some evidence for all the outcomes of interest, the evidence is suboptimal: several limitations included the lack of studies with a comparison group, and the risk of bias and imprecision, resulting in low or very low certainty evidence for all outcomes.

The applicability of the evidence may also be limited. Although we only rated down for indirectness when it was considered a serious problem (i.e., in evidence about the effects of surgeries, which was collected from people who were importantly older than the target population in this report), there are also potential applicability issues to consider in the evidence regarding the effects of puberty blockers and cross-sex hormones. It is not clear to what extent the people included in the studies were similar enough to the people seeking these treatment options today. For example, some of the included studies were conducted in people who had a diagnosis of gender dysphoria confirmed with strict criteria, as well as a supportive environment. It is important to take into account to what extent this may compromise the applicability of the results to people who are not in the same situation.

5.3 Strengths and limitations of the process for developing this report

We followed a reproducible process for developing this report. We used the highest methodological standards and the approach to evidence synthesis we generally use when supporting organizations in the development of their guidelines. This approach is based on prioritizing the sources of evidence most likely to be informative (i.e., to identify and use the evidence with the highest certainty level).

To follow the principles for evidence-based decision making, which require using the best available evidence to inform decisions, we summarized the best available evidence. Because knowing the best

available evidence necessitates being aware of all the available evidence, we based this report on systematic reviews of the literature. We chose the most trustworthy and relevant systematic reviews among many published reviews.

One potential limitation of the process is that, due to feasibility concerns, we relied on the information reported by the systematic reviewers. Most of the systematic reviews we used, unfortunately, were judged at moderate or low methodological quality, which may raise concerns about the trustworthiness of the evidence presented in this report. We believe, however, that the results and conclusions of this report would not be importantly different had the systematic reviews been conducted following higher methodological standards. Because there are no randomized controlled trials, well-conducted comparative observational studies, or very large case series (which include a large sample of consecutive patients who are representative of the whole population) addressing the effects of puberty blockers, cross-sex hormones, and surgeries; the certainty of the evidence about the effects of these interventions is likely to continue being low or very low, even if a few more studies are included (as observed after searching for primary studies published after the reviews were conducted) or some data points were reported inaccurately in the systematic reviews.

Also due to feasibility concerns, the scope of this report was limited to outcomes that are important to patients. Although some may question the decision of not including surrogate outcomes for which there is evidence available (e.g. bone density, blood pressure), decision makers should rarely consider these outcomes and should instead focus on outcomes that do matter to people and stakeholders (e.g., fractures, cardiovascular events).

5.4 Implications

The evidence evaluating the effects of puberty blockers, cross-sex hormones, and surgeries in people with gender dysphoria has important limitations. Therefore, decisions regarding their use should carefully consider other relevant factors. At a patient level, these factors include patients' values and preferences (how patients trade off the potential benefit and harms - what outcomes are more important to them), and resources needed to provide the interventions (and the availability of such resources). At a population level, in addition to these factors, it would be important to consider resources needed to implement the interventions, feasibility, acceptability by relevant stakeholders, and equity.

It is important to note that when there is low or very low certainty evidence, it is rarely appropriate to make decisions that will be applied to the majority of the patients (equivalent to strong recommendations). This implies, at the patient level, that shared decision making is a key part of the decision-making process. At a policy level, extensive debate may be needed.

6. Conclusions

Due to the important limitations in the body of evidence, there is great uncertainty about the effects of puberty blockers, cross-sex hormones, and surgeries in young people with gender dysphoria. This evidence alone is not sufficient to support whether using or not using these treatments. We encourage decision makers to be explicit and transparent about which factors play an important role in their decision, and how they are weighed and traded off.

Methods

To ensure completeness and feasibility of the evidence review, we used an approach in which we prioritized the types of studies according to the design that was more likely to provide the best available evidence. First, we searched for systematic reviews of the literature. Second, we appraised all existing systematic reviews to select the most trustworthy (highest methodological quality, most up-to-date, most applicable) from which to draw conclusions. Third, we used the information presented in the systematic reviews to abstract information regarding the effects of the interventions of interest. Fourth, we assessed the certainty of the evidence (also known as quality of the evidence) abstracted from the selected systematic reviews. We planned to search for primary studies if systematic reviews were not found.

Information sources: We searched for existing systematic reviews in:

1. Epistemonikos (https://www.epistemonikos.org), an electronic database that focuses on systematic reviews. We used a comprehensive search strategy based on the population, using the terms "gender dysphoria", "gender identity disorder" and "transgender". We conducted this search on April 23, 2022.
2. OVID Medline. We used a search strategy based on the population and the interventions of interest, as well as an adaptation of a filter for systematic reviews from the Health Information Research Unit at McMaster University. We conducted this search on April 23, 2022.
3. Grey literature; we conducted a manual search in the websites of specific health agencies: National Institutes for Health and Care Excellence (NICE), Agency for Healthcare Research and Quality (AHRQ), Canada's Drug and Health Technology Agency (CADTH), and the website from the Society for Evidence-Based Gender Medicine (SEGM). We conducted these searches between April 27-30, 2022.

We used no date limits for the searches, but we did limit to systematic reviews published in English. Search strategies are available in Appendix 1.

Eligibility criteria: We included systematic reviews, which we defined as:

1. Reviews in which the authors searched for studies to include in at least one electronic database, and in which there were eligibility criteria for including studies and a methodology for assessing and synthesizing the evidence, or
2. Reviews in which the authors searched for studies to include in at least one electronic database, and although there was no description of eligibility criteria or methodology, the presentation of the results strongly suggested that the authors used systematic methods (e.g. flow chart depicting study selection, tables with the same information from all included studies, synthesis of data at the outcome level).

We screened systematic reviews using the following criteria for inclusion:

- ***Type of participants:*** Young individuals (< 25 years old) with a diagnosis of gender dysphoria/gender identity disorder. We included reviews in which authors used any label and diagnostic criteria for this condition. We included reviews in which the participants in the reported studies were older if it was the only evidence available for a specific question. We excluded reviews with mixed populations (i.e. with and without gender dysphoria) in which people without gender dysphoria constituted more than 20% of the total sample.

- ***Type of Interventions***: Puberty blockers, cross-sex hormones, gender affirming surgeries. We included any type of puberty blockers and cross-sex hormones, provided with any regimen. We included the following surgeries: phalloplasty, vaginoplasty, and chest surgery (mastectomy or breast implants/augmentation). We only included these when they were performed for the first time (i.e., not revision surgeries).

- ***Type of comparison:*** When the systematic reviews included comparative studies, the comparator of interest was no intervention. Participants could have received psychotherapy or counselling as a cointervention (in both groups).

- ***Type of outcomes:*** Gender dysphoria, mental health outcomes (depression and anxiety), quality of life, suicidal ideation, suicide, adverse effects (for puberty blockers and cross-sex hormones only), and satisfaction, complications, reoperation, and regret (for surgeries only). We included any length of follow-up. We excluded surrogate outcomes such as blood pressure, bone mineral density, kidney or liver function test values, etc.

- ***Type of studies included in the systematic reviews:*** Any clinical study (studies in which the researchers recruited and measured outcomes in humans) regardless of study design. This included randomized clinical trials, comparative observational studies, and case series. Because we could not quantify effect measures, incidence, or prevalence, we excluded case reports.

We excluded systematic reviews published only in abstract format, and those that we could not retrieve in full text (no access through the McMaster University library, or open access online).

Selection process: The two reviewers screened all titles and abstracts independently and in duplicate, followed by screening of full texts of potentially eligible systematic reviews independently and in duplicate, using the systematic review online application Covidence (https://www.covidence.org). We solved disagreements by consensus.

To select the most useful systematic reviews among all of those that met the eligibility criteria, we used the following prioritization criteria:

1. Date of publication: we prioritized systematic reviews published within the last 3 years (2020-2022)

2. Match between eligibility criteria of the review and the question of interest: we prioritized reviews in which the authors specifically included the population, intervention, comparison, and outcomes of interest for this evidence review
3. Outcome data available: we prioritized systematic reviews in which the authors report outcome data
4. Methodological quality: we used a modified version of the items in AMSTAR 2.[1] We modified the items to ensure assessment of methodological rather than reporting quality (Table 1). We rated each systematic review as having high, moderate, low, or critically low methodological quality, according to the guidance from the developers of the tool.[1] We reached consensus on critical items that determined this rating (Table 1). We prioritized selection of systematic reviews with highest methodological quality.

For surgical interventions, in addition, we prioritized systematic reviews that covered all gender affirming surgeries (instead of focusing on a specific type of surgery).

We selected a systematic review specifically for each of the outcomes of interest. In other words, we chose the best systematic review to inform each outcome. Each systematic review, however, could inform more than one outcome.

Table 1: Items used to rate the methodological quality of the eligible systematic reviews

AMSTAR Item	Modification to measure methodological quality
1. Did the research questions and inclusion criteria for the review include the components of PICO?	Does the review have a clear question and are the eligibility criteria for studies consistent with the question?
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	No modification needed
3. Did the review authors explain their selection of the study designs for inclusion in the review?	No modification needed
4. Did the review authors use a comprehensive literature search strategy?	Did the authors search in at least 2 electronic databases, using a reproducible search strategy?
5. Did the review authors perform study selection in duplicate?	No modification needed
6. Did the review authors perform data extraction in duplicate?	No modification needed
7. Did the review authors provide a list of excluded studies and justify the exclusions?	No modification needed
8. Did the review authors describe the included studies in adequate detail?	No modification needed
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	No modification needed

10. Did the review authors report on the sources of funding for the studies included in the review?	Did the review authors consider conflicts of interest and how they may have affected the results of the primary studies?
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?	Was the synthesis of evidence done appropriately? (outcome level, appropriate meta analysis or narrative synthesis)
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Did authors use subgroup or sensitivity analysis to assess the effect of risk of bias in meta-analytic results? Likely not applicable to most cases
13. Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review?	Did the review authors incorporate an assessment of risk of bias at the outcome level when drawing conclusions?
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Did the review authors incorporate an assessment of heterogeneity at the outcome level when drawing conclusions?
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	Did the authors address publication bias? (regardless of whether synthesis was using a meta-analysis or narrative)
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Did the authors report conflicts of interest and did they manage any existing conflict of interest appropriately?

Shaded items were items considered critical.

Data abstraction: We abstracted outcome data from each of the systematic reviews. To ensure feasibility, we used the data as reported by the authors of the review and did not re-abstract data from the primary studies. One reviewer abstracted the data and a second reviewer checked the data for accuracy.

Data synthesis: Using the systematic reviews prioritized, we synthesized the evidence at the outcome level. Because of the higher likelihood of it resulting in higher certainty of evidence (details below) for each outcome, when there was comparative data (i.e. comparison of outcomes between an untreated and a treated group) and non-comparative data (i.e. changes from before to after treatment in one group, or only outcomes after treatment), we prioritized comparative data.

We prioritized numerical results (i.e. magnitudes of effect) and reported estimates and their 95% confidence intervals (CIs). When results were not reported in that way, we calculated the estimates and CIs when systematic review authors provided sufficient information. When necessary, we assumed moderate correlation coefficients for the changes between baseline and follow up (coefficient= 0.4). When this information was not available we reported narratively the effect estimates and ranges.

When a specific study reported the same outcome measured by more than one scale, we chose the scale presented first. We highlighted situations when the results obtained with other scales were importantly different.

When the same outcome was reported by more than one study but we could not pool the results, we created narrative syntheses.

Certainty of evidence: For each outcome, we assessed the certainty of the evidence (also known as quality of the evidence) using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[2] The certainty of evidence can be rated as high, moderate, low, or very low (Table 2). For effects of interventions, the certainty of the evidence started as high and could be rated down due to serious concerns about risk of bias, inconsistency, indirectness, imprecision, and publication bias. For inferences about the effect of using a treatment versus no treatment, when there was no comparison group, we assessed risk of bias as very serious and rated down the certainty of the evidence 2 levels by default. We used the same principles when assessing the certainty of the evidence in estimates of prevalence or rates, but did not judge risk of bias as resulting in very serious concerns due to lack of a comparison group. For all assessments, we used the information presented by the authors of the systematic review (e.g. assessments of risk of bias of the included studies, effect estimates from studies).

