EXHIBIT 43

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

* * *

BRIANNA BOE, et al.,
Plaintiffs,
UNITED STATES OF AMERICA,
Intervenor Plaintiff,
vs. CASE NO. 2:22-cv-184-LCB
HON. STEVE MARSHALL, in his Official capacity as Attorney General, of the State of Alabama, et al.,

Defendants.

* * *

Deposition of ARMAND H. ANTOMMARIA, M.D., Ph.D., FAAP, HEC-C, Witness herein, called by the Defendants for examination pursuant to the Rules of Civil Procedure, taken before me, Monica K. Schrader, a Notary Public in and for the State of Ohio, at the U.S. Attorney's Office, Cleveland Branch Office, Atrium II Building, 221 East Fourth Street, Suite 400, Cincinnati, Ohio, on Friday, April 21, 2023, at 9:03 a.m.

* * *

INDEX

WITNESS: ARMAND H. ANTOMMARIA, M.D., Ph.D., FAAP, HEC-C

APPEARANCES:

On behalf of the Intervenor Plaintiff:

U.S. Department of Justice

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ALSO PRESENT:

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Shannon Minter, Esq.

* * *

ARMAND H. ANTOMMARIA, M.D., Ph.D., FAAP, HEC-C
of lawful age, Witness herein, having been first duly cautioned and sworn, as hereinafter certified, was examined and said as follows:

EXAMINATION

BY MR. FRAMPTON:

Q. Good morning, Dr. Antommaria. 09:03:33
A. Good morning. 09:03:35
Q. How are you? 09:03:35
A. I am all right, thank you. 09:03:36
Q. Very good. I introduced myself earlier, but I am Hal Frampton. I am representing the State of Alabama, and I am going to ask you some questions over the course of the day. Have you had your deposition taken before? 09:03:37 09:03:40 09:03:42 09:03:44 09:03:46 09:03:50
A. I have. 09:03:50
Q. How many times about? 09:03:51
A. Twice. 09:03:53
Q. Twice. What cases were those in, to the best of your recollection? 09:03:54 09:03:57
A. The case in Arkansas and the case in Florida. 09:03:58 09:04:01
Q. Okay, got it. The case in Arkansas, the Brandt case; is that right? 09:04:02 09:04:07

A. Correct. 09:04:09
Q. And Florida, was that a recent 09:04:09
deposition? 09:04:12
A. Yes. 09:04:13
Q. When was it? 09:04:13
A. About two weeks ago. 09:04:14
Q. Okay, got it. Well, you know 09:04:17
basically how this process works. This will 09:04:20
work the same as your others. I am going to 09:04:22
ask you a series of questions. You understand 09:04:25
that you are under oath this morning, correct? 09:04:27
A. I do. 09:04:28
Q. Fair enough. Dr. Antommaria, I am 09:04:45
going to hand you what I am marking as 09:04:52
Exhibit 1. 09:04:53
(Thereupon, Exhibit 1, curriculum 09:05:01
vitae, was marked for purposes of identification.) 09:05:02
BY MR. FRAMPTON: 09:05:02
Q. All right. Dr. Antommaria, is 09:05:17
Exhibit 1 a current copy of your CV? 09:05:18
A. Yes, it's a current copy of my CV. 09:05:21
Q. Thank you, sir. 09:05:41
MR. CHEEK: And, Mr. Frampton, my 09:05:42
apologies, can I put something on the record 09:05:45
before we go further? That we are not agreeing to 09:05:46

the usual stipulations. We will take this 09:05:49
deposition according to the Federal Rules. 09:05:51
MR. FRAMPTON: Okay. 09:05:53
MR. CHEEK: And we will also reserve 09:05:53
the right to read and sign. 09:05:55
MR. FRAMPTON: Okay. 09:05:57
MR. CHEEK: My apologies. 09:05:57
BY MR. FRAMPTON: 09:05:58
Q. All right. Dr. Antommaria, I see 09:06:01
on the second page of your CV that you are in 09:06:04
the Department of Surgery; is that correct? 09:06:07
A. I have a secondary appointment in 09:06:11
the Department of Surgery. 09:06:15
Q. Okay. Are you a surgeon? 09:06:17
A. No, I am not. 09:06:19
Q. What is your specialty? 09:06:20
A. My clinical specialty is as a 09:06:24
pediatric hospitalist. 09:06:31
Q. And so that means you manage the 09:06:33
care of pediatric patients while they are 09:06:36
inpatients; is that correct? 09:06:39
A. That is an aspect of what a 09:06:40
pediatric hospitalist does or how a pediatric 09:06:47
hospitalist is defined. 09:06:50
Q. Okay. What did I miss in that 09:06:52

definition? 09:06:54
A. Oh, we don't care for all types of 09:06:55
pediatric inpatients. 09:06:58
Q. Okay. What types of pediatric 09:06:59
inpatients do you not care for? 09:07:03
A. We don't care for surgical 09:07:04
patients or patients exclusively admitted for a 09:07:12
single subspecialty condition. 09:07:17
Q. Is it the case in your clinical 09:07:19
practice that all of your patients are 09:07:25
inpatients? 09:07:27
A. So all the patients that I care 09:07:28
for were admitted as an inpatient. We are 09:07:38
increasingly managing transitions to home and 09:07:43
do receive phone calls for patients following 09:07:49
their discharge. So all of the patients that I 09:07:51
am providing medical care for are not 09:07:55
concurrently inpatients but were inpatients at 09:07:58
one point in time. 09:08:02
Q. It looked to me on the website for 09:08:02
Cincinnati Children's that child psychiatry has 09:08:15
its own inpatient facilities; is that correct? 09:08:18
A. Yes. There are specific inpatient 09:08:20
psychiatric beds at Cincinnati Children's. 09:08:28
Q. And do you service those patients? 09:08:31

MR. CHEEK: Objection, form. 09:08:37
THE WITNESS: So I am sorry that this 09:08:43
is complicated. So as a pediatric hospitalist, I 09:08:45
do admit psychiatric patients either awaiting 09:08:49
medical clearance or who have been medically 09:08:54
cleared and are awaiting psychiatric admission. 09:08:57
And as a bioethicist, I consult on patients 09:09:03
admitted to -- so the name of the facility at 09:09:10
Cincinnati Children's where the inpatient 09:09:13
psychiatric beds are located is called College 09:09:16
Hill. I consult on patients who are admitted at 09:09:19
College Hill. 09:09:22
BY MR. FRAMPTON: 09:09:23
Q. In your capacity as a medical 09:09:23
ethicist? 09:09:25
A. Yes. 09:09:26
Q. What about in your capacity as a 09:09:26
pediatric hospitalist? 09:09:31
A. No. 09:09:33
Q. Approximately what percentage of 09:09:33
your time is spent on your practice as a 09:09:41
pediatric hospitalist? 09:09:44
A. 30 percent of my effort is 09:09:45
dedicated to my work as a pediatric 09:09:49
hospitalist. 09:09:51

Page 14

Q. And what percentage as a medical ethicist? 09:09:52 09:09:54
A. So 70 percent of my time is dedicated to my role as the director of the Ethics Center at Cincinnati Children's. 09:09:55 09:09:59 09:10:04
Q. You do not perform the initial diagnosis of gender dysphoria in a patient, do you? 09:10:05 09:10:11 09:10:14
A. That is correct, I don't perform the initial diagnosis. 09:10:14 09:10:17
Q. And you do not initiate medical treatment; is that correct? 09:10:18 09:10:22
MR. CHEEK: Objection, form. 09:10:24
THE WITNESS: Could you be more -- what do you mean by medical treatment, sir? 09:10:28 09:10:29
BY MR. FRAMPTON: 09:10:32
Q. Do you initiate the treatment of puberty-suppressing medication in patients with gender dysphoria? 09:10:33 09:10:35 09:10:39
A. No, I do not. 09:10:39
Q. What about cross-sex hormones? 09:10:40
A. I don't initiate the use of gender affirming hormone therapy. 09:10:43 09:10:49
Q. Your medical ethics practice, what all does that consist of? 09:10:50 09:11:04

Page 15

A. So I direct the Ethics Center at Cincinnati Children's, so I have oversight for the center's activities. The center has activities related to research, clinical and organizational ethics. I would be happy to provide more specific information about any of those areas. 09:11:05 09:11:16 09:11:19 09:11:23 09:11:28 09:11:33 09:11:39
Q. Sure. About what percentage of your time is spent actually consulting on clinical care? 09:11:39 09:11:43 09:11:46
A. I think it's hard to identify a particular percentage of my time because I don't track time in the way lawyers track billable hours, so I don't -- it would be difficult for me to give an estimate of that. 09:11:46 09:11:58 09:12:02 09:12:07 09:12:10
Q. Is it the majority of your time? 09:12:12
A. Probably not the majority of my time. 09:12:15 09:12:22
Q. Are you compensated separately for your clinical practice and your practice as director of ethics or director of the Ethics Center? 09:12:23 09:12:28 09:12:31 09:12:34
A. By compensated separately, can I ask what you mean? 09:12:34 09:12:41
Q. Sure. I am simply asking are 09:12:42