Table 2: GRADE levels of certainty of the evidence

Certainty level	Definition
High ⊕⊕⊕⊕	We are very confident that the true result (effect estimate/ prevalence/ mean, etc.) lies close to that of the estimate of the result
Moderate ⊕⊕⊕◯	We are moderately confident in the result: the true result is likely to be close to the estimate of the result, bur there is a possibility that it is substantially different
Low ⊕⊕◯◯	Our confidence in the result is limited: the true result may be substantially different from the estimate of the result
Very low ⊕◯◯◯	We have very little confidence in the result: the true result is likely to be substantially different from the estimate of the result

Presentation of results: We created GRADE Summary of Findings tables in which we describe the evidence available for each of the outcomes, and the certainty of the evidence. These tables contain the following information:

- Outcomes: measurement method (including scales, if applicable) and follow-up
- Estimates of effect: absolute and relative estimates of effect, and their corresponding 95% CIs.
- Number of studies and participants providing evidence for the outcome
- GRADE certainty of the evidence, with a link to detailed explanations (provided at the bottom of the table) of why the certainty of the evidence was rated at a specific level
- A narrative statement about what happens with the outcome, based on the estimate of effect and certainty of evidence.

Searching for new evidence not included in the systematic reviews: To assess if newer evidence not included in the included systematic reviews would change the conclusions importantly, we searched for and assessed primary studies answering the questions of interest that were published after the authors of such systematic reviews conducted their searches. We defined an important change in conclusions as a change in the certainty of the evidence (from low/ very low/ not available to high/ moderate).

We searched OVID Medline from January 1, 2019 through May 12, 2022, for studies published in English. We included studies if they enrolled young individuals (< 25 years old, with at least 20% of the people being this age) with a diagnosis of gender dysphoria/gender identity disorder, who received puberty blockers, cross-sex hormones, or surgeries; and measured any of the outcomes of interest.

For outcomes that should be evaluated in a comparative manner (e.g., depression, anxiety, etc.), because they are the only type of study design that would change the conclusions importantly, we selected comparative clinical studies (studies in which the researchers recruited and measured outcomes in humans, and compared a group of people who received the intervention with another one who did not receive the intervention). This included randomized clinical trials, and comparative observational studies. For outcomes that can only occur when the treatment is administered, we included non-comparative observational studies (case series). For these to change conclusions, they should have a sufficiently large sample size, and therefore we excluded case series in which the researchers reported information from <100 people.

Two reviewers screened the potentially relevant articles at title and abstract and full text screening stage. We abstracted relevant study characteristics and outcome data, and assessed risk of bias of comparative studies using the most relevant domains of the Risk of Bias for non-Randomized studies of Interventions (ROBINS-I) tool[3] (table 3). For non-comparative studies, we used a list of custom items that captured the most important potential risk of bias concerns of case series (table 4). We judged the risk of bias of each study as the highest risk of bias of any of the domains assessed (e.g., one domain judged at critical risk of bias resulted in the study judged at critical risk of bias). We summarized this information at the study and judged whether it would have changed the conclusions importantly if added to the body of evidence from the systematic reviews.

Table 3: Domains used to assess risk of bias of comparative studies

Domain	Low	Critical
Confounding	Adjusted for all relevant confounding factors	No adjustment
Classification of intervention	Intervention recorded prospectively or from medical records	Asked patients to recall whether they received the intervention
Deviation from intended interventions	No cointerventions or cointerventions balanced between the groups	Cointerventions unbalanced between the groups

Missing data	More than 90% of patients who started the study provided outcome data	Less thank 50% of patients who started the study provided outcome data
Measurement of outcome	All outcomes measured in the same way in both groups	Outcomes measured differently in both groups

Each domain could be judged at low, moderate, serious, or critical risk of bias. In addition, information could be insufficient to make a judgment. The table describes the criteria used to judge a domain in the extreme categories.

Table 4: Domains used to assess risk of bias of non- comparative studies

Domain	Low	High
Representativeness of the sample	Included all consecutive patients	Highly selected sample based on specific characteristics related with the prognosis after treatment
Classification of the intervention	Intervention recorded prospectively or from medical records	Asked patients to recall whether they received the intervention
Deviation from intended interventions	No cointerventions outside what would be observed in practice (or in a small proportion of patients)	Most patients received co interventions that could influence the outcomes
Missing data	More than 90% of patients who started the study provided outcome data	Less thank 50% of patients who started the study provided outcome data
Measurement of outcome	Outcomes measured prospectively or from medical records	Outcomes reported by the patients and/ or needed to recall what happened a long time ago

Each domain could be judged at low, moderate, or high risk of bias. In addition, information could be insufficient to make a judgment. The table describes the criteria used to judge a domain in the extreme categories.

References

1. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *Bmj* 2017;358:j4008. doi: 10.1136/bmj.j4008 [published Online First: 2017/09/25]
2. Blashem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of the evidence. *Journal of clinical epidemiology* 2011;64:401-06.
3. Sterne JA, Hernan MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ (Clinical research ed)* 2016;355:i4919. doi: 10.1136/bmj.i4919 [published Online First: 2016/10/14]

Search Strategies

Questions Covered:

PICO questions:

1. For children, adolescents, and young adults (<21) with gender dysphoria, what are the effects of treatment with **puberty blockers (gonadotrophin releasing hormone (GnRH) analogues)** compared to no puberty blockers?
2. For children, adolescents, and young adults (<21) with gender dysphoria, what are the effects of treatment with **cross-sex hormones** compared to no cross-sex hormones?
3. For children, adolescents, and young adults (<21) with gender dysphoria, what are the effects of **gender-affirming surgeries** compared to no surgery?

Search Strategies:

Note: Population, puberty blocker, cross-sex hormones search blocks adapted from NICE (2020) evidence reviews. Gender-affirming search block adapted from Wernick *et al.* 2019. Systematic reviews filter adapted from McMaster University Health Information Research Unit (HIRU).

Databases: Medline, Epistemonikos
Grey Literature: CADTH, AHRQ, SEGM, NICE

Medline

OVERVIEW	
Interface:	Ovid
Databases:	OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Study Types:	Systematic Reviews
Search Run:	April 23, 2022
Search Strategy: search terms [number of results]	

Population

1 exp "Sexual and Gender Minorities"/ 12385
2 Gender Dysphoria/ 774
3 Gender Identity/ 20481
4 Gender Role/ 197
5 "Sexual and Gender Disorders"/ 81
6 Transsexualism/ 4236
7 Transgender Persons/ 5303
8 Health Services for Transgender Persons/ 186

1

9 exp Sex Reassignment Procedures/ 1208
10 gender identity disorder.mp. 492
11 non-binary.mp. 566
12 transgender.mp. 9989
13 (gender* adj3 (dysphori* or disorder* or distress or nonconform* or non-conform* or atypical or incongru* or identi* or disorder* or confus* or minorit* or queer* or variant or diverse or creative or explor* or question* or expan* or fluid)).tw. 16428
14 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition* or expression*)).tw. 13749
15 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. 19665
16 (genderfluid or genderqueer or agender).mp. 130
17 ((correct or chosen) adj3 name).mp. 591
18 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. 135313
19 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition* or expression*)).tw. 13749
20 (male-to-female or m2f or female-to-male or f2m).tw. 148579
21 or/1-20 342948

Cross-Sex Hormones

22 Hormones/ad, tu, th 4676
23 exp Progesterone/ad, tu, th 11265
24 exp Estrogens/ad, tu, th 29635
25 exp Gonadal Steroid Hormones/ad, tu, th 35375
26 (progesteron* or oestrogen* or estrogen*).tw. 223307
27 ((cross-sex or crosssex or gender-affirm*) and (hormon* or steroid* or therap* or treatment* or prescri* or pharm* or medici* or drug* or intervention* or care)).tw. 1488
28 exp Estradiol/ad, tu, th 11197
29 exp Testosterone/ad, tu, th 8710
30 (testosteron* or sustanon* or tostran or testogel or testim or restandol or andriol or testocaps* or nebido or testavan).tw. 86509
31 (oestrad* or estrad* or evorel or ethinyloestrad* or ethinylestrad* or elleste or progynova or zumenon or bedol or femseven or nuvelle).tw. 100252
32 or/22-31 345895

Puberty Blockers

33 Gonadotropin-Releasing Hormone/ 28809
34 (pubert* adj3 block*).ti,ab. 141
35 ((gonadotrophin or gonadotropin) and releasing).ti,ab. 20121
36 (GnRH adj2 analog*).ti,ab. 2878
37 GnRH*.ti,ab. 24390
38 "GnRH agonist*".ti,ab. 4749
39 Triptorelin Pamoate/ 1981
40 triptorelin.ti,ab. 821
41 arvekap.ti,ab. 1

42 ("AY 25650" or AY25650).ti,ab. 1
43 ("BIM 21003" or BIM21003).ti,ab. 0
44 ("BN 52014" or BN52014).ti,ab. 0
45 ("CL 118532" or CL118532).ti,ab. 0
46 Debio.ti,ab. 119
47 diphereline.ti,ab. 28
48 moapar.ti,ab. 0
49 pamorelin.ti,ab. 1
50 trelstar.ti,ab. 3
51 triptodur.ti,ab. 1
52 ("WY 42422" or WY42422).ti,ab. 0
53 ("WY 42462" or WY42462).ti,ab. 0
54 gonapeptyl.ti,ab. 0
55 decapeptyl.ti,ab. 225
56 salvacyl.ti,ab. 0
57 Buserelin/ 2137
58 buserelin.ti,ab. 1395
59 onist.ti,ab. 0
60 ("hoe 766" or hoe-766 or hoe766).ti,ab. 72
61 profact.ti,ab. 2
62 receptal.ti,ab. 31
63 suprecur.ti,ab. 5
64 suprefact.ti,ab. 25
65 tiloryth.ti,ab. 0
66 histrelin.ti,ab. 78
67 "LHRH-hydrogel implant".ti,ab. 1
68 ("RL 0903" or RL0903).ti,ab. 1
69 ("SPD 424" or SPD424).ti,ab. 1
70 goserelin.ti,ab. 1016
71 Goserelin/ 1643
72 ("ici 118630" or ici118630).ti,ab. 51
73 ("ZD-9393" or ZD9393).ti,ab. 0
74 zoladex.ti,ab. 388
75 leuprorelin.ti,ab. 525
76 carcinil.ti,ab. 0
77 enanton*.ti,ab. 26
78 ginecrin.ti,ab. 0
79 leuplin.ti,ab. 15
80 Leuprolide/ 3018
81 leuprolide.ti,ab. 2004
82 lucrin.ti,ab. 16
83 lupron.ti,ab. 183
84 provren.ti,ab. 0
85 procrin.ti,ab. 3
86 ("tap 144" or tap144).ti,ab. 41
87 (a-43818 or a43818).ti,ab. 3
88 Trenantone.ti,ab. 2
89 staladex.ti,ab. 0