Page 16

you -- do you have sort of a compensation line item for your clinical practice and a line item for your role as director of the Ethics Center? 09:12:45 09:12:48 09:12:50
Is it broken out in that way? 09:12:54
A. So within the Ethics Center budget, there is compensation for my clinical time, which comes from the Division of Hospital Medicine. And there is our other budget lines for my effort related to being the director of the Ethics Center. 09:12:56 09:13:00 09:13:05 09:13:09 09:13:14 09:13:18
Q. In your clinical consultation practice, that is not limited as an ethicist -- that is not limited to gender dysphoria issues, correct? 09:13:18 09:13:28 09:13:34 09:13:37
MR. CHEEK: Objection, form. 09:13:37
THE WITNESS: No, it is not limited in that way. 09:13:39 09:13:41
BY MR. FRAMPTON: 09:13:41
Q. About what percentage of your time do you believe you spend on gender dysphoria issues in your role as an ethicist? 09:13:43 09:13:44 09:13:46
A. So, again, it's difficult for me to put a percentage. I would say that I attend and participate in Adolescent Medicine Clinic that cares for transgender patients, 09:13:50 09:14:00 09:14:06 09:14:12

Page 17

multidisciplinary team meeting. I consult on patients on an as-needed basis when particular ethical issues arise, which may be two to three patients. I may have separate conversations about patients that don't arise to a formal ethics consult. And I am engaged in institutional issues related to policies and procedures related to the care of patients with gender dysphoria, which are not individual patient consultation. 09:14:17 09:14:20 09:14:28 09:14:31 09:14:36 09:14:40 09:14:45 09:14:53 09:14:55 09:15:03
Q. Would you say all of that adds up to a majority of your time? 09:15:04 09:15:10
A. It does not. 09:15:11
Q. You said two to three patients. What number -- what number are you referring to there? 09:15:12 09:15:17 09:15:20
A. It would be two to three patients per year. 09:15:20 09:15:21
Q. Got it, fair enough. You are not a psychiatrist; is that correct? 09:15:22 09:15:27
A. That is correct. 09:15:28
Q. You are not a psychologist; is that correct? 09:15:30 09:15:33
A. That is correct. 09:15:33
Q. I have got a few of these. You 09:15:33

are not an endocrinologist; is that correct? 09:15:37
A. That is correct. 09:15:39
Q. All right. What training do you 09:15:40
have in adolescent developmental psychology? 09:15:44
A. I have training in adolescent 09:15:48
development psychology as part of my medical 09:15:55
school education, as part of my pediatric 09:15:59
residency training, and as part of my ongoing 09:16:02
professional education. 09:16:06
Q. Do you consider yourself an expert 09:16:07
in adolescent developmental psychology? 09:16:12
A. No, I don't consider myself an 09:16:15
expert in that area. 09:16:19
Q. What is your training in the study 09:16:20
of cognitive development? 09:16:32
A. Again, I have training in the 09:16:33
study of cognitive development as a result of 09:16:40
my medical school education, my residency 09:16:43
training, and my ongoing professional 09:16:46
development. 09:16:49
Q. Do you consider yourself an expert 09:16:50
in that area? 09:16:53
A. So I don't consider myself an 09:16:54
expert in that area colloquially. There are 09:17:02
particular areas related to, say, adolescent 09:17:07

capacity to make decisions that are a narrow 09:17:11
subset of the entire field in which I have a 09:17:16
greater knowledge. 09:17:20
MR. FRAMPTON: Let's go off the
record because I don't want to burn time on people
joining.
(Thereupon, an off-the-record
discussion was had.)
BY MR. FRAMPTON:
Q. Back on. Dr. Antommaria, you do 09:18:04
not have any peer-reviewed publications on any 09:18:06
issues of transgender medicine; is that 09:18:08
correct? 09:18:10
A. That is correct. 09:18:10
Q. You have not been an investigator 09:18:13
in any study of the safety or efficacy of any 09:18:17
hormonal interventions as treatment for gender 09:18:20
dysphoria; is that correct? 09:18:23
A. That is correct. 09:18:24
Q. All right. Can you tell me the 09:18:27
difference between suicide and suicidality, if 09:18:52
you know? I mean, if I ask questions that are 09:18:57
outside your expertise, just tell me. 09:18:58
A. So if by suicide you mean 09:19:06
completed suicide, that would be somebody who 09:19:09

attempts to take their life and is successful 09:19:14
and has died, and suicidality would be that 09:19:16
someone has thoughts of committing suicide or 09:19:22
potentially attempts to commit suicide. 09:19:28
Q. Suicidality is far more common 09:19:37
than completed suicide; is that correct? 09:19:40
A. That is correct. 09:19:41
Q. Do you consider yourself an expert 09:19:42
in suicide or suicidality? 09:19:47
A. No, I don't consider myself an 09:19:50
expert on those topics. 09:19:52
Q. When -- are you aware of any study 09:19:53
demonstrating that the medical transition of 09:20:12
any type, whether it's hormonal, surgical, 09:20:17
whatever, reduces the rate of completed suicide 09:20:20
among any population of transgender 09:20:24
individuals? 09:20:29
MR. CHEEK: Objection. I didn't hear 09:20:29
the last part of your question, Counsel. 09:20:31
MR. FRAMPTON: I'll just do it again. 09:20:40
BY MR. FRAMPTON: 09:20:41
Q. Are you aware of any study -- I'll 09:20:42
speak up -- are you aware of any study 09:20:43
demonstrating that medical transition of any 09:20:46
kind reduces the rate of completed suicides 09:20:48

among any population of transgender 09:20:52
individuals? 09:20:54
A. I am not aware of such a study. 09:20:54
Q. When we treat an adolescent -- a 09:21:00
gender dysphoric adolescent with hormone 09:21:15
therapy, the hope certainly is that they are 09:21:19
going to have far more adult years in their 09:21:20
life than teenage years, correct? 09:21:23
A. Yes, we would anticipate that 09:21:26
individuals have more adult years than teenage 09:21:36
years. 09:21:38
Q. And so the effect of the hormonal 09:21:38
intervention over the course of adult years is 09:21:45
at least as important as the short-term effect 09:21:48
of the intervention, would you agree? 09:21:52
A. Both the short term and long-term 09:21:54
effects of the intervention are important 09:21:58
considerations. 09:22:00
Q. Equally important? 09:22:01
A. It would depend on the clinical 09:22:10
context, sir. 09:22:12
Q. How is that? 09:22:13
A. For someone with less severe 09:22:13
dysphoria, the long-term effects may have a 09:22:26
greater weight. And for somebody with a severe 09:22:31

dysphoria, the short-term effects might have greater weight. 09:22:37 09:22:40

Q. Even in the latter case, the long-term effects are important, are they not? 09:22:40 09:22:45

A. In the latter case, being someone with severe dysphoria? 09:22:47 09:22:53

Q. Yes. 09:22:54

A. Yes. 09:22:55

(Thereupon, Exhibit 2, Hormone Therapy, Mental Health, and Quality of Life Among Transgender People: A Systematic Review, was marked for purposes of identification.) 09:23:06 09:23:06 09:23:06 09:23:07

BY MR. FRAMPTON: 09:23:07

Q. All right. Dr. Antommaria, I am going to show you what I am marking as Exhibit 2. What I marked is a paper entitled Hormone Therapy, Mental Health, and Quality of Life Among Transgender People, A Systematic Review. The lead author is Kellan Baker. And, Dr. Antommaria, first question, is this an article that you are familiar with? 09:23:21 09:23:23 09:23:24 09:23:58 09:24:01 09:24:04 09:24:07 09:24:10

A. No, sir, it is not. 09:24:11

Q. So this wasn't something that you reviewed in preparing your expert report? 09:24:13 09:24:17

A. No, sir, it is not. 09:24:22

Q. Then my questions about it are going to be very limited. But I would like you to turn to page 13. 09:24:24 09:24:29 09:24:32

A. I am on page 13, sir. 09:24:44

Q. Look under acknowledgements. Do you see where it says Financial Support: This review was partly funded by the World Professional Association for Transgender Health? 09:24:46 09:24:49 09:24:51 09:24:53 09:24:56