90 prostap.ti,ab. 6
91 Nafarelin/ 327
92 nafarelin.ti,ab. 263
93 ("76932-56-4" or "76932564").ti,ab. 0
94 ("76932-60-0" or "76932600").ti,ab. 0
95 ("86220-42-0" or "86220420").ti,ab. 0
96 ("rs 94991 298" or rs94991298).ti,ab. 0
97 synarel.ti,ab. 13
98 deslorelin.ti,ab. 306
99 gonadorelin.ti,ab. 237
100 ("33515-09-2" or "33515092").ti,ab. 0
101 ("51952-41-1" or "51952411").ti,ab. 0
102 ("52699-48-6" or "52699486").ti,ab. 0
103 cetrorelix.ti,ab. 520
104 cetrotide.ti,ab. 52
105 ("NS 75A" or NS75A).ti,ab. 0
106 ("NS 75B" or NS75B).ti,ab. 0
107 ("SB 075" or SB075).ti,ab. 1
108 ("SB 75" or SB75).ti,ab. 67
109 gonadoliberin.ti,ab. 151
110 kryptocur.ti,ab. 7
111 cetrorelix.ti,ab. 520
112 cetrotide.ti,ab. 52
113 antagon.ti,ab. 18
114 ganirelix.ti,ab. 160
115 ("ORG 37462" or ORG37462).ti,ab. 3
116 orgalutran.ti,ab. 26
117 ("RS 26306" or RS26306).ti,ab. 5
118 ("AY 24031" or AY24031).ti,ab. 0
119 factrel.ti,ab. 13
120 fertagyl.ti,ab. 12
121 lutrelef.ti,ab. 5
122 lutrepulse.ti,ab. 3
123 relefact.ti,ab. 10
124 fertiral.ti,ab. 0
125 (hoe471 or "hoe 471").ti,ab. 6
126 relisorm.ti,ab. 4
127 cystorelin.ti,ab. 19
128 dirigestran.ti,ab. 5
129 or/33-128 47108

Gender-affirming Surgeries

130 virilization/ 2309
131 (virilism or virili?ation or masculini?ation).mp. 5657
132 feminization/ 797
133 femini?ation.mp. 3420
134 (vaginoplasty or vaginoplasties).mp. 1022

135 exp Vagina/ or *Reconstructive Surgical Procedures/ 78841
136 (vaginoplasty or vaginoplasties).mp. 1022
137 (phalloplasty or phalloplasties).mp. 561
138 exp Penile Prosthesis/ 1636
139 "penile reconstruction".mp. 292
140 (vagina reconstruction or vaginal reconstruction).mp. 549
141 (genitoplasty or genitoplasties).mp. 263
142 transsexualism/su [Surgery] 1007
143 sex reassignment.mp. 1668
144 sex transformation.mp. 42
145 or/130-144 91560

Systematic Review Filter

147 meta-analysis/ 158633
148 (meta anal* or meta-anal* or metaanal*).ti,ab. 231876
149 ((systematic or evidence) adj2 (review* or overview*)).ti,ab. 279806
150 ((pool* or combined) adj2 (data or trials or studies or results)).ab. 65411
151 (search strategy or search criteria or systematic search or study selection or data extraction).ab. 70886
152 (search* adj4 literature).ab. 84593
153 or/146-152 521554

Combine Interventions and Population

154 32 or 129 or 145 459771
155 21 and 154 17838

Limit to Systematic Reviews in English Language

156 153 and 155 295
157 limit 156 to english language 288

Epistemonikos

OVERVIEW	
Interface:	https://www.epistemonikos.org/
Database:	Epistemonikos
Study Types:	Systematic Reviews
Search Run:	April 23, 2022
Search Strategy: search terms [number of results]	
Population (title:((title:(gender dysphoria) OR abstract:(gender dysphoria)) OR (title:(gender identity disorder) OR abstract:(gender identity disorder)) OR (title:(transgender) OR abstract:(transgender))) OR abstract:((title:(gender dysphoria) OR abstract:(gender dysphoria)) OR (title:(gender identity disorder) OR abstract:(gender identity disorder)) OR (title:(transgender) OR abstract:(transgender)))) *Limit to Systematic Reviews* *Limited by publication type "systematic review" [425]	

Canadian Agency for Drugs and Technologies in Health (CADTH)

OVERVIEW	
Interface:	https://www.cadth.ca/
Database:	CADTH
Study Types:	Systematic Reviews, Health Technology Reviews
Search Run:	April 27, 2022
Search Strategy: search terms [number of results]	
"gender dysphoria" [10] *Limit to Health Technology Review* [2] "transgender" [9] *Limit to Health Technology Review* [5] "gender identity disorder" [1]	

Agency for Healthcare Research and Quality (AHRQ)

OVERVIEW	
Interface:	https://search.ahrq.gov/
Database:	AHRQ
Study Types:	Evidence Based Practice (EPC) Centre Reports, Full Research Reports, Health Technology Assessments
Search Run:	April 29, 2022
Search Strategy: search terms [number of results]	
Search titles only: "gender identity disorder" "gender dysphoria" "transgender" [7]	

Society for Evidence-based Gender Medicine (SEGM)

OVERVIEW	
Interface:	https://segm.org/news
Database:	SEGM News
Study Types:	Systematic Reviews
Search Run:	April 30, 2022
Search Strategy: search terms [number of results]	
Find in page: "systematic" [5]	

National Institute for Health and Care Excellence (NICE)

OVERVIEW	
Interface:	https://www.nice.org.uk/
Database:	NICE
Study Types:	Systematic Reviews, Guidelines with Systematic Reviews
Search Run:	April 30, 2022
Search Strategy: search terms [number of results]	
gender dysphoria [1] *Limit to Guidance* [1] transgender [10] *Limit to Guidance* [7]	

gender identity disorder [9] *Limit to Guidance* [8]

Search Strategies – Individual Studies

Questions Covered:

PICO questions:

1. For children, adolescents, and young adults (<21) with gender dysphoria, what are the effects of treatment with **puberty blockers (gonadotrophin releasing hormone (GnRH) analogues)** compared to no puberty blockers?

2. For children, adolescents, and young adults (<21) with gender dysphoria, what are the effects of treatment with **cross-sex hormones** compared to no cross-sex hormones?

3. For children, adolescents, and young adults (<21) with gender dysphoria, what are the effects of **gender-affirming surgeries** compared to no surgery?

Search Strategies:

Note: Population, puberty blocker, cross-sex hormones search blocks adapted from NICE (2020) evidence reviews. Gender-affirming search block adapted from Wernick *et al.* 2019.

Databases: Medline

Medline

OVERVIEW	
Interface:	Ovid
Databases:	OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Study Types:	Any
Search Run:	May 12, 2022
Search Strategy: search terms [number of results]	

Population

1	exp "Sexual and Gender Minorities"/	12631
2	Gender Dysphoria/	781
3	Gender Identity/	20586
4	Gender Role/	204
5	"Sexual and Gender Disorders"/	81
6	Transsexualism/	4259
7	Transgender Persons/	5371
8	Health Services for Transgender Persons/	187
9	exp Sex Reassignment Procedures/	1211
10	gender identity disorder.mp.	492

11 non-binary.mp. 574
12 transgender.mp. 10079
13 (gender* adj3 (dysphori* or disorder* or distress or nonconform* or non-conform* or atypical or incongru* or identi* or disorder* or confus* or minorit* or queer* or variant or diverse or creative or explor* or question* or expan* or fluid)).ti,ab. 16546
14 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).ti,ab. 9375
15 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).ti,ab. 19788
16 (genderfluid or genderqueer or agender).mp. 132
17 ((correct or chosen) adj3 name).mp. 591
18 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).ti,ab. 135744
19 (male-to-female or m2f or female-to-male or f2m).ti,ab. 149067
20 or/1-19 341083

Cross-sex Hormones

21 Hormones/ad, tu, th 4690
22 exp Progesterone/ad, tu, th 11270
23 exp Estrogens/ad, tu, th 29646
24 exp Gonadal Steroid Hormones/ad, tu, th 35401
25 (progesteron* or oestrogen* or estrogen*).ti,ab. 223689
26 ((cross-sex or crosssex or gender-affirm*) and (hormon* or steroid* or therap* or treatment* or prescri* or pharm* or medici* or drug* or intervention* or care)).ti,ab. 1507
27 exp Estradiol/ad, tu, th 11200
28 exp Testosterone/ad, tu, th 8722
29 (testosteron* or sustanon* or tostran or testogel or testim or restandol or andriol or testocaps* or nebido or testavan).ti,ab. 86670
30 (oestrad* or estrad* or evorel or ethinyloestrad* or ethinylestrad* or elleste or progynova or zumenon or bedol or femseven or nuvelle).ti,ab. 100411
31 or/21-30 346508

Puberty Blockers

32 Gonadotropin-Releasing Hormone/ 28845
33 (pubert* adj3 block*).ti,ab. 142
34 ((gonadotrophin or gonadotropin) and releasing).ti,ab. 20158
35 (GnRH adj2 analog*).ti,ab. 2879
36 GnRH*.ti,ab. 24437
37 "GnRH agonist*".ti,ab. 4763
38 Triptorelin Pamoate/ 1983
39 triptorelin.ti,ab. 822
40 arvekap.ti,ab. 1
41 ("AY 25650" or AY25650).ti,ab. 1
42 ("BIM 21003" or BIM21003).ti,ab. 0
43 ("BN 52014" or BN52014).ti,ab. 0
44 ("CL 118532" or CL118532).ti,ab. 0

45 Debio.ti,ab. 119
46 diphereline.ti,ab. 28
47 moapar.ti,ab. 0
48 pamorelin.ti,ab. 1
49 trelstar.ti,ab. 3
50 triptodur.ti,ab. 1
51 ("WY 42422" or WY42422).ti,ab. 0
52 ("WY 42462" or WY42462).ti,ab. 0
53 gonapeptyl.ti,ab. 0
54 decapeptyl.ti,ab. 225
55 salvacyl.ti,ab. 0
56 Buserelin/ 2137
57 buserelin.ti,ab. 1396
58 onist.ti,ab. 0
59 ("hoe 766" or hoe-766 or hoe766).ti,ab. 72
60 profact.ti,ab. 2
61 receptal.ti,ab. 31
62 suprecur.ti,ab. 5
63 suprefact.ti,ab. 25
64 tiloryth.ti,ab. 0
65 histrelin.ti,ab. 78
66 "LHRH-hydrogel implant".ti,ab. 1
67 ("RL 0903" or RL0903).ti,ab. 1
68 ("SPD 424" or SPD424).ti,ab. 1
69 goserelin.ti,ab. 1017
70 Goserelin/ 1644
71 ("ici 118630" or ici118630).ti,ab. 51
72 ("ZD-9393" or ZD9393).ti,ab. 0
73 zoladex.ti,ab. 388
74 leuprorelin.ti,ab. 529
75 carcinil.ti,ab. 0
76 enanton*.ti,ab. 26
77 ginecrin.ti,ab. 0
78 leuplin.ti,ab. 15
79 Leuprolide/ 3018
80 leuprolide.ti,ab. 2003
81 lucrin.ti,ab. 16
82 lupron.ti,ab. 183
83 provren.ti,ab. 0
84 procrin.ti,ab. 3
85 ("tap 144" or tap144).ti,ab. 41
86 (a-43818 or a43818).ti,ab. 3
87 Trenantone.ti,ab. 2
88 staladex.ti,ab. 0
89 prostap.ti,ab. 6
90 Nafarelin/ 327
91 nafarelin.ti,ab. 263
92 ("76932-56-4" or "76932564").ti,ab. 0