A. Yes, sir, I do see that. 09:25:00

Q. Are you familiar with that organization? 09:25:02 09:25:03

A. I am, sir. 09:25:04

Q. Do you know if this was a review commissioned by WPATH for Standards of Care 8? 09:25:04 09:25:13

MR. CHEEK: Objection, speculation. 09:25:19

THE WITNESS: As I said, sir, I am not familiar with the article, so I am not familiar with that aspect of the article. 09:25:20 09:25:21 09:25:22

BY MR. FRAMPTON: 09:25:24

Q. Okay. Well, then I am not going to ask you anything terribly substantive about this. What I will -- look on page 12 under discussion. At the bottom of that first paragraph, it says: It was impossible to draw 09:25:25 09:25:27 09:25:30 09:25:34 09:25:42

conclusions about the effects of hormone therapy on death by suicide. Do you see that? 09:25:46 09:25:48

A. I do see that sentence, sir. 09:25:50

Q. And my question is simply are you aware of any systematic reviews that have been able to draw conclusions about the effects of hormone therapy on suicide? 09:25:53 09:25:55 09:25:59 09:26:04

A. So I believe that my answer to the prior question was that I wasn't aware of any individual studies. And not being aware of any individual studies, I am also not aware of any meta-analyses of individual studies. 09:26:05 09:26:13 09:26:17 09:26:22 09:26:29

Q. Fair. Okay, we are done with that one. 09:26:30 09:27:13

(Thereupon, Exhibit 3, Psychosocial Functioning in Transgender Youth after 2 Years of Hormones, was marked for purposes of identification.) 09:27:13 09:27:13 09:27:13 09:27:13

BY MR. FRAMPTON: 09:27:13

Q. I think we'll have a little better luck with this one. I am going to show you, Dr. Antommaria, what I am marking as Defendants' Exhibit 3. I found my exhibit sticker, so we are starting off on the right foot. 09:27:13 09:27:13 09:27:14 09:27:17 09:27:22 09:27:24

And what I have marked as Exhibit 3 is an article entitled Psychosocial Functioning in Transgender Youth after 2 Years of Hormones. The lead author is Diane Chen. And, Dr. Antommaria, are you familiar with this article? 09:27:36 09:27:39 09:27:42 09:27:45 09:27:54 09:27:56

A. Yes, I am. 09:27:56

Q. You cited this one in your expert report, correct? 09:28:00 09:28:02

A. So I don't have my expert report before me. I believe so. 09:28:03 09:28:09

Q. We will. You are familiar with the article. It doesn't matter for purposes of this line of questioning. Let's -- first, are you familiar with any of the researchers listed here? 09:28:11 09:28:15 09:28:17 09:28:25 09:28:29

A. Familiar in what way, sir? 09:28:31

Q. Do you know any of them? 09:28:34

A. I have met Dr. Rosenthal, as Dr. Rosenthal has lectured at Cincinnati Children's. 09:28:35 09:28:43 09:28:45

Q. Does he have a strong reputation? 09:28:45

MR. CHEEK: Objection, form. 09:28:57

THE WITNESS: A strong reputation for what, sir? 09:28:58 09:29:04

BY MR. FRAMPTON: 09:29:04
Q. For this kind of research. 09:29:07
A. My general understanding is that 09:29:12
Dr. Rosenthal is an expert in the field of 09:29:14
transgender health care. 09:29:17
Q. Are you familiar with Dr. Chen? 09:29:18
Have you read other publications by her? 09:29:25
A. So given that many articles have 09:29:28
multiple authors, and I may not always be as 09:29:38
attentive to the middle authors of a 09:29:44
publication, I may have read articles by 09:29:47
Dr. Chen, but none immediately come to mind. 09:29:51
Q. Okay, fair. This is published in 09:29:57
the New England Journal of Medicine, correct? 09:30:04
A. It is, sir. 09:30:06
Q. Is that a prestigious medical 09:30:09
journal, in your understanding? 09:30:12
A. It is, sir. 09:30:13
Q. All right. Let's talk about this 09:30:14
study. This is a perspective cohort study; is 09:30:18
that correct, in terms of research design? 09:30:29
A. Yes, sir. 09:30:31
Q. And that means that the 09:30:31
researchers are sort of monitoring the 09:30:34
participants as the experiment proceeds, 09:30:37

correct? 09:30:40
A. Yes, they establish a cohort of 09:30:41
patients and follow them over time. One might 09:30:48
refer to it as an observational study. 09:30:54
Q. Fair enough. This study, we have 09:30:56
got 315 participants, correct? 09:31:02
A. Yes, sir. 09:31:05
Q. The mean age is 16; is that right? 09:31:11
A. Yes, sir. I believe that would be 09:31:17
a reference to their mean age at the time of 09:31:26
enrollment. 09:31:29
Q. Right. And if you flip to page 09:31:29
241, about halfway down the second column. Is 09:31:37
it your understanding that these patients were 09:31:49
followed for 24 months? 09:31:52
A. Yes, sir. 09:31:55
Q. Flip to page 243, please, sir. 09:31:56
The first column under sample characteristics 09:32:17
towards the bottom, do you see where it says 09:32:19
two participants died by suicide during the 09:32:20
study, one after six months of follow-up and 09:32:22
the other after 12 months of follow-up and six 09:32:25
participants withdrew from the study? 09:32:29
A. So I'm sorry, which subsection in 09:32:31
the article are you reading that? 09:32:33

Q. I'm sorry, that's sample 09:32:34
characteristics. 09:32:35
A. Okay. 09:32:36
Q. Next to last sentence from the 09:32:36
bottom of that particular section, I'll read it 09:32:40
one more time. Two participants died by 09:32:42
suicide during the study, one after six months 09:32:45
of follow-up and the other after 12 months of 09:32:48
follow-up, and six participants withdrew from 09:32:51
the study. Did I read that correctly? 09:32:55
A. Yes, sir. 09:32:56
Q. Okay. The authors recognized 09:32:56
those suicide deaths as adverse events; is that 09:33:08
correct? 09:33:11
A. I would have to look at their 09:33:11
methods and results to confirm that, sir. 09:33:22
Q. Yeah, let me help you out. Go to 09:33:24
page 245, Table 2, top left-hand corner. 09:33:30
A. Okay. 09:33:33
Q. Based on that table, do you agree 09:33:33
that they recognized these deaths as adverse 09:33:40
events in their protocol? 09:33:43
A. Yes, so Table 2 is titled Adverse 09:33:48
Events. An event is listed by death by 09:33:51
suicide. 09:33:54

Q. What is an adverse event in a 09:33:54
research study? 09:33:57
A. So an adverse event in a research 09:33:57
study would be a negative outcome in the study, 09:34:05
although it may not necessarily be attributable 09:34:12
to the intervention in the study. 09:34:16
Q. Right. Whether it's attributable 09:34:18
or not is unknown; is that correct? 09:34:23
A. There would be efforts made to 09:34:25
determine whether it's attributable or not. 09:34:33
Q. So the suicide rate in this 09:34:36
particular study is 2 out of 315; is that 09:34:45
correct? 09:34:50
A. So there would be multiple ways to 09:34:50
report a suicide rate, and they are frequently 09:35:01
reported as rate per individual years. And so 09:35:05
one way to describe the rate might be 2 out of 09:35:13
115, but I don't know that that would 09:35:19
necessarily be the way it would be typically 09:35:22
reported in the literature. 09:35:24
Q. If we -- understood. If we did 09:35:25
patient years, it would be 2 out of 630, 09:35:29
correct, because we have got two patient years 09:35:37
per patient? 09:35:39
A. Correct. 09:35:40

Page 30

Q. And that would be 0.3 percent per patient year, my math roughly, correct? 09:35:40 09:35:42
A. I would need to take your word that your math is correct, sir. 09:35:47 09:35:49
Q. Do you have any sense of whether that is a particularly high suicide rate? 09:35:50 09:35:54
A. Based on other literature that I have read, I would have reason to believe that it is higher than the population average, sir. 09:35:58 09:36:12 09:36:14
Q. Can you think of any study that has found that high of a rate of death by suicide among gender dysphoric children or youth who were not given hormonal interventions? 09:36:17 09:36:24 09:36:28 09:36:34 09:36:36
A. Can you repeat your question, sir? 09:36:38
Q. I am happy to. 09:36:44
A. Just so I understand. 09:36:45
Q. Understood. Can you think of any study as you sit here today that has found that high of a suicide rate among gender dysphoric children or youth who were not given hormonal interventions? 09:36:46 09:36:47 09:36:50 09:36:55 09:36:58
MR. CHEEK: Objection, form. 09:37:03
THE WITNESS: So, sir, I can't think of a study of the suicide rate in individuals who 09:37:07 09:37:08

Page 31

did not receive gender affirming medical care, so I am unable to make a comparison between the rate of such a study and the rate reported in this study. 09:37:14 09:37:19 09:37:22 09:37:24
BY MR. FRAMPTON: 09:37:25
Q. You would agree that in a study of this nature, suicide is the most serious adverse event possible, would you not? 09:37:32 09:37:34 09:37:37
MR. CHEEK: Object to form. 09:37:50
THE WITNESS: So I would agree that death is the most adverse event possible. I would have to give greater consideration to whether death by suicide is more severe or not than death in general. 09:37:52 09:37:55 09:37:57 09:38:01 09:38:05
BY MR. FRAMPTON: 09:38:06
Q. Fair enough. Would you agree the suicide rate reported in this study is unexpected? 09:38:07 09:38:10 09:38:13
A. No, sir. 09:38:13
Q. And why is that? 09:38:26
A. I don't know that I have a particular expectation of what the rate would be in order for the rate that the investigators reported to be unexpected. 09:38:27 09:38:30 09:38:34 09:38:37
Q. Had you -- I know you said you 09:38:38

Page 32

were familiar with this study. Had you -- in reading it before today, had you noticed the suicide point, that two of the participants had committed suicide? Is that something that stuck out to you? 09:38:42 09:38:45 09:38:50 09:38:56 09:38:59
A. So, sir, it's included in the abstract. So yes, it was something I was aware of. 09:38:59 09:39:04 09:39:06
Q. Did you in reviewing it find any explanation that the authors provided as to the suicide rate? 09:39:06 09:39:12 09:39:16
A. So it's been a while since I have read this study. I would need to review the authors' discussion to determine how they discussed the suicide rate in their study. So, sir, in scanning the discussion without rereading it thoroughly, I don't see a specific discussion of the two participants who unfortunately committed suicide during the study. 09:39:18 09:39:22 09:39:25 09:39:29 09:41:09 09:41:14 09:41:16 09:41:20 09:41:23
Q. That's fine. You can put that one aside for now. We will probably come back to it at some point. Dr. Antommaria, in your understanding, is the term evidence-based medicine a term of art that has a particular 09:41:23 09:41:25 09:41:28 09:41:34 09:41:38

Page 33

meaning? 09:41:43
A. So by term of art, you then mean has a particular meaning in the field of medicine? 09:41:44 09:41:48 09:41:50
Q. Yes. 09:41:50
A. Yes, it is. 09:41:51
Q. Okay. And tell me, what is evidence-based medicine, to your understanding? 09:41:52 09:41:54
A. Evidence-based medicine would be the effort to base clinical decision making on the best available evidence and to improve that evidence base over time. 09:41:56 09:42:01 09:42:06 09:42:11
Q. Did evidence-based medicine as a paradigm replace some sort of paradigm that came before it? 09:42:12 09:42:19 09:42:22
MR. CHEEK: Objection, form. 09:42:28
THE WITNESS: So presumably, the paradigm for medical care in the 18th century was not based on evidence-based medicine because there were not clinical trials at that time. 09:42:34 09:42:35 09:42:41 09:42:45
BY MR. FRAMPTON: 09:42:47
Q. Have you taken any particular courses on evidence-based medicine? 09:42:52 09:42:58
A. So evidence-based -- so particularly as medical education has changed 09:43:00 09:43:10

Page 34

over time, there is less of an emphasis on 09:43:13
individual courses and the integration of 09:43:18
knowledge into larger blocks of courses. So 09:43:22
no, I have not taken a individual course on 09:43:25
evidence-based medicine, but it has been a 09:43:29
component then of my undergraduate medical 09:43:31
education, my residency, and my continuing 09:43:35
medical education. And I teach medical 09:43:39
evidence-based medicine to the trainees that I 09:43:42
supervise. 09:43:47
Q. And you teach that they are to 09:43:47
base their care to the greatest extent possible 09:43:57
on the best available evidence; is that 09:43:59
correct? 09:44:03
A. Yes. 09:44:03
(Thereupon, Exhibit 4, Users' Guides 09:44:09
to the Medical Literature, was marked for purposes 09:44:09
of identification.) 09:44:09
BY MR. FRAMPTON: 09:44:09
Q. All right. I am going to hand 09:44:40
you, Dr. Antommaria, what I am marking as 09:44:41
Defense Exhibit 4. We are going to go through 09:44:43
this page by page. I am joking, we are not. 09:44:50
What I have marked as Exhibit 4 is called 09:44:55
User's Guides to the Medical Literature. The 09:44:58

Page 35

lead author is Gordon Guyatt. Dr. Antommaria, 09:45:03
is this a document you have seen before? 09:45:09
A. So I am familiar with JAMA's 09:45:10
Users' Guides to the Medical Literature, and -- 09:45:22
but not necessarily this compilation. 09:45:27
Q. Okay. Does -- okay. So this one 09:45:31
is subtitled Essentials of Evidence-Based 09:45:37
Clinical Practice. Does JAMA publish other 09:45:40
users' guides to the literature? 09:45:46
A. So you will see that this is the 09:45:49
third edition -- 09:45:51
Q. Oh, okay. 09:45:52
A. -- and that this is a book. There 09:45:53
are individual articles about topics in 09:45:59
evidence-based medicine that JAMA has published 09:46:03
in the past. And so I just -- to be specific, 09:46:08
just trying to be specific, I haven't seen the 09:46:15
third edition of -- 09:46:18
Q. Fair enough. 09:46:19
A. -- this book, but I am familiar 09:46:21
with JAMA's Users' Guides to the Medical 09:46:22
Literature, having read articles in this series 09:46:25
in the past. 09:46:28
Q. Got it. And do you recognize the 09:46:30
name Gordon Guyatt? 09:46:35

Page 36

A. I do. 09:46:36
Q. What do you know about Dr. Guyatt? 09:46:37
A. I know that Dr. Guyatt works in 09:46:39
the area of evidence-based medicine, and I am 09:46:45
familiar with his role in the development of 09:46:48
the GRADE methodology. 09:46:51
Q. Got it. Turn in the preface if 09:46:56
you would to page 26, but it's Roman numeral 09:47:03
XXVI. 09:47:11
A. I am there, sir. 09:47:29
Q. Okay. And in that first full 09:47:30
paragraph, do you see the sentence: We have 09:47:35
added a fundamental principle to the hierarchy 09:47:42
of evidence and the necessity for value and 09:47:46
preference judgments; that optimal clinical 09:47:50
decision making requires systematic summaries 09:47:54
of the best available evidence, do you see 09:47:58
that? 09:48:00
A. I do see that sentence, sir. 09:48:01
Q. Do you agree with that sentence? 09:48:02
A. So it's hard for me to necessarily 09:48:03
understand a sentence removed from its broader 09:48:22
context, sir. 09:48:26
Q. Do you agree in general with the 09:48:27
principle that optimal clinical decision making 09:48:33

Page 37

requires systematic summaries of the best 09:48:36
available evidence? 09:48:41
A. I would in principle agree with 09:48:42
that statement, sir, recognizing that 09:48:56
frequently systematic summaries of the best 09:49:00
available evidence are not available when 09:49:03
clinical decisions must be made. 09:49:05
Q. But when they are available, they 09:49:07
are important to the decision-making process, 09:49:14
correct? 09:49:16
A. Yes, sir. 09:49:16
Q. Let's unpack a few of the concepts 09:49:19
in that sentence. So what do you understand by 09:49:26
hierarchy of evidence? 09:49:30
A. So I understand by hierarchy of 09:49:33
evidence that there are a variety of types of 09:49:40
evidence that can be used to support clinical 09:49:43
decision making and that some types of evidence 09:49:46
are stronger than other types of evidence and 09:49:50
that there are a variety of different ways to 09:49:55
characterize the types of evidence and their 09:49:59
relative strength. 09:50:04
Q. What is a systematic review of 09:50:05
evidence? 09:50:27
A. As the name suggests, a systematic 09:50:29

review of the evidence uses a systematic 09:50:35
process to collect and review evidence 09:50:39
generally related to a specific clinical 09:50:45
decision so that there would be mechanisms for 09:50:49
searching the literature, reviewing abstracts 09:50:58
and titles and then reviewing full texts of 09:51:01
articles, abstracting data from the articles, 09:51:03
and then summarizing that information in some 09:51:08
systematic reviews may also then involve a 09:51:13
meta-analysis, the analysis of the data from a 09:51:15
number of individuals. 09:51:19
Q. So typically, the methodology for 09:51:20
searching for potentially relevant evidence 09:51:25
would be disclosed in the review, correct? 09:51:28
A. So there are published 09:51:30
recommendations for best practices for 09:51:41
performing systematic reviews of the 09:51:43
literature. And I am not going to remember 09:51:45
which of the appropriate guidelines it is, but 09:51:47
there are guidelines and checklists for 09:51:50
recommending what is a best practice for 09:51:54
performing a systematic review. 09:51:57
Q. And do you know sitting here 09:51:59
whether disclosing the methodology, the search 09:52:04
methodology, is one of those best practices? 09:52:06