93 ("76932-60-0" or "76932600").ti,ab. 0
94 ("86220-42-0" or "86220420").ti,ab. 0
95 ("rs 94991 298" or rs94991298).ti,ab. 0
96 synarel.ti,ab. 13
97 deslorelin.ti,ab. 310
98 gonadorelin.ti,ab. 238
99 ("33515-09-2" or "33515092").ti,ab. 0
100 ("51952-41-1" or "51952411").ti,ab. 0
101 ("52699-48-6" or "52699486").ti,ab. 0
102 cetrorelix.ti,ab. 520
103 cetrotide.ti,ab. 52
104 ("NS 75A" or NS75A).ti,ab. 0
105 ("NS 75B" or NS75B).ti,ab. 0
106 ("SB 075" or SB075).ti,ab. 1
107 ("SB 75" or SB75).ti,ab. 67
108 gonadoliberin.ti,ab. 152
109 kryptocur.ti,ab. 7
110 cetrorelix.ti,ab. 520
111 cetrotide.ti,ab. 52
112 antagon.ti,ab. 18
113 ganirelix.ti,ab. 161
114 ("ORG 37462" or ORG37462).ti,ab. 3
115 orgalutran.ti,ab. 26
116 ("RS 26306" or RS26306).ti,ab. 5
117 ("AY 24031" or AY24031).ti,ab. 0
118 factrel.ti,ab. 13
119 fertagyl.ti,ab. 12
120 lutrelef.ti,ab. 5
121 lutrepulse.ti,ab. 3
122 relefact.ti,ab. 10
123 fertiral.ti,ab. 0
124 (hoe471 or "hoe 471").ti,ab. 6
125 relisorm.ti,ab. 4
126 cystorelin.ti,ab. 19
127 dirigestran.ti,ab. 5
128 or/32-127 47179

Surgery

129 virilization/ 2309
130 (virilism or virili?ation or masculini?ation).mp. 5664
131 feminization/ 798
132 femini?ation.mp. 3425
133 (vaginoplasty or vaginoplasties).mp. 1032
134 (vaginoplasty or vaginoplasties).mp. 1032
135 (phalloplasty or phalloplasties).mp. 561
136 exp Penile Prosthesis/ 1642
137 "penile reconstruction".mp. 292

138 (vagina reconstruction or vaginal reconstruction).mp. 550
139 (genitoplasty or genitoplasties).mp. 263
140 transsexualism/su [Surgery] 1007
141 sex reassignment.mp. 1674
142 sex transformation.mp. 42
143 or/129-142 14290

Any intervention AND population

144 31 or 128 or 143 386835
145 20 and 144 16516

Limit to Humans

146 animals/ not humans/ 4972586
147 145 not 146 9281
148 limit 147 to humans 7901

Limit to Publication Year 2019 to Current

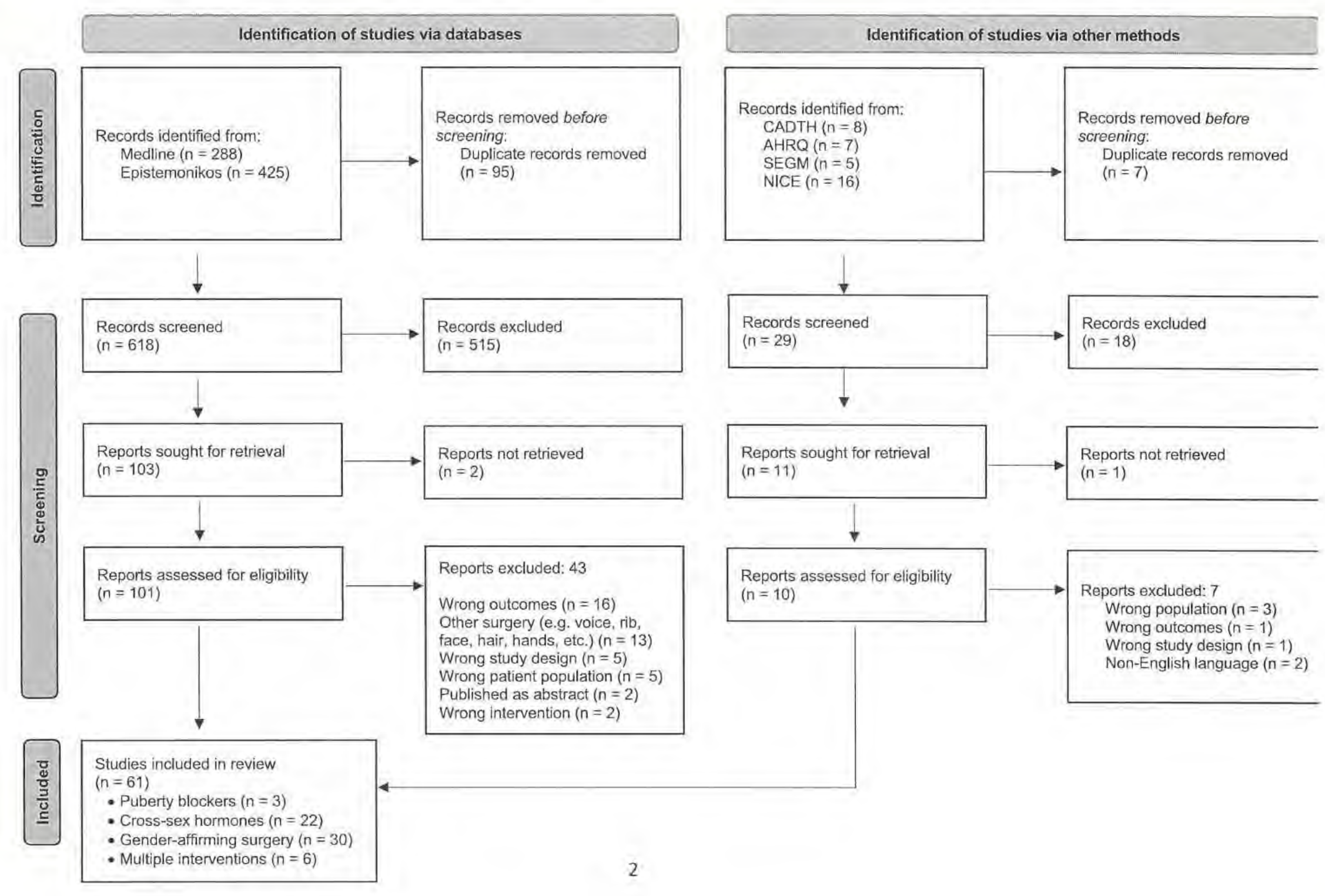
149 limit 148 to yr="2019 -Current" 1859

Results

Search results and eligible reviews: After screening 647 records found through our searches, we found 61 eligible systematic reviews. From these, 27 were published between 2020 and 2022 (Figure 1). Overall, 4% (1/27) of the reviews were judged to be of high methodological quality, 15% (4/27) were moderate methodological quality, 37% (10/27) were low methodological quality, and 44% (12/27) were critically low methodological quality.

We provide reasons for excluding systematic reviews in appendix 1.

Effects of gender affirming therapies in people with gender dysphoria: evaluation of the best available evidence. Dr. Romina Brignardello-Petersen and Dr. Wojtek Wiercioch; Results; May 16, 2022



2

Figure 1: PRISMA flow diagram for the selection of systematic reviews. *From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Outcomes:

1. **Puberty blockers:** We found 4 systematic reviews assessing the effects of puberty blockers published between 2020 and 2022.[1-4] From these, we judged 2 as having moderate methodological quality, and 2 as having critically low methodological quality. Details of the assessment are provided in Figure 2.

   Table 1 summarizes the evidence about the effects of puberty blockers on the outcomes of interest. We used information from 2 systematic reviews.[2 3] For most outcomes (except suicidality), there is no evidence about the effect of puberty blockers compared to not using puberty blockers. In other words, no studies compared the outcomes between a group of people with gender dysphoria using puberty blockers and another not using them. Therefore, it is unknown whether people with gender dysphoria who use puberty blockers experience more improvement in gender dysphoria, depression, anxiety, and quality of life than those with gender dysphoria who do not use them. There is very low certainty about the effects of puberty blockers on suicidal ideation (see details in Table 1).

   Studies, however, reported outcomes among a group of people with gender dysphoria after receiving puberty blockers. The findings are:
   - There is low certainty evidence suggesting that treatment with puberty hormones may slightly increase gender dysphoria severity (mean change score in the Utrecht Gender Dysphoria scale, 0.7 points [95% CI, -4.2 to 5.6], range 12-60, with higher scores reflecting more severe gender dysphoria)
   - There is low certainty evidence suggesting that treatment with puberty blockers may decrease depression (mean change score in the Beck Depression Inventory, -3.4 [95% CI, -5.7 to -1.0], range 0-63, with higher scores reflecting more severe depression)
   - There is low certainty evidence suggesting that treatment with puberty blockers may decrease anxiety (mean change score in the Trait Anxiety Scale, trait subscale, -1.5 [95% CI, -4.7 to -1.8], range 0-80, with higher scores reflecting more severe anxiety)
   - There is low certainty evidence suggesting a moderate percentage of patients reporting adverse events after treatment with puberty blockers (see Table 1 for details)
   - There is very low certainty evidence about how puberty blockers affect suicidality

Figure 2: AMSTAR assessment judgements for systematic reviews addressing puberty blockers

Review ID	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16	Methodological quality
AHRQ 2021																	MODERATE
NICE 2020a																	MODERATE
Ramos 2020																	CRITICALLY LOW
Rew 2020																	CRITICALLY LOW

Figure legend:

Yes

Probably yes

Probably no

No

Not applicable

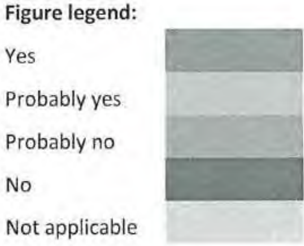


Table 1: Puberty blockers (gonadotrophin releasing hormone analogues) compared to no puberty blockers in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: puberty blockers (gonadotrophin releasing hormone analogues)
Comparison: no puberty blockers

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no puberty blockers	Risk / mean with puberty blockers				
Gender dysphoria assessed with: difference (effect) in gender dysphoria proportion or severity	Not reported					The effects of puberty blockers on gender dysphoria are unknown
Gender dysphoria assessed with: mean change score in the Utrecht Gender Dysphoria Scale (12-60, higher scores reflect more gender dysphoria, 40 points or more indicate a diagnosis of gender dysphoria) (NICE, 2020a) Follow up: mean 1.9 years (range 0.4 to 5.1 years)	NA	0.7 (-4.2 to 5.6)	NA	41 (1 study)	⊕⊕◯◯ LOW[1]	The mean gender dysphoria score may increase by 0.7 points after puberty blockers
Depression assessed with: difference (effect) in depression proportion or severity	Not reported					The effects of puberty blockers on depression are unknown

Table 1: Puberty blockers (gonadotrophin releasing hormone analogues) compared to no puberty blockers in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: puberty blockers (gonadotrophin releasing hormone analogues)
Comparison: no puberty blockers

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no puberty blockers	Risk / mean with puberty blockers				
Depression assessed with: mean change score in Beck Depression Inventory-II scale (0-63, higher scores represent more severe depression) (NICE, 2020a) Follow up: mean 1.9 years (range 0.4 to 5.1 years)	NA	-3.4 (-5.7 to -1.0)	NA	41 (1 study)	⊕⊕◯◯ LOW[1]	The mean depression score may decrease by 3.4 points after puberty blockers
Anxiety assessed with: difference (effect) in anxiety proportion or severity	Not reported					The effects of puberty blockers on anxiety are unknown
Anxiety assessed with: mean change score in STAI-Trait scale (0-80, higher scores represent more severe anxiety) (NICE, 2020a) Follow up: mean 1.9 years (range 0.4 to 5.1 years)	NA	-1.5 (-4.7 to 1.8)	NA	41 (1 study)	⊕⊕◯◯ LOW[1]	The mean anxiety score may decrease by 1.5 points after puberty blockers

Table 1: Puberty blockers (gonadotrophin releasing hormone analogues) compared to no puberty blockers in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: puberty blockers (gonadotrophin releasing hormone analogues)
Comparison: no puberty blockers

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no puberty blockers	Risk / mean with puberty blockers				
Quality of life assessed with: any measure	Not reported					The effects of puberty blockers on quality of life are unknown
Suicidal ideation difference (effect) in suicidal ideation (Rew, 2020) Follow-up: cross-sectional survey	The authors report that "compared to youth who did not receive pubertal suppression, those who did showed lower lifetime rates of suicidal ideation".			89 (1 study)	⊕◯◯◯ VERY LOW[2]	We are very uncertain about the effect of puberty blockers on suicidal ideation
Adverse effects assessed with: proportion of patients reporting adverse effects (NICE, 2020a) Follow up: mean 2.3 years (range 0.0 to 11.3 years)	NA	11%[3] (2% to 29%)	NA	27 (1 study)	⊕⊕◯◯ LOW[4]	The proportion of patients reporting adverse effects after treatment with puberty blockers may be 11%