A. I believe it would be, sir. 09:52:08
Q. Will a systematic review often 09:52:12
rate the quality of the evidence or assess the 09:52:19
quality of the evidence? 09:52:22
A. Some systematic reviews rate the 09:52:23
quality of evidence, and others do not. 09:52:31
Q. What is the value of a systematic 09:52:33
review compared to sort of a more traditional 09:52:43
narrative review of the literature? 09:52:49
A. By being systematic, it decreases 09:52:51
the likelihood of omitting relevant evidence in 09:52:59
the summary of the available evidence. 09:53:04
Q. Have you ever conducted or 09:53:05
supervised a systematic review on the effects 09:53:13
of a medical intervention? 09:53:16
A. So I have conducted systematic -- 09:53:18
a systematic review of the literature, but I 09:53:24
have not conducted a systematic review of the 09:53:27
literature of an effect of a medical 09:53:33
intervention. 09:53:35
Q. And have you ever conducted a 09:53:35
systematic review in which you assessed the 09:53:41
quality of evidence using the GRADE 09:53:45
methodology? 09:53:45
A. So if I have not conducted a 09:53:52

systematic review of the literature on a 09:53:57
medical intervention, I will not have utilized 09:53:57
the GRADE methodology to assess the quality of 09:53:59
that evidence, sir. 09:54:03
Q. Okay. Well, as a methodology, is 09:54:06
GRADE limited to medical interventions? 09:54:09
A. So it may also be applicable to 09:54:10
diagnostic tests, as well as treatments. 09:54:21
Q. But you have not done that kind of 09:54:25
systematic review, either, correct? 09:54:30
A. No, I have not, sir. 09:54:31
Q. Okay, fair enough. It looked like 09:54:32
you have done two systematic reviews; is that 09:54:39
right? 09:54:42
A. So can I refer to my CV, sir? 09:54:42
Q. Yeah, let me -- in fact, let's go 09:54:57
ahead and -- 09:55:01
MR. FRAMPTON: Grab 110 and 111. 09:55:02
THE WITNESS: So, sir, one systematic 09:55:16
review immediately comes to mind. I have 09:55:18
hesitance regarding the characterization that I 09:55:24
have performed two. 09:55:28
MR. FRAMPTON: We'll just go ahead 09:55:28
and mark them. That way, we are all clear. 09:55:36
(Thereupon, Exhibit 5, A Systematic 09:55:36

Literature Review of Individuals' Perspectives on 09:55:36
Broad Consent and Date Sharing in the United 09:55:36
States, was marked for purposes of 09:55:36
identification.) 09:55:37
BY MR. FRAMPTON: 09:55:37
Q. I hand you what I am marking as 09:55:41
Defendants' Exhibit 5. 09:55:43
A. Oh, yes, sir, two. 09:55:45
Q. Okay. What I have marked as 09:55:58
Exhibit 5 is called a Systematic Literature 09:56:01
Review of Individuals' Perspectives on Broad 09:56:04
Consent and Data Sharing in the United States. 09:56:09
The lead author is Dr. Garrison. 09:56:12
Dr. Antommaria, is this one of the systematic 09:56:16
reviews that you have been involved in? 09:56:18
A. Yes, sir. 09:56:19
Q. And were you involved in assessing 09:56:20
the quality of the studies? 09:56:29
A. No, sir, I was not. 09:56:45
(Thereupon, Exhibit 6, Systematic 09:56:52
Review of Typologies Used to Characterize Clinical 09:56:52
Ethics Consultations, was marked for purposes of 09:56:52
identification.) 09:56:52
BY MR. FRAMPTON: 09:56:52
Q. Then I am going to hand you what I 09:56:52

Page 42

am marking as Defendants' Exhibit 6. That one 09:56:58
is titled Systematic Review of Typologies Used 09:57:04
to Characterize Clinical Ethics Consultations. 09:57:09
And you will have to help me pronounce your -- 09:57:15
the lead author's last name. 09:57:18
A. deSante-Bertkau, sir. 09:57:22
Q. Thank you, de-Sante-Bertkau. Is 09:57:23
this the other systematic review you were 09:57:29
involved with, Dr. Antommaria? 09:57:30
A. Yes, sir. 09:57:31
Q. Okay. And this one did not assess 09:57:31
the quality of evidence; is that right? 09:57:33
A. Because of the nature of the 09:57:35
systematic review and the types of articles 09:57:39
that we were reviewing, no, it did not assess 09:57:44
the quality of the evidence. 09:57:48
Q. Okay, fair enough. You agree that 09:57:49
clinical practice guidelines should be based on 09:57:59
systematic reviews of the evidence, correct? 09:58:02
A. Ideally, clinical practice 09:58:04
guidelines should be based on systematic 09:58:11
reviews, yes, sir. 09:58:13
Q. Are you familiar with the Cochrane 09:58:14
Library? 09:58:16
A. I am, sir. 09:58:16

Page 43

Q. Tell me what it is, please, to the 09:58:17
extent you know. 09:58:19
A. So the Cochrane Collaboration is a 09:58:21
group that does methodological research related 09:58:26
to systematic reviews and supports the 09:58:33
performance of systematic reviews, and the 09:58:36
systematic reviews that they publish are then 09:58:39
published in the Cochrane Library. 09:58:43
Q. And are they recognized in the 09:58:46
community of experts as doing good work in 09:58:59
publishing systematic reviews, conducting and 09:59:01
publishing systematic reviews? 09:59:04
A. Yes, they are recognized as 09:59:05
producing high quality or publishing high 09:59:08
quality systematic reviews. 09:59:10
Q. Go back to that JAMA guide. 09:59:11
That's Exhibit 4 for you, please. Turn to page 09:59:18
15, if you would, the normal 15. 09:59:26
A. I am on page 15, sir. 09:59:35
Q. All right. Bottom of the page, I 09:59:36
think it's the last -- next to last full 09:59:40
sentence. It says: Returning to the hierarchy 09:59:42
of therapy, noting the limitations of human 09:59:46
intuition, EBM places the unsystematic 09:59:49
observations of individual clinicians lowest on 09:59:55

Page 44

the hierarchy. Did I read that correctly? 09:59:58
A. You did, sir. 10:00:01
Q. And in this context, does EBM mean 10:00:01
evidence-based medicine? 10:00:06
A. Yes, sir. 10:00:06
Q. What do they mean by unsystematic 10:00:06
observations of individual clinicians? 10:00:12
A. So based on the figure above, they 10:00:18
describe that presumably as the clinical 10:00:21
experience of individual clinicians. 10:00:23
Q. And they place that lowest on the 10:00:26
rung of evidence that one might consider, 10:00:31
correct? 10:00:35
MR. CHEEK: Objection, form. 10:00:35
THE WITNESS: So it's just to say, 10:00:43
sir, that we are moving back and forth between a 10:00:44
couple of different ways of understanding the 10:00:48
hierarchy of evidence and the way in which 10:00:50
systematic reviews may grade the evidence. And so 10:00:56
this is a particular way of describing that 10:01:03
hierarchy which is different than the GRADE 10:01:06
methodology. But within the way they are choosing 10:01:14
to describe the hierarchy, yes, they are putting 10:01:16
the clinical experience as the lowest level of 10:01:19
evidence. 10:01:21

Page 45

BY MR. FRAMPTON: 10:01:22
Q. Right. Below laboratory and 10:01:23
physiology research, correct? 10:01:31
A. Based on Figure 2-3, yes, sir. 10:01:32
Q. Below observational studies, 10:01:37
right? 10:01:39
A. Again, based on that figure, yes, 10:01:39
sir. 10:01:42
Q. And even beyond the figure, is 10:01:42
that your understanding as someone who -- as an 10:01:46
expert that that is sort of how the hierarchy 10:01:51
of evidence works? 10:01:54
A. So there are likely to be some 10:01:56
nuances within this hierarchy, particularly the 10:02:08
relationship between basic research and 10:02:11
clinical experience that I don't have a 10:02:13
particular opinion on. But in general, in 10:02:17
general, randomized trials are a higher level 10:02:24
of evidence than observational studies than 10:02:28
would be individual clinical experience, sir. 10:02:31
Q. We have -- we mentioned a few 10:02:34
minutes ago the GRADE methodology. Could you 10:02:48
tell me sort of in general terms, what is the 10:02:50
GRADE methodology? 10:02:53
A. The GRADE methodology is 10:02:54

methodology for grading the quality of evidence and the strength of recommendations. 10:02:58 10:03:02