STAI-Trait: Trait Anxiety Scale. Range: 0-80
CI: Confidence interval
NA: Not applicable

Table 1: Puberty blockers (gonadotrophin releasing hormone analogues) compared to no puberty blockers in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: puberty blockers (gonadotrophin releasing hormone analogues)
Comparison: no puberty blockers

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no puberty blockers	Risk / mean with puberty blockers				

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

1. Mean change rated down due to risk of bias and imprecision. According to the systematic review authors, the study had poor methodological quality. In addition, there are too few participants included, which is not sufficient to make trustworthy inferences (does not meet the optimal information size).
2. The authors of Rew 2020 narratively summarized the outcome of Turban *et al.* 2020; a cross-sectional online survey study. According to the systematic review authors, Turban et al. did not describe the study participants and the setting in detail and it was unclear whether outcomes were measured in a valid and reliable way. We therefore, downgraded the certainty of evidence by one level from low to very low due to high risk of bias.
3. The authors reported 3/27 (11%) participants treated with GnRHa developed side effects: 1 participant developed sterile abscesses; they were switched from leuprolide acetate to triptorelin, 1 participant developed leg pains and headaches, which eventually resolved without treatment, 1 participant gained 19 kg within 9 months of initiating GnRH analogues.
4. Proportion of adverse effects rated down due to risk of bias and imprecision. According to the systematic review authors, the cohort study Khatchadourian *et al.* 2014 was assessed at high risk of bias due to incomplete reporting of its cohort. In addition, there are too few participants included, which is not sufficient to make trustworthy inferences (does not meet the optimal information size).

2. **Cross-sex hormones:** We found 9 systematic reviews assessing the effects of cross-sex hormones published between 2020 and 2022.[4-11] One of these, however, included both puberty blockers and cross-sex hormones combined in their evidence synthesis as was not prioritized.[5] From the 8 remaining reviews, we judged 1 as having high methodological quality, 2 as having moderate methodological quality, 2 as having low methodological quality, and 3 as having critically low methodological quality. Details of the assessment are provided in Figure 3. Because of its eligibility criteria related to study design, the systematic review judged at high methodological quality[7] did not include any studies and therefore we could not use it to inform any outcome.

   Table 2 summarizes the evidence about the effects of cross-sex hormones on the outcomes of interest. We used information from 4 systematic reviews.[6 9 11 12] For most outcomes (all except risk of breast cancer), there is no evidence about the effect of cross-sex hormones compared to not using cross-sex hormones. In other words, no studies compared the outcomes between a group of people with gender dysphoria using cross-sex hormones and another not using it. Therefore, it is unknown whether people with gender dysphoria who use cross-sex hormones experience more improvement in gender dysphoria, depression, anxiety, quality of life, and suicidality than those with gender dysphoria who do not use them. There is low certainty evidence suggesting that cross-sex hormones may not increase or decrease the risk of breast cancer (see details in Table 2).

   Studies, however, reported outcomes among a group of people with gender dysphoria after receiving cross-sex hormones. The findings are:
   - There is low certainty evidence suggesting that treatment with cross-sex hormones may decrease gender dysphoria severity (mean change score in the Utrecht Gender Dysphoria scale, -42.4 points [95% CI, -44.1 to -40.1], range 12-60, with higher scores reflecting more severe gender dysphoria)
   - There is low certainty evidence suggesting that treatment with cross-sex hormones may decrease depression (measured with different scales, see Table 4 for details) and the need for treatment for depression (change in percentage, -39%)
   - There is low certainty evidence suggesting that treatment with cross-sex hormones may decrease anxiety (measured with different scales, see Table 4 for details) and the need for treatment for anxiety (change in percentage, -32%)
   - There is very low certainty about the change in quality of life after treatment with cross-sex hormones.
   - There is low certainty evidence suggesting that treatment with cross-sex hormones may decrease suicidality degree (mean change score in the Ask Suicide-Screening questions scale, -0.84 points [95% CI, -1.30 to -0.44], range 0-4, with higher scores reflecting more severe suicidality) and the percentage of patients with need for treatment due to suicidality/self-harm (change in percentage, -31%). There is very low certainty evidence about the percentage of people with suicidal ideation and suicide attempts after treatment with cross-sex hormones.

- There is low certainty evidence suggesting a low prevalence of venous thromboembolism after treatment with cross-sex hormones (see Table 2 for details)

Figure 3: AMSTAR assessment judgements for systematic reviews addressing cross-sex hormones

Review ID	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16	Methodological quality
AHRQ 2021																	MODERATE
Baker 2021																	MODERATE
Fledderus 2020																	CRITICALLY LOW
Haupt 2020																	HIGH
Karalexi 2020																	LOW
Kotamarti 2021																	CRITICALLY LOW
Mattawanon 2021																	CRITICALLY LOW
NICE 2021b																	MODERATE
Totaro 2021																	LOW

Figure legend:

Table 2: Cross-sex hormones compared to no cross-sex hormones in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: cross-sex hormones
Comparison: no cross-sex hormones

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no cross-sex hormones	Risk/ mean with cross-sex hormones				
Gender dysphoria assessed with: difference (effect) in gender dysphoria percentage or severity	Not reported					The effects of cross-sex hormones on gender dysphoria are unknown
Gender dysphoria assessed with: mean change score in the Utrecht Gender Dysphoria Scale (12-60, higher scores reflect more gender dysphoria, 40 points or more indicate a diagnosis of gender dysphoria) (NICE, 2020b) Follow up: 1 year	NA	-42.4 (-44.1 to -40.1)	NA	23 (1 study)	⊕⊕◯◯ LOW[1]	The mean gender dysphoria score may decrease by 42 points after cross-sex hormones
Depression assessed with: difference (effect) in depression percentage or severity	Not reported					The effects of cross-sex hormones on depression are unknown

Table 2: Cross-sex hormones compared to no cross-sex hormones in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: cross-sex hormones
Comparison: no cross-sex hormones

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no cross-sex hormones	Risk/ mean with cross-sex hormones				
Depression assessed with: mean change score in depression scales (higher scores represent more severe depression) (NICE, 2020b) Follow up: 1 year	NA	The mean depression score reduction was 9.6 points when using the BDI-II scale (n=23) and 7.5 when using the CESD-R scale (n=50). The authors report that both reductions were statistically significant[2]	NA	73 (2 studies)	⊕⊕◯◯ LOW[1]	The mean depression score may decrease after cross-sex hormones
Depression assessed with: change in percentage of patients with need for treatment (NICE, 2020b) Follow-up: 1 year	NA	The percentage of participants requiring treatment was reduced by 39% (from 54% at baseline), which was statistically significant	NA	52 (1 study)	⊕⊕◯◯ LOW[1]	The percentage of participants requiring treatment may be reduced by 39% after cross-sex hormones
Anxiety assessed with: difference (effect) in anxiety percentage or severity	Not reported					The effects of cross-sex hormones on anxiety are unknown

Table 2: Cross-sex hormones compared to no cross-sex hormones in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: cross-sex hormones
Comparison: no cross-sex hormones

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no cross-sex hormones	Risk/ mean with cross-sex hormones				
Anxiety assessed with: mean change score in anxiety scales (higher scores represent more severe anxiety) (NICE, 2020b) Follow up: 1 year	NA	The mean anxiety score reduction was 16.5 points when using the STAI-State scale and 14.5 when using the STAI-Trait scale. The authors report that both reductions were statistically significant	NA	23 (1 study)	⊕⊕◯◯ LOW[1]	The mean anxiety score may decrease after cross-sex hormones
Anxiety assessed with: change in percentage of patients with need for treatment (NICE, 2020b) Follow-up: 1 year	NA	The percentage of participants requiring treatment was reduced by 32% (from 48% at baseline), which was statistically significant	NA	52 (1 study)	⊕⊕◯◯ LOW[1]	The percentage of participants requiring treatment may be reduced by 32% after cross-sex hormones
Quality of life assessed with: difference (effect) in quality of life improvement	Not reported					The effects of cross-sex hormones on quality of life are unknown

Table 2: Cross-sex hormones compared to no cross-sex hormones in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: cross-sex hormones
Comparison: no cross-sex hormones

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no cross-sex hormones	Risk/ mean with cross-sex hormones				
Quality of life assessed with: mean change score in QLES-Q-SF score (higher scores represent better quality of life) (NICE, 2020b) Follow up: 1 year	NA	The mean quality of life score improved, but the differences were not statistically significant. The magnitudes were not reported	NA	50 (1 study)	⊕◯◯◯ VERY LOW[3]	We are very uncertain about the quality of life change after cross-sex hormones
Suicide/ suicidal ideation assessed with: difference (effect) in suicide or suicidal ideation	Not reported					The effects of cross-sex hormones on suicide/ suicidal ideation are unknown
Suicidality assessed with: change in score from ASQ instrument (higher scores represent greater degree of suicidality) (NICE, 2020b) Mean follow up: 1 year	NA	-0.84 (-1.30 to -0.44)	NA	39 (1 study)	⊕⊕◯◯ LOW[1]	Suicidality scores may decrease by 0.84 points after cross-sex hormones

Table 2: Cross-sex hormones compared to no cross-sex hormones in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: cross-sex hormones
Comparison: no cross-sex hormones

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no cross-sex hormones	Risk/ mean with cross-sex hormones				
Suicidal ideation assessed with: percentage of participants with suicidal ideation measured with PHQ-9 (NICE, 2020b) Follow-up: 1 year	NA	The percentage of participants with suicidal ideation decreased by 6% (from 10% at baseline). The authors did not conduct a statistical analysis	NA	50 (1 study)	⊕◯◯◯ VERY LOW[3]	We are very uncertain about the change in percentage of patients in suicidal ideation after cross-sex hormones
Suicide attempts assessed with: not reported (NICE, 2020b) Follow up: not reported	NA	The percentage of people with lifetime suicide attempts was 15%, those with attempts 3 months before treatment was 2%, and those with attempts at follow up was 5%	NA	130 (1 study)	⊕◯◯◯ VERY LOW[3]	We are very uncertain about the percentage of people with suicide attempts after cross-sex hormones
Suicidality/ self-harm assessed with: change in percentage of patients with need for treatment (NICE, 2020b) Follow-up: 1 year	NA	The percentage of participants requiring treatment was reduced by 31% (from 35% at baseline), which was statistically significant	NA	52 (1 study)	⊕⊕◯◯ LOW[1]	The percentage of participants requiring treatment may be reduced by 31% after cross-sex hormones
Venous thromboembolism assessed with: Risk of VTE	Not reported					The effects of cross-sex hormones on the risk of VTE are unknown

Table 2: Cross-sex hormones compared to no cross-sex hormones in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: cross-sex hormones
Comparison: no cross-sex hormones

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no cross-sex hormones	Risk/ mean with cross-sex hormones				
Venous thromboembolism assessed with: Prevalence among assigned males at birth (Totaro, 2021) Mean follow up: 4.1 years	NA	**20 per 1,000** (10 to 30)	NA	11,542 (18 studies)	⊕⊕⊕◯ MODERATE[4]	The prevalence of VTE among assigned males at birth is probably 2% after cross-sex hormones
Venous thromboembolism assessed with: Prevalence among assigned females at birth (Kotamarti, 2021) Mean follow up: 5.7 years	NA	**6 per 1,000** (CI not reported)[5]	NA	4,218 (8 studies)	⊕⊕⊕◯ MODERATE[6]	The prevalence of VTE among assigned females at birth is probably 0.6% after cross-sex hormones
Breast cancer assessed with: Risk of breast cancer (Fledderus, 2020) Follow up: not reported	Two studies compare the risk of beast cancer between assigned females at birth using versus not using testosterone, and found no differences (0 vs 1 case [total n= 130], and 1 vs 6 [total n=1579]). A third study compared assigned females at birth with non transgender women and found a lower risk in the former (magnitude not reported)		NA	2,938 (3 studies)	⊕⊕◯◯ LOW[7]	The risk of breast cancer may not increase or decrease due to the use of cross-sex hormones