Q. And is it a well-recognized method within the community of experts that you inhabit? 10:03:04 10:03:13 10:03:17

A. It is a well-recognized methodology within medicine, sir. 10:03:18 10:03:22

(Thereupon, Exhibit 7, GRADE guidelines: 3. Rating the Quality of Evidence, was marked for purposes of identification.) 10:03:36 10:03:36 10:03:37

BY MR. FRAMPTON: 10:03:37

Q. I show you what we will mark as Exhibit 7. Dr. Antommaria, what I am marking as Exhibit 7 is an article from the Journal of Clinical Epidemiology called GRADE guidelines: 3. Rating the Quality of Evidence. I believe you are familiar with this one, correct? 10:03:37 10:03:39 10:03:53 10:03:58 10:04:00 10:04:03

A. Yes, I am, sir. 10:04:05

Q. And just so we sort of set the stage, the Journal of Clinical Epidemiology in 2011 published a whole series of GRADE guidelines, correct? 10:04:06 10:04:12 10:04:15 10:04:18

A. So there is a series of approximately I want to say 12 articles. To the best of my memory, I don't recall if they 10:04:21 10:04:24 10:04:30

were all published in a single year or over time. 10:04:32 10:04:34

Q. Right. 10:04:34

A. But yes, there are a series of -- there was an initial publication describing the GRADE guidelines and subsequent publications describing the guidelines in greater detail, and this is one of the individual articles describing a particular aspect of the guidelines. 10:04:35 10:04:39 10:04:42 10:04:45 10:04:48 10:04:51 10:04:54

Q. And the author group are the developers of the GRADE guidelines, correct? 10:04:54 10:05:01

A. So it's hard for me to be specific about that, sir, given that there are multiple publications over time and that all of the authors may not have participated in the development of the methodology at all phases in its development. 10:05:03 10:05:19 10:05:22 10:05:25 10:05:27 10:05:29

Q. Would you consider this article series an authoritative explanation of the GRADE methodology? 10:05:30 10:05:38 10:05:42

A. Yes, sir. 10:05:43

Q. All right. Turn to 402, and let's look at key points in the box up there. 10:05:43 10:05:51

A. I am on 402, sir. 10:05:58

Q. Thank you. Third bullet says: The optimal application of GRADE requires systematic review of the impact of alternative management strategies on all patient-important outcomes. Did I read that correct? 10:05:59 10:06:02 10:06:06 10:06:09 10:06:13

A. You did, sir. 10:06:14

Q. What -- to your understanding, what is meant by patient-important outcomes? 10:06:15 10:06:25

A. So, again, I would have to review the article again in detail for the authors' definition of that term, but it would be the relevant outcomes of a medical intervention. 10:06:29 10:06:36 10:06:40 10:06:46

Q. And that would include potential benefits of the intervention; is that correct? 10:06:49 10:06:54

A. Yes, sir. 10:06:57

Q. And would it also include potential risks of the intervention? 10:06:59 10:07:02

A. Yes, sir. 10:07:04

Q. In sort of lay terms, the outcomes that would matter to a reasonable patient; is that fair? 10:07:06 10:07:13 10:07:16

MR. CHEEK: Objection, form. 10:07:17

THE WITNESS: So as an ethicist, I might say the outcomes that would be relevant to obtaining informed consent from a patient. 10:07:21 10:07:23 10:07:26

BY MR. FRAMPTON: 10:07:28

Q. Which would include potential risks and benefits, correct? 10:07:37 10:07:39

A. Yes, sir. 10:07:41

Q. And GRADE as a general matter is a method for rating the strength of the evidence to predict the outcome of the tested intervention; is that right? 10:07:42 10:07:49 10:07:56 10:08:01

A. So I think it's important to recognize that GRADE has two components, both rating the quality of the evidence as well as the strength of recommendations and that rating quality -- the quality of the evidence does not have the sole determinant of the strength of a recommendation, sir. 10:08:03 10:08:04 10:08:08 10:08:10 10:08:15 10:08:17 10:08:23

Q. Let's talk for a moment about the quality of evidence piece, the rating the quality of evidence piece. That's essentially rating how well -- how well we are able to predict the effects of the tested intervention, correct? 10:08:24 10:08:28 10:08:30 10:08:36 10:08:43 10:08:46

A. Yes, sir, both the kind of magnitude of the effect and the certainty that that estimate is correct. 10:08:47 10:08:50 10:08:53

Q. Turn to page 404, please, and look 10:08:55

Page 50

at Table 2. 10:09:05
A. I am there, sir. 10:09:09
Q. Thank you. Is Table 2 -- well, 10:09:10
it's got in it quality levels high, moderate, 10:09:15
low, and very low, correct? 10:09:18
A. Correct, sir. 10:09:19
Q. And in the GRADE methodology, you 10:09:21
assign one of those quality levels to the piece 10:09:24
of evidence, correct? 10:09:29
A. The body of evidence, sir. 10:09:30
Q. And have you, yourself, ever done 10:09:34
that exercise? 10:09:45
A. No, sir, I have not. 10:09:46
Q. And so high quality evidence means 10:09:48
essentially that there is a high level of 10:09:55
confidence that the true effect of the 10:10:01
intervention lies close to the estimate of the 10:10:06
effect of the intervention, correct? 10:10:09
A. You read that correctly, sir. 10:10:11
Q. And sort of in lay terms, that 10:10:12
means if the evidence tells us that the effect 10:10:15
of an intervention will be X, we are pretty 10:10:21
confident that it's going to be close to that, 10:10:26
right? 10:10:28
A. Correct, sir. 10:10:28

Page 51

Q. Then explain in your own terms 10:10:29
what sort of a moderate quality level of 10:10:36
evidence means. 10:10:38
A. So, sir, my general understanding 10:10:43
is that there are qualitative differences in 10:10:46
the degree of certainty between the various 10:10:50
quality levels. 10:10:54
Q. And low means that the true effect 10:10:55
may be substantially different from the 10:11:01
estimate, correct? 10:11:04
A. You read that correctly, sir. 10:11:05
Q. And so essentially, if the 10:11:07
estimate is a moderately beneficial effect, the 10:11:10
reality might be a profound beneficial effect, 10:11:16
correct? 10:11:20
A. Yes, sir, the variation might be 10:11:20
either higher or lower. 10:11:26
Q. Right. Or it might be a no 10:11:27
effect, right? 10:11:30
A. Correct, sir. 10:11:31
Q. And then low is then even 10:11:31
qualitatively worse than that. We believe that 10:11:36
it's likely to be substantially different from 10:11:39
the estimate, correct? 10:11:42
A. Correct. 10:11:43

Page 52

Q. And you mentioned strength of 10:11:43
recommendation earlier. You would agree that 10:11:50
the quality of evidence informs the strength of 10:11:52
recommendation, correct? 10:11:57
A. That is correct, but it is but one 10:11:57
factor that informs the direction of the 10:12:00
strength of recommendations. 10:12:04
Q. Got it. Let's go to Table 3. So 10:12:05
if I understand, it should be -- is it on your 10:12:11
next page or is it at the bottom of the page 10:12:14
you are looking at? 10:12:17
A. It's at the bottom of the page, 10:12:18
sir. 10:12:19
Q. That's what I thought. Basic 10:12:19
flowchart if you are applying the GRADE 10:12:20
methodology is that you start with an initial 10:12:23
quality rating based on the methodology in the 10:12:26
body of evidence, correct? 10:12:32
A. Yes, sir. 10:12:34
Q. High if you are dealing with 10:12:37
randomized controlled trials, low if you are 10:12:38
dealing with observational studies, right? 10:12:41
A. Correct, sir. 10:12:43
Q. But then you may lower the quality 10:12:43
rating based on any of five factors, correct? 10:12:48