Table 2: Cross-sex hormones compared to no cross-sex hormones in youth (<21 years old) with gender dysphoria

Patient or population: youth (<21 years old) with gender dysphoria
Intervention: cross-sex hormones
Comparison: no cross-sex hormones

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no cross-sex hormones	Risk/ mean with cross-sex hormones				

ASQ: Ask Suicide-Screening Questions. Range 0-4
BDI-II: Beck Depression Inventory. Range: 0-63
CESD-R: Center for Epidemiological Studies Depression Scale. Range: 0-60
CI: Confidence interval
NA: Not applicable
PHQ-9: Patient Health Questionnaire (PHQ) Modified for Teens. For suicidal ideation, it is a single question (yes/no)
QLES-Q-SF: Quality of Life Enjoyment and Satisfaction Questionnaire. Range: 15-75
STAI: State-Trait Anxiety Inventory. Range: 0-80

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

1. Mean change rated down due to risk of bias and imprecision. According to the systematic review authors, the studies had poor methodological quality. In addition, there are too few participants included, which is not sufficient to make trustworthy inferences (does not meet the optimal information size)
2. Similar results when this outcome was measured using the Patient Health Questionnaire (PHQ) Modified for Teens in one of the same studies
3. Rated down due to risk of bias, imprecision, and indirectness. According to the systematic review authors, the studies had poor methodological quality. In addition, there are too few participants included, which is not sufficient to make trustworthy inferences (does not meet the optimal information size). Finally, 30% of the participants did not have a diagnosis of gender dysphoria.
4. Prevalence rated down due to risk of bias. According to the systematic review authors, only 6 out of the 18 studies (representing 16.5% of the weight of the studies) were at low risk of bias.

5. A meta-analysis of independent studies reported in this systematic review suggested that the prevalence of VTE in non-transgender females at birth was 1.7% (based on 7 studies and 18,748 persons)
6. Prevalence rated down doe to risk of bias. According to the systematic review authors, all studies had at least one domain judged as problematic.
7. Risk rated down 2 levels because of risk of bias. The researchers did not account for confounding in any of the studies.

3. **Surgeries:** We found 15 systematic reviews assessing the effects of gender-affirming surgeries published between 2020 and 2022. We judged 8 as having low methodological quality and 7 as having critically low methodological quality. Details of the assessment are provided in Figure 4. We present the results regarding the effects of surgeries in three parts. First, we describe the effects of all surgeries on mental health outcomes in all patients. Second, we describe the effects of all surgeries on surgical outcomes in assigned females at birth (transgender males). Finally, we describe the effects of all surgeries on surgical outcomes in assigned males at birth (transgender females).

3.1 **Effects of surgeries on mental health outcomes:** Table 3 summarizes the evidence about the effects of all surgeries on mental health outcomes in all patients. We used information from 2 systematic reviews.[13 14] There were no systematic reviews and studies reporting on gender dysphoria, depression, anxiety, and suicidality. Therefore, the effects of surgeries on these outcomes (when compared to a group of patients with gender dysphoria who do not undergo surgery), or the changes in these outcomes (improvements or deterioration) among patients who undergo surgeries is unknown.

The systematic reviews addressed quality of life and depression, but none of the included studies included a comparison group. Thus, it is unknown whether people with gender dysphoria who undergo surgeries experience more improvement in quality of life or less regret than those with gender dysphoria who do not undergo surgeries.

Studies, however, reported the following outcomes among a group of people with gender dysphoria after undergoing surgeries. The findings are:

- There is low certainty evidence suggesting that the percentage of people who experience regret after surgery is low (1%)
- There is very low certainty evidence about how surgeries affect quality of life (see Table 3 for details)

Figure 4: AMSTAR assessment judgements for systematic reviews addressing gender-affirming surgery

Review ID	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16	Methodological quality
Bustos SS 2021																	LOW
Bustos VP 2021																	LOW
Bustos VP 2021b																	LOW
Dunford 2021																	LOW
Eftekhar, 2020																	LOW
Falcone 2021																	CRITICALLY LOW
Hu, 2022																	CRITICALLY LOW
Huayllani 2021																	CRITICALLY LOW
Jolly 2021																	LOW
Nassiri 2020																	CRITICALLY LOW
Oles 2022																	LOW
Oles 2022b																	LOW
Salibian 2021																	CRITICALLY LOW
Sijben 2021																	CRITICALLY LOW
Tay 2021																	CRITICALLY LOW

Figure legend:

Table 3: All surgeries compared to no surgeries in young people (<21 years old) with gender dysphoria

Patient or population: young people (<21 years old) with gender dysphoria
Intervention: surgeries
Comparison: no surgeries
Outcomes: Mental health and regret

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no surgery	Risk/ mean with surgery				
Gender dysphoria assessed with: any measure	Not reported					The effects of surgery on gender dysphoria, the changes in gender dysphoria severity after surgery, and the prevalence of gender dysphoria after surgery are unknown
Depression assessed with: any measure	Not reported					The effects of surgery on depression, the changes in depression severity after surgery, and the prevalence of depression after surgery are unknown
Anxiety assessed with: any measure	Not reported					The effects of surgery on anxiety, the changes in anxiety severity after surgery, and the prevalence of anxiety after surgery are unknown
Suicidality assessed with: any measure	Not reported					The effects of surgery on suicidality, the changes in anxiety severity after surgery, and the prevalence of anxiety after surgery are unknown
Quality of life assessed with: difference (effect) in quality of life	Not reported					The effects of surgery on quality of life are unknown
Quality of life assessed with: change in quality of life	Not reported					The change in quality of life after surgery is unknown

Quality of life assessed with: mean score in the Short Form-36 Scale (0-100, higher scores reflect better quality of life) (Eftekhar Ardebili, 2020) Follow up: cross-sectional	NA	59.17 (48.59 to 69.74)[1]	NA	633 (5 studies)	⨁◯◯◯ VERY LOW[2]	We are very uncertain about the quality of life after surgeries
Regret assessed with: difference (effect) in percentage of people with regret	Not reported					The effects of surgery on regret are unknown
Regret assessed with: percentage of people with regret (Bustos, 2021) Mean follow up: 4 years	NA	1% (0 to 2%)[3]	NA	7928 (27 studies)	⨁⨁◯◯ LOW[4]	The percentage of people who experience regret is low

CI: Confidence interval
NA: Not applicable

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

1. Similar scores for assigned males at birth and assigned females at birth.
2. Mean score rated down for risk of bias and inconsistency. According to the systematic review authors, all studies had concerns related to risk of bias. In addition, the smaller studies showed better quality of life than the larger study.
3. Similar percentage for assigned males at birth and assigned females at birth, and for different types of surgeries (all pooled percentages below 2%).
4. Percentage rated down due to risk of bias and indirectness. According to the authors, many of the studies had moderate or high risk of bias. The mean age of the participants at the time of surgery was higher than the target population. Because it was considered to not have an important effect on the pooled estimate, we did not rate down for statistical heterogeneity

3.2 **Effects of surgeries on assigned females at birth:** Table 4 summarizes the evidence about the effects of all surgeries on surgical outcomes among assigned at birth females. We used information from 3 systematic reviews.[13-17] Due to the nature of the outcomes (i.e. they can only be experienced by people who undergo surgeries), there cannot be studies comparing the outcomes between a group of people with gender dysphoria who undergo surgeries and another who does not.

Studies, therefore, assessed the outcomes among a group of people with gender dysphoria after surgery. The findings are:

- There is low certainty evidence suggesting that the percentage of people who are satisfied after chest surgery is high (92%)
- There is very low certainty evidence about the rate of surgical complications after chest surgery
- There is very low certainty evidence about the percentage of people who are satisfied, and the rate of surgical complications after bottom surgeries (see Table 4 for details)

Table 4: All surgeries compared to no surgeries in assigned females at birth (<21 years old) with gender dysphoria

Patient or population: assigned females at birth (<21 years old) with gender dysphoria
Intervention: surgeries
Comparison: no surgeries

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no surgery	Risk/ mean with surgery				
Chest surgery						
Satisfaction assessed with: percentage of people who reported being satisfied (Bustos VP, 2020b) Range of follow up: 6 weeks to 46 months[1]	NA	92% (88% to 96%)[2]	NA	733 (14 studies)	⊕⊕◯◯ LOW[3]	The percentage of people who reports being satisfied may be 92%
Surgical complications assessed with: rate of complications across patients (Oles, 2022) Range of follow up: 8 weeks to 1 year	NA	16.8% Range (5.5% to 80.0%)	NA	1255 (7 studies)	⊕◯◯◯ VERY LOW[4]	We are very uncertain about the rate of surgical complications
Reoperation assessed with: rate of reoperation across patients (Oles, 2022) Range of follow up: 8 weeks to 1 year	NA	6.2% Range (0.7% to 11.2%)	NA	1214 (6 studies)	⊕◯◯◯ VERY LOW[4]	We are very uncertain about the rate of reoperation
Bottom surgery						

Table 4: All surgeries compared to no surgeries in assigned females at birth (<21 years old) with gender dysphoria

Patient or population: assigned females at birth (<21 years old) with gender dysphoria
Intervention: surgeries
Comparison: no surgeries

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no surgery	Risk/ mean with surgery				
Satisfaction assessed with: percentage of people who reported being satisfied (Oles, 2022b) Range of follow up: 6 weeks to 46 months	NA	89.6% (45% to 100%)[5]	NA	1458 (27 studies)	⊕◯◯◯ VERY LOW[4]	We are very uncertain about the percentage of people who reports being satisfied
Surgical complications-Major assessed with: percentage of people experiencing major complications (Oles, 2022b) follow up: not reported	NA	The percentage was - 2.3% (range 0 to 20%) experiencing total flap loss - 19.5% (range 0 to 72%) experiencing prosthesis issues - 24.5% (range 0 to 86%) experiencing urethral issues	NA	3177 (42 studies)[6]	⊕◯◯◯ VERY LOW[4]	We are very uncertain about the percentage of people who experience major surgical complications
Surgical complications-Minor assessed with: percentage of people experiencing major complications (Oles, 2022b) follow up: not reported	NA	The percentage varied from 9.3% (range 0% to 45.5%) experiencing donor site issues, to 24% (range 10 to 93%) experiencing urethral issues[7]	NA	4466 (52 studies)[8]	⊕◯◯◯ VERY LOW[4]	We are very uncertain about the percentage of people who experience minor surgical complications

Table 4: All surgeries compared to no surgeries in assigned females at birth (<21 years old) with gender dysphoria

Patient or population: assigned females at birth (<21 years old) with gender dysphoria
Intervention: surgeries
Comparison: no surgeries

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no surgery	Risk/ mean with surgery				
Reoperation assessed with: rate of reoperation across patients (Oles, 2022b) follow up: not reported	NA	27.6% Range (2.5% to 40%)	NA	1624 (15 studies)	⊕◯◯◯ VERY LOW[4]	We are very uncertain about the percentage of people who undergo reoperations

CI: Confidence interval
NA: Not applicable

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

1. Studies used different scales to assess satisfaction
2. The percentage was similar when the analysis was done by type of surgery and by follow up time (< 1 year vs 1 year or more). Another systematic review (Oles, 2022) also investigated this outcome, and reported a very similar percentage of satisfaction (91.8%, range 73% to 100%)
3. Percentage of patients satisfied rated down due to risk of bias and indirectness. According to the systematic review authors, several studies were judged at moderate and high risk of bias. In addition, the median of the mean age of patients included in the studies was 28 years
4. Rated down due to risk of bias, inconsistency/ imprecision, and indirectness. Even though the review authors did not assess risk of bias, these studies were included in other systematic reviews in which the authors judged several of them at high risk of bias. The studies report inconsistent results (some high and other low rates). The patients are older than the target population.
5. Results for phalloplasty. Similar results for metoidioplasty (91.3%).

Effects of gender affirming therapies in people with gender dysphoria: evaluation of the best available evidence. Dr. Romina Brignardello-Petersen and Dr. Wojtek Wiercioch; Results; May 16, 2022

6. People and studies for urethral complications. 2671 people (37 studies) for prosthesis issues, and 1548 people (22 studies) for total flap loss.
7. Percentage of wound dehiscence 9.8% (range, 2.9% to 75%), percentage of infection/ partial necrosis 10.3% (range, 0 to 45.8%), percentage of prosthesis issues 14.2% (range, 1.6 to 41.9%), percentage of incontinence 15.3% (range, 5.4% to 59.1%)
8. People and studies for infection/ partial necrosis. 2389 people (31 studies) for urethral issues, 1736 people (17 studies) for wound dehiscence, 1080 (10 studies) for prosthesis issues, 1053 people (8 studies) for donor site issues, 131 people (3 studies) for incontinence

3.3 **Effects of surgeries on assigned males at birth**: Table 5 summarizes the evidence about the effects of all surgeries on surgical outcomes among assigned at birth males. We used information from 3 systematic reviews.[16 18 19] Due to the nature of the outcomes (i.e. they can only be experienced by people who undergo surgeries), there cannot be studies comparing the outcomes between a group of people with gender dysphoria who undergo surgeries and another who does not.

Studies, therefore, assessed the outcomes among a group of people with gender dysphoria after surgery. The findings are:

- There is low certainty evidence suggesting that the percentage of people who are satisfied after vaginoplasty is high (91%)
- There is very low certainty evidence about the percentage of people who are satisfied, the rate of complications, and the rate of reoperations after chest surgery (see Table 5 for details)
- There is low certainty evidence suggesting that the percentage of people who have regret after vaginoplasty is low (2%)
- There is very low certainty evidence about the rate of complications and the rate of reoperations after vaginoplasty (see Table 5 for details)

Table 5: All surgeries compared to no surgeries in assigned males at birth (<21 years old) with gender dysphoria

Patient or population: assigned males at birth (<21 years old) with gender dysphoria
Intervention: surgeries
Comparison: no surgeries

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no surgery	Risk/ mean with surgery				
Chest surgery						
Satisfaction assessed with: percentage of people who reported being satisfied (Oles 2022) Range of follow up: 12 months to 17 years	NA	Range 75% (80/107) to 95% (33/35)[1]	NA	142 (2 studies)	⊕◯◯◯ VERY LOW[2]	We are very uncertain about the percentage of people who report being satisfied
Surgical complications assessed with: rate of complications across patients (Oles 2022) Range of follow up: 2 weeks to 16 years	NA	The complication rates were: - 3.8% (range 0% to 5.5%) of capsular contracture - 2.2% of major hematoma - 2.2% of implant extrusion[3]	NA	432 (5 studies)	⊕◯◯◯ VERY LOW[2]	We are very uncertain about the rate of surgical complications
Reoperation assessed with: rate of reoperation across patients (Oles 2022) Range of follow up: Not reported	NA	8.6% Range (4.4% to 10.4%)	NA	291 (2 studies)	⊕◯◯◯ VERY LOW[2]	We are very uncertain about the rate of reoperation
Bottom surgery						

Table 5: All surgeries compared to no surgeries in assigned males at birth (<21 years old) with gender dysphoria

Patient or population: assigned males at birth (<21 years old) with gender dysphoria
Intervention: surgeries
Comparison: no surgeries

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no surgery	Risk/ mean with surgery				
Satisfaction assessed with: percentage of people who reported being satisfied for overall outcomes (Bustos SS, 2021) Range of follow up: 1 week to 11.3 years	NA	91% (81% to 98%)[4]	NA	1230 (12 studies)	⊕⊕◯◯ LOW[5]	The percentage of people who report being satisfied with overall outcomes may be 91%
Regret assessed with: percentage of people who reported regret (Bustos SS, 2021) Range of follow up: 2 months to 24.1 years	NA	2% (1% to 3%)	NA	1137 (15 studies)	⊕⊕◯◯ LOW[6]	The percentage of people who report regret may be 2%
Surgical complications assessed with: rate of complications across patients (Bustos SS, 2021) Range of follow up: 3 weeks to 24.1 years	NA	The complication rates were: - 1% (95% CI, <0.1% to 2%) of fistula - 11% (95% CI, 8% to 14%) of stenosis and/or strictures - 4% (95% CI, 1% to 9%) of tissue necrosis - 3% (95% CI, 1% to 4%) of prolapse[7]	NA	4196 (42 studies)[3]	⊕◯◯◯ VERY LOW[8]	We are very uncertain about the rate of surgical complications

Table 5: All surgeries compared to no surgeries in assigned males at birth (<21 years old) with gender dysphoria

Patient or population: assigned males at birth (<21 years old) with gender dysphoria
Intervention: surgeries
Comparison: no surgeries

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Risk / mean with no surgery	Risk/ mean with surgery				
Reoperation assessed with: rate of reoperation across patients (Tay, 2021) Range of follow up: 6 weeks to 14.8 months	NA	One study reported a surgical revision rate of 9% (1/11 patients), and a second study reported that 13% (19/145) patients required repeat surgery due to complications.	NA	156 (2 studies)	⊕◯◯◯ VERY LOW[9]	We are very uncertain about the percentage of people who undergo reoperations

CI: Confidence interval
NA: Not applicable

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

1. Another systematic review, Sijben 2021, reported satisfaction from 3 additional studies: 82% (113/138) were satisfied or very satisfied, 93% (32/34) were happier and more satisfied with their chest, and 79% (28/36) were very satisfied with the overall cosmetic result (very low certainty of evidence due to risk of bias, imprecision, and indirectness).
2. Rated down due to risk of bias, indirectness (the included studies were not restricted to youth or young adults), and imprecision (too few participants included, not meeting optimal information size).

3. Another systematic review, Sijben 2021, reported similar ranges for rates of complication requiring reoperation from 7 studies (835 patients): capsular contraction (range 0.0-5.6%), asymmetry (3.6%), hematoma (range 0.0-2.9%), infection (range 0.0-0.9%), striae distensae (0.7%), implant rupture (0.7%), abscess (0.4%), scarring (0.0%), hypersensitivity (0.0%), and numbness (0.0%) (very low certainty of evidence due to risk of bias, imprecision, and indirectness)
4. Bustos SS *et al.* 2021 additionally reported on satisfaction for functional (87%, 95% CI 77% to 94%) and aesthetic (90%, 95% CI 84% to 94%) outcomes. Another systematic review and meta-analysis, Oles 2022b, similarly reported that 92.3% (range 23.1% to 100%) of patients (2410/2601) were satisfied after vaginoplasty (very low certainty of evidence due to risk of bias, imprecision, and indirectness).
5. Rated down due to risk of bias (the systematic review authors reported the quality of the included studies to be low to moderate using the New Castle Ottawa scale), and indirectness as the included studies were not restricted to youth or young adults. We did not rate down for imprecision or inconsistency despite high I^2 values as a satisfaction rate of 80% or above was deemed as a minimum threshold for clinical importance.
6. Rated down due to risk of bias (the systematic review authors reported the quality of the included studies to be low to moderate using the New Castle Ottawa scale), and indirectness as the included studies were not restricted to youth or young adults.
7. Another systematic review, Oles 2022b, similarly reported the percentage of patients experiencing complications from 51 studies, ranging from 2.4% to 12.0% (range 0% to 88%) for minor complications (intraoperative injury, wound dehiscence, superficial necrosis, infection, urinary issues, vaginal prolapse, stenosis, and bleeding) and 1.6% to 2.1% (range 0% to 31%) for major complications (flap/graft necrosis and infection) after genitoplasty (very low certainty of evidence due to risk of bias, imprecision, and indirectness).
8. Rated down due to risk of bias (the systematic review authors reported the quality of the included studies to be low to moderate using the New Castle Ottawa scale), imprecision and inconsistency, with wide confidence intervals and I^2 values ranging from 65.8% to 94.3%, and indirectness as the included studies were not restricted to youth or young adults.
9. Rated down due to risk of bias, indirectness (the age range of patients in the included studies was 24 to 39 years; the studies included were restricted to those that investigated the use of peritoneum in neovagina construction), and imprecision (too few participants included, not meeting optimal information size).

Results from search for studies not included in the systematic reviews: After screening 1854 records found through our searches, we found 10 eligible studies (figure 5). From these, 8 were comparative observational studies[20-27] and 2 were non- comparative[28 29]. We provide reasons for excluding studies in appendix 2.

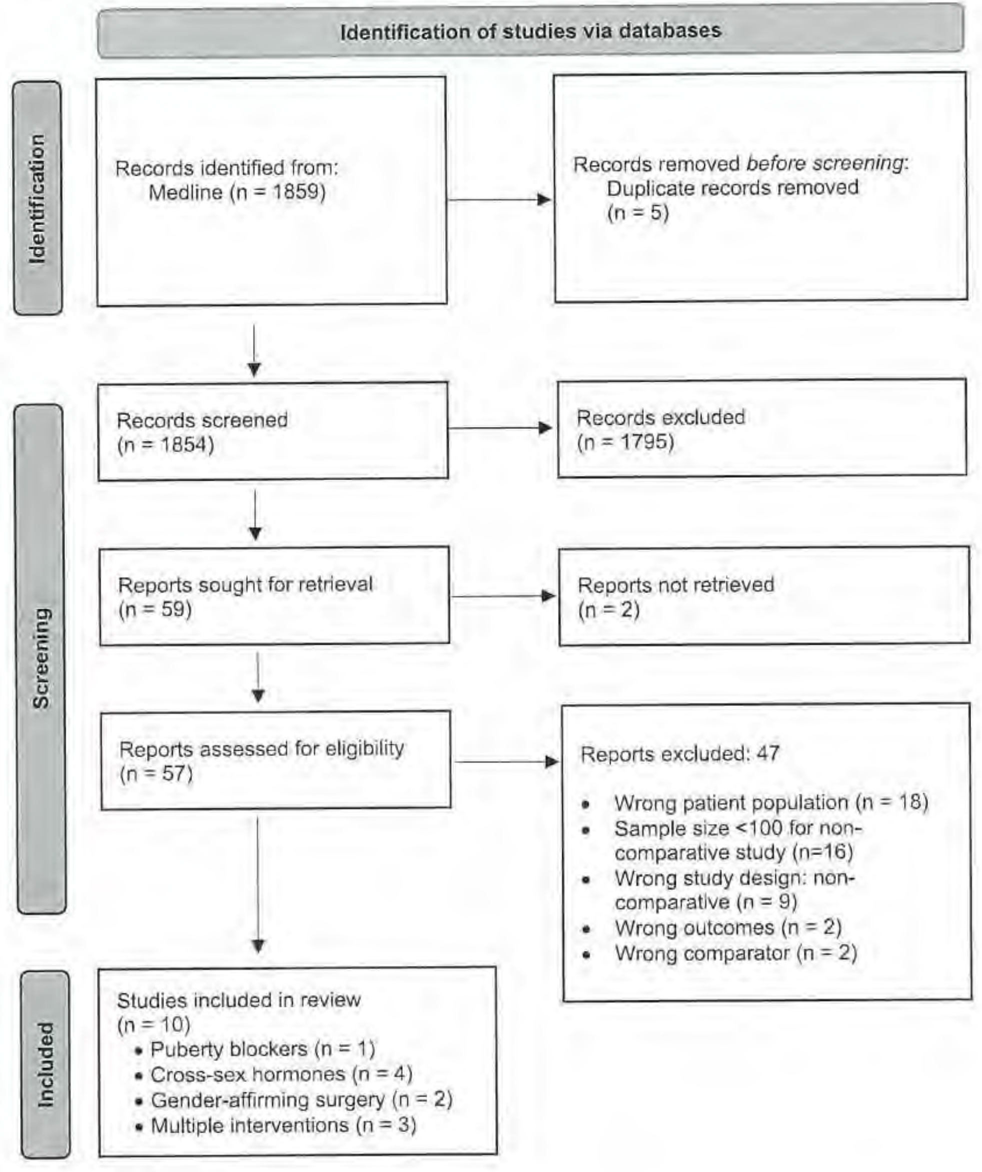


Figure 5: PRISMA flow diagram for the selection of primary studies. *From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

None of the studies were judged as likely to importantly change the conclusions obtained from the systematic reviews (Tables 6 and 7). The main limitations of the comparative studies were risk of bias concerns (Figures 6 and 7) due to confounding, classification of intervention, and missing data; as well as small sample sizes. Although non-comparative studies were at lower risk of bias, because their results were consistent with those of the included evidence, they were also judged as unlikely to change the conclusions importantly.