Page 53

A. Correct, sir. 10:12:51
Q. And you also may raise the quality 10:12:56
rating based on one of three factors, one or 10:13:01
more of three factors, right? 10:13:05
A. Correct, sir. 10:13:06
Q. And then once you have sort of 10:13:08
done all of that, you assign a quality rating 10:13:11
based on where you landed, right? 10:13:13
A. Yes, sir. 10:13:15
Q. And so because of this process of 10:13:17
upgrading and downgrading, randomized control 10:13:21
trials will not necessarily end up providing 10:13:27
high quality evidence, correct? 10:13:29
A. That is correct, sir. 10:13:30
Q. And observational studies will not 10:13:34
necessarily end up providing low quality 10:13:36
evidence, correct? 10:13:38
A. Correct, it is possible for 10:13:39
observational studies to produce high quality 10:13:41
evidence. 10:13:44
THE WITNESS: Can we take a 10:13:58
three-minute break, sir? 10:13:59
MR. FRAMPTON: Of course. Let's go 10:14:00
off the record real quick. 10:14:00
(Recess taken.) 10:14:02

Page 54

(Thereupon, Exhibit 8, GRADE guidelines: 4. Rating the Quality of Evidence - Study Limitations (Risk of Bias), was marked for purposes of identification.) 10:14:02 10:14:02 10:19:40

BY MR. FRAMPTON: 10:19:40

Q. We are back on the record. 10:19:40

Dr. Antommaria, I am handing you what I am marking as Defendants' Exhibit 8. Exhibit 8 is also from the Journal of Clinical Epidemiology. It is titled GRADE guidelines for Rating the Quality of Evidence - Study Limitations (Risk of Bias). Are you familiar with this one, Doctor? 10:19:42 10:19:43 10:20:00 10:20:03 10:20:03 10:20:09 10:20:11

A. Yes, I am, sir. 10:20:11

Q. All right. This is from that same series of GRADE guidelines we just looked at; is that right? 10:20:12 10:20:14 10:20:16

A. It's in the same series as the previous exhibit, sir. 10:20:17 10:20:20

Q. Thank you. All right. Turn to page 409, please. 10:20:21 10:20:28

A. One moment. I am on page 409, sir. 10:20:33 10:20:38

Q. All right. Bottom right-hand of the page, right above Table 2. 10:20:38 10:20:40

Page 55

A. Okay. 10:20:45

Q. Do you see where it says: 10:20:45

Ideally, observational studies will choose contemporaneous comparison groups that, as far as possible, differ from intervention groups only in the decision typically by patient or clinician not to use the intervention. Did I read that correctly? 10:20:47 10:20:50 10:20:54 10:20:59 10:21:01 10:21:03

A. You did, sir. 10:21:04

Q. Okay. And the idea they are getting at there is that when you are doing an observational study, it's best to include some kind of control or comparison group, right? 10:21:05 10:21:09 10:21:11 10:21:14

A. Within the limitations of as far as possible and ideally, sir. 10:21:16 10:21:22

Q. And why is that important? Why is a comparison group important? 10:21:25 10:21:32

A. To be able to potentially differentiate the effects of the intervention from other effects in the environment. 10:21:33 10:21:46 10:21:50

Q. Right. Difficult to infer causation on the part of the intervention without some kind of comparison group, correct? 10:21:55 10:22:01 10:22:05

A. So it would be to say that there are differences between observational studies 10:22:07 10:22:16

Page 56

and randomized controlled trials in terms of the ability to infer causation so that simply having a comparison group might not be sufficient. 10:22:19 10:22:22 10:22:27 10:22:29

Q. Necessary, but not sufficient? 10:22:31

A. Yes, necessary, but not sufficient to -- well, so I would have to -- I would have to think about that, sir. 10:22:35 10:22:43 10:22:49

Q. Well, still on 410 which we flipped to, the top left-hand corner, first full paragraph. Do you see where it says: To make inferences regarding intervention effects, case series must still refer to results in a comparison group? Did I read that correctly? 10:22:50 10:22:55 10:23:00 10:23:02 10:23:06 10:23:09

A. Yes, sir. 10:23:13

Q. Do you agree with that statement? 10:23:14

A. I think referring to a comparison group is one way to make such inferences, sir. 10:23:16 10:23:29

Q. Well, the sentence uses the word must, does it not? 10:23:32 10:23:39

A. May I read the full paragraph, sir? 10:23:42 10:23:59

Q. Of course. 10:24:00

A. So, sir, I would agree that there needs to be a reference to a comparison group 10:24:59 10:25:01

Page 57

but that those comparison groups might be the general population or historic controls. 10:25:03 10:25:06

Q. And that generally should be explicit in a study if they are referencing a historic control or a general population, right? 10:25:10 10:25:13 10:25:16 10:25:18

A. So the study would be stronger if those references were more explicit. 10:25:18 10:25:25

Q. Turn back to 409. Let's look at Table 2. 10:25:27 10:25:36

A. Yes, sir. 10:25:40

Q. Do you agree generally that this table lists things that might cause a risk of bias in an observational study? 10:25:41 10:25:43 10:25:48

A. So the table is entitled Study Limitations in Observational Studies. I don't necessarily know that all limitations result in a risk of bias. 10:25:51 10:25:55 10:26:01 10:26:06

Q. Would you agree that a failure to adequately control confounding can create a risk of bias? 10:26:07 10:26:18 10:26:22

A. So a failure to adequately control confounding is a potential study limitation, sir. 10:26:23 10:26:32 10:26:37

Q. This article is about risk of 10:26:37

Page 58

bias, so I am asking does that study limitation 10:26:42
potentially create a risk of bias, as GRADE 10:26:45
uses that phrase? 10:26:47
A. Again, I would have to review the 10:26:49
article in order to see. The table is not 10:26:59
entitled Bias in Observational Studies. So I 10:27:01
am just uncertain as to why the authors have 10:27:05
chosen to title it in a different way. And so 10:27:09
I would just need -- in order to be certain, 10:27:12
sir, I would need to review the article in 10:27:14
order to understand why they are shifting the 10:27:18
terminology. That's my hesitance, sir. 10:27:21
Q. Can you tell me generally what 10:27:27
risk of bias is within the GRADE methodology? 10:27:29
A. So in reading the title, sir, and 10:27:33
in reading the introduction, they are using 10:27:51
study limitations and risk of bias it appears 10:27:55
synonymously. So the answer to your question 10:27:58
would be, yes, failure to adequately control 10:28:02
for confounding would be a potential source of 10:28:06
bias. 10:28:09
Q. And what are confounding factors? 10:28:10
What does that phrase mean? 10:28:14
A. So a confounding factor would be a 10:28:16
unmeasured variable that would potentially 10:28:27

Page 59

influence the outcome. 10:28:30
Q. So, for example, if you were doing 10:28:30
a study on people with depression and one group 10:28:46
received some kind of medication, SSRIs plus 10:28:53
cognitive behavioral therapy and another group 10:29:00
just received cognitive behavioral therapy, you 10:29:03
wouldn't be able to determine -- I'm sorry, bad 10:29:08
example, strike all of that. 10:29:12
One arm, one arm study. People 10:29:16
with depression, they receive both SSRIs and 10:29:18
cognitive behavioral therapy, and they improve 10:29:23
over time. You wouldn't be able to tell 10:29:26
whether it was the medication or the therapy 10:29:29
that led to the improvement, correct? 10:29:32
MR. CHEEK: Objection, form. 10:29:34
THE WITNESS: So, sir, we talked 10:29:38
previously about implicit controls. So it would 10:29:40
be -- it would depend on what implicit control 10:29:44
there was and what data there was about the 10:29:49
utility of cognitive behavioral therapy itself. 10:29:53
So one might be able to draw a conclusion, but it 10:30:00
would require more information about the entire 10:30:03
body of evidence. 10:30:08
BY MR. FRAMPTON: 10:30:10
Q. One way or another, you would have 10:30:10

Page 60

to have information on cognitive behavioral 10:30:13
therapy alone, correct? 10:30:14
A. You would have to have more 10:30:15
information about that patient population and 10:30:25
their clinical course over time. 10:30:29
Q. Would you need information about 10:30:30
the effect of cognitive behavioral therapy 10:30:34
alone? 10:30:36
A. Just so I answer your question 10:30:37
correctly, sir, can you repeat your question? 10:30:57
Q. Sure. Again, the example is if 10:30:59
you did a study of people with depression, you 10:31:02
treated them with medication and therapy, found 10:31:05
that over, say, 24 months they improved in some 10:31:10
form or fashion, you would not be able to 10:31:14
disentangle the effects of the medication 10:31:19
versus the therapy, would you? 10:31:21
MR. CHEEK: Objection, form. 10:31:23
THE WITNESS: Again, it would depend 10:31:27
on what available evidence outside of that study 10:31:28
was available about that patient population. So 10:31:33
if there was evidence that individuals who receive 10:31:39
cognitive behavioral therapy did not have 10:31:50
sufficient remission in their symptoms, one might 10:31:54
be able to then draw conclusions about the 10:31:57