Table 6: Characteristics of eligible comparative observational studies

Study ID	Sample size*	Study design	Intervention	Comparator	Outcomes measured	Likely to change conclusions	Reasons
VanDerMiesen, 2020	450	Retrospective cohort study	Puberty blockers	Waiting for puberty blockers	Self-harm/ suicidality, internalizing behaviors	No	Reports a small benefit on suicidality and moderate on internalizing behaviours, but high risk of bias
Becker-Hebly, 2021	75	Prospective cohort study	1. Puberty blockers 2. Cross-sex hormones 3. Surgery	No medical intervention yet; psychosocial intervention only	Health-related quality of life	No	Critical risk of bias (missing data due to low response rate, and confounding). Reports small benefit in mean change score for mental and physical dimension QoL as compared to no medical treatment. Imprecision; the 95% CIs for mean change scores are wide.
Green, 2021	3235	Cross-sectional study	Cross-sex hormones	Would like to take cross-sex hormones	Depression, suicidality	No	Critical risk of bias, no follow up of patients (measurement of current outcomes and not adjusting for baseline)
Tordoff, 2022	84	Prospective cohort study	1. Puberty blockers 2. Cross-sex hormones	No intervention	Depression, anxiety, suicidal thoughts	No	Moderate risk of bias, small sample size
Turban, 2022	9341	Cross-sectional study	Cross-sex hormones	Desired but never accessed gender affirming hormones	Suicidal ideation, suicidal attempt	No	Critical risk of bias, no follow up of patients (measurement of current outcomes and not adjusting for baseline)
Grannis, 2021	47	Cross-sectional study	Cross-sex hormones	No intervention yet	Anxiety, depression	No	Critical risk of bias, no follow up of patients, small sample size
Fontanari, 2020	350	Cross-sectional study	1. Cross-sex hormones 2. Cross-sex hormones or surgery	1. Waiting for cross-sex hormones 2. No intervention	Anxiety, depression, gender distress	No	Critical risk of bias (confounding, self-reported classification of interventions). Online cross-sectional survery reported small benefit in anxiety and depression mean scores, and little to no effect on gender distress with cross-sex hormones and/or surgery. Non-randomized comparative study provides very low certainty evidence due to

							very serious risk of bias and serious imprecision (95% CIs include little to no effect)
Castelo-Branco, 2021	205	Cross-sectional study	Cross-sex hormones	No intervention	Anxiety, depression	No	Critical risk of bias due to confounding (non-adjusted analysis). Reported no difference observed in anxiety and depression mean scores (Symptom Checklist-90-Revised scale) between groups. Non-randomized comparative study provides low certainty evidence.

*Considered the number of participants relevant to the questions of this report, not all people included in the studies

Table 7: Characteristics of eligible non- comparative observational studies

Study ID	Sample size	Intervention	Outcomes measured	Likely to change conclusions	Reasons
Bordas, 2021	813	FtM bottom surgery	Surgical complications, satisfaction	No	Reports rate of complications (10.5%) and satisfaction (79% totally satisfied, 20% mainly satisfied) within range of effects reported by studies already included in systematic reviews. Unlikely to reduce imprecision and inconsistency within body of evidence (3177 and 1458 people, respectively) of non-comparative studies (42 and 27, respectively) to increase certainty of evidence
Elias, 2022	110	FtM top surgery	Complications	No	Reports rate of complications (16%) and revision surgery (5%), which is consistent with the rates reported in the studies included. Unlikely to increase the certainty of evidence

Figure 6: Risk of bias judgements for comparative studies

Study ID	Intervention	Confounding	Classification of the intervention	Deviations from intended interventions	Missing data	Measurement of outcome	Overall
Becker-Hebly, 2021	Puberty blockers, cross-sex hormones, or surgery						CRITICAL
Castelo-Branco, 2021	Cross-sex hormones						CRITICAL
Fontanari, 2020	Cross-sex hormones, cross-sex hormones or surgery						CRITICAL
Grannis, 2021	Cross-sex hormones						CRITICAL
Green, 2021	Cross-sex hormones						CRITICAL
Tordoff, 2022	Puberty blockers, cross-sex hormones						MODERATE
Turban, 2022	Cross-sex hormones						CRITICAL
Van Der Miesen, 2020	Puberty blockers						SERIOUS

Figure legend:

- Low
- Moderate
- Serious
- Critical
- Unclear

Figure 7: Risk of bias judgements for non-comparative studies

Study ID	Intervention	Representativeness of sample	Classification of intervention	Deviation from intended interventions	Missing data	Measurement of outcome	Overall
Bordas, 2021	FtM bottom surgery						LOW
Elias, 2022	FtM top surgery						MODERATE

Figure legend:

Low

Moderate

High

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ID	Study	Reason
#534	Abu-Ghname 2020	Wrong population: non transgender men
#434	Aires 2022	Wrong interventions: Other type of surgery: glottoplasty
#514	Angus 2021	Wrong outcomes: It does not include any outcome of interest. Includes: serum total testosterone concentration, body fat redistribution, breast development, and facial/body hair reduction
#318	Baddredine 2022	Wrong intervention. Continuing vs stopping estrogen during perioperative period of vaginoplasty
#40	Baram 2019	Wrong outcomes: only clinical outcomes are sperm count, testicular histology, hormone levels, etc.
#145	Barcelos 2022	Wrong outcomes: sexual satisfaction, desire, and function outcomes only
#60	Boczar 2021	No outcome data
#386	Bouman 2014	Wrong population: unclear that more than 80% are transgender
#208	Bustos 2021	Wrong intervention: niple areola reconstruction
#54	Connelly 2021	Wrong outcomes: Blood pressure
#43	Coon 2022	Wrong intervention: facial gender surgery
#34	D'Angelo 2018	Wrong design: narrative review
#165	Delgado-Ruiz 2019	Wrong outcomes: bone density
#355	Escandon 2022	Other type of surgery: facial surgery
#129	Fighera 2019	Wrong outcomes: bone mass
#597	Hembree 2017	Practice guideline, does not report the methods/ results of the systematic review in details
#120	Kakadekar 2021	Wrong outcomes: histological findings
#451	Kennedy 2021	Wrong intervention: self administered hormones
#375	Kloer 2021	Wrong outcomes: sexual health and satisfaction outcomes only
#439	Kovar 2019	More than 20% participants did not have gender dysphoria
#297	Kristensen 2021	Wrong outcomes: agression and hostility
#637	Leclere 2015	Wrong design: commentary of a systematic review
#293	Miranda 2021	Published in abstract format only
#624	Morrison 2016	Wrong intervention: facial feminization surgery
#270	Narayan 2021	Wrong design: narrative review
#119	Nolan 2019	Wrong intervention: phonosurgery
#167	Patel 2021	Wrong intervention: facial hair transplantation
#287	Ray 2020	Wrong population: cisgender is the population of interest, transgender included as indirect evidence and not in a systematic manner
#518	Rozga 2020	Published in abstract format only
#265	Sariyaka 2017	Wrong population: More than 20% participants did not have gender dysphoria
#35	Sayegh 2019	Wrong intervention: facial mascullnization surgery
#124	Schwarz 2017	Wrong intervention: laryngeal surgery

#97	Siringo 2021	Wrong intervention: facial feminization surgery
#253	Song 2016	Wrong intervention: phonosurgery
#250	Song 2017	Wrong intervention: phonosurgery
#104	Spanos 2020	Wrong outcomes: lean mass, fat mass or insulin resistance
#257	Therattil 2017	Wrong intervention: thyroid chartilage reduction surgery
#328	Tirrell 2022	Wrong intervention: facial feminization surgery
#676	Traish 2010	Wrong design: narrative review
#279	VanDamme 2017	Wrong intervention: voice pitch raising surgery
#171	Vellho 2017	Wrong outcomes: BMI, blood pressure, hematocrit, hemoglobin, lipid profile, and liver enzymes
#112	Wilson 2020	Wrong outcomes: prolactine related outcomes (levels, hyperprolactinemia, prolactinoma)
#245	Worth 2018	Unable to access full text
#122	Ziegler 2018	Wrong outcomes: voice parameters and satisfaction with voice
#499	Zucker 2021	Unable to access full text

ID	Study	Reason
#1458	Al-Tamimi 2019	Wrong patient population
#287	Al-Tamimi 2020	Wrong study design: non comparative
#403	Alcon 2021	Wrong study design: non comparative
#214	Aldridge 2021	Wrong study design: non comparative
#54	Almazan 2021	Wrong patient population
#1387	Boas 2019	Wrong patient population
#1323	Branstrom 2020	Wrong patient population
#1447	Breidenstein 2019	Wrong study design: non comparative
#114	Briles 2022	Insufficient Sample Size <100
#1804	Butler 2019	Wrong patient population
#716	Carmichael 2021	Wrong study design: non comparative
#622	Cocchetti 2021	Wrong outcomes
#1067	Coon 2020	Wrong patient population
#1835	Cristofari 2019	Wrong patient population
#1486	Cuccolo 2019	Wrong patient population
#1276	deBlok 2020	Wrong patient population
#577	deRooij 2021	Wrong patient population
#1625	DeWolf 2019	Wrong patient population
#1759	Djordjevic 2019	Wrong patient population
#244	Falcone 2020	Insufficient Sample Size <100
#258	FosterSkewis 2021	Wrong comparator
#1583	Gallagher 2019	Wrong patient population
#139	Gumussoy 2022	Wrong study design: non comparative
#515	Hisle-Gorman 2021	Wrong study design: non comparative
#350	Hougen 2021	Insufficient Sample Size <100
#1007	Meyer 2020	Wrong study design: non comparative
#499	Miller 2021	Wrong patient population
#621	Mullins 2021	Wrong study design: non comparative
#1653	Naeimi 2019	Insufficient Sample Size <100
#1691	Namba 2019	Insufficient Sample Size <100
#1770	Neuville 2019	Insufficient Sample Size <100
#623	Neuville 2021	Insufficient Sample Size <100
#644	Nieder 2021	Insufficient Sample Size <100
#1624	Nikkels 2019	Wrong patient population
#353	Opsomer 2021	Wrong patient population
#1306	Papadopulos 2020	Wrong comparator
#640	Papadopulos 2021	Insufficient Sample Size <100
#1472	Pigot 2019	Wrong patient population
#899	Pigot 2020	Insufficient Sample Size <100
#1212	Segev-Becker 2020	Insufficient Sample Size <100
#1351	Staples 2020	Wrong outcomes
#645	Staud 2021	Insufficient Sample Size <100
#864	Terrier 2020	Insufficient Sample Size <100
#1083	vanderSluis 2020	Insufficient Sample Size <100