Page 61

efficacy of the pharmacological intervention. 10:32:00
BY MR. FRAMPTON: 10:32:04
Q. And you are assuming if you had 10:32:04
evidence about people who had undergone 10:32:07
cognitive behavioral therapy alone, correct? 10:32:11
MR. CHEEK: Objection, form. 10:32:15
THE WITNESS: Yes, evidence broadly 10:32:16
understood. 10:32:23
BY MR. FRAMPTON: 10:32:23
Q. What does that mean? 10:32:26
A. Well, we have talked about the 10:32:26
variety of levels of evidence. One wouldn't 10:32:31
need a randomized control trial of cognitive -- 10:32:36
a randomized placebo control trial of cognitive 10:32:40
behavioral therapy to potentially draw that 10:32:44
inference. 10:32:46
Q. But you would want more than 10:32:46
individual clinician experience, would you not? 10:32:49
A. That would be a form of evidence, 10:32:51
sir. 10:32:54
Q. You would not want more than 10:32:54
individual clinician experience? 10:32:57
MR. CHEEK: Objection, form. 10:32:59
THE WITNESS: So as we discussed 10:33:02
earlier, sir, individual clinician experience is a 10:33:03

Page 62

form of evidence. There is a large difference 10:33:06
between making decisions in clinical practice in 10:33:12
the real world and what ideally one might want as 10:33:16
we have read in these guidelines, the use of 10:33:20
ideally in their language. 10:33:26
BY MR. FRAMPTON: 10:33:32
Q. My question is would you want 10:33:32
better evidence than clinician experience 10:33:34
alone? 10:33:35
A. Clinician experience alone might 10:33:38
in the clinical context be the evidence that 10:33:41
one had available and needed to make a clinical 10:33:45
judgment. 10:33:49
Q. So you would not necessarily want 10:33:50
better evidence than that? 10:33:52
A. One might always want higher 10:33:53
quality evidence than lower quality evidence. 10:34:01
But, unfortunately, that's not always available 10:34:04
to clinicians. 10:34:06
Q. What do you understand the phrase 10:34:06
regression to the mean to mean? 10:34:18
A. That if -- if a, say, cohort is 10:34:22
followed over time and they have a parameter 10:34:33
which is significantly different from the 10:34:38
general population, that over time that 10:34:42

Page 63

parameter might move more toward the value in 10:34:45
the general population. 10:34:49
Q. And that -- let me ask you, have 10:34:58
you ever looked at regression to the mean in 10:35:05
the context of depression or anxiety or any 10:35:09
similar mental health condition? 10:35:14
A. I'm sorry, sir, I am not sure what 10:35:15
you are asking. 10:35:21
Q. Have you ever looked at anything 10:35:21
looking -- have you ever looked at a study 10:35:23
attempting to measure the extent to which 10:35:29
regression to the mean affects results in 10:35:31
studies on mental health? 10:35:35
A. No, sir, I haven't investigated 10:35:37
the extent to which that particular factor 10:35:44
occurs over time. 10:35:48
Q. Do you agree it's at least a 10:35:49
potential confounder in studies on mental 10:35:56
health? 10:35:59
A. So, again, in terms of 10:36:00
terminology, I don't know that I would describe 10:36:07
it as a confounder. I would describe it as a 10:36:09
potential study limitation or a risk of bias. 10:36:13
Q. Fair. Going back to our earlier 10:36:15
discussion, relying on what you have called 10:36:22

Page 64

implicit controls is a reason a study might be 10:36:27
legitimately downgraded in the GRADE 10:36:32
methodology, correct? 10:36:36
A. May I, sir? 10:36:36
Q. Uh-huh. 10:36:41
A. So I believe we made reference to 10:36:57
Exhibit 7, Table 3. I think that that would be 10:37:00
considered under a risk of bias and the result 10:37:07
of potentially lowering the quality of 10:37:11
evidence. 10:37:13
Q. Tell me what is meant in the 10:37:14
literature, the methodological literature, by 10:37:23
lost to follow up. 10:37:28
A. So in a observational study, one 10:37:32
would develop a cohort of individuals and 10:37:36
follow them over time. I think we discussed 10:37:40
the Chen study. They developed a cohort of 10:37:47
individuals and followed them over a period of 10:37:50
two years. And lost to follow up would be 10:37:53
individuals for whom data is not available at 10:38:00
the end of that period of time. 10:38:03
Q. And is that a study limitation, or 10:38:04
at least a potential study limitation? 10:38:12
A. So depending on the degree to 10:38:15
which lost to follow up occurs, it can be a 10:38:21

Page 65

study limitation. 10:38:26
Q. Right. And is that because we 10:38:28
don't know if the group that was lost to follow 10:38:30
up would have the same results as the group 10:38:34
that we are still able to study? 10:38:36
A. Yes, sir. 10:38:39
Q. And if those groups had vastly 10:38:41
different results, it would pretty seriously 10:38:52
bias the study, correct? 10:38:55
A. Again, it depends on the degree of 10:38:56
the lost to follow up. Studies will at times 10:39:03
make assumptions about individuals lost to 10:39:05
follow up in their outcomes in order to 10:39:08
potentially examine those implications. And if 10:39:10
the lost to follow up is not large, it may have 10:39:15
limited implications on the results of the 10:39:19
study. 10:39:22
Q. Right. There is only so much 10:39:22
effect a 5 percent lost to follow up can have, 10:39:24
right? 10:39:28
A. Again, not wanting to be specific 10:39:29
about particular percentages. But yes, a 10:39:31
smaller lost to follow up would have a less 10:39:34
effect potentially than a larger lost to follow 10:39:37
up. 10:39:39

Page 66

Q. Right. Larger than if, say, you lost half of your participants, correct? 10:39:39 10:39:42
A. Correct. 10:39:44
Q. What about too short of a follow up, how can that bias results? 10:39:44 10:39:55
A. So that's a difficult question to answer because short is a relative term. Too short relative to what, sir? 10:39:56 10:40:05 10:40:11
Q. To -- yeah, I know what you mean. If, for example, you study a population for two years and there are significant effects at five years, you would miss those in the two-year study, correct? 10:40:14 10:40:23 10:40:28 10:40:33 10:40:35
A. That is correct, sir. 10:40:36
Q. And so particularly in a medical intervention that people are going to take, people are going to undergo for the rest of their life, you would want to make sure you are studying it long enough to capture those effects, correct? 10:40:38 10:40:46 10:40:49 10:40:51 10:40:53 10:40:55
A. You would want -- you would want to study it in order to do what, sir? 10:40:56 10:41:05
Q. In order to understand what the effects are going to be over the course of someone's life. 10:41:09 10:41:11 10:41:13

Page 67

A. So I will give an example of vaccines. So once you give somebody a vaccine, you cannot unvaccinate them. The COVID vaccines were studied for a finite period of time prior to FDA approval. There is post-marketing surveillance to look at what happens in a larger population of individuals and for a longer period of time. But in that case, even though the vaccine is going to be -- in some ways be with individuals for the rest of their lives, it wasn't necessary to study the vaccines for 40 years prior or 70 years prior to their approval. 10:41:19 10:41:22 10:41:27 10:41:34 10:41:38 10:41:43 10:41:47 10:41:51 10:41:56 10:42:01 10:42:03 10:42:07 10:42:13
Q. If we discovered in that follow up that, say, 10 years after vaccination people started experiencing significant adverse effects, that would then start -- that would then have implications for clinical decision making going forward, would it not? 10:42:14 10:42:23 10:42:27 10:42:30 10:42:33 10:42:38
A. It would, sir. So it is to say that is a reason to continue ongoing studies but is not a reason that those studies need to be completed before, say, FDA approval or before a clinician is utilizing the intervention. 10:42:39 10:42:46 10:42:50 10:42:54 10:42:57 10:43:03

Page 68

Q. I mean, that depends on the risk profile of the intervention we are talking about, correct? 10:43:03 10:43:05 10:43:07
A. That's why short is a relative term, sir. 10:43:09 10:43:12
Q. Are you familiar with the phrase, I have seen it in the literature, quasi RCT? Have you ever seen that? 10:43:13 10:43:22 10:43:25
A. I may have, sir. 10:43:25
Q. Do you have any understanding of its meaning? 10:43:29 10:43:31
A. I can only speculate based on those words, sir. There are increasingly novel study designs that are utilized over time, but I don't know that -- I am not aware that quasi RCT is a specific study design, sir. 10:43:32 10:43:38 10:43:49 10:43:53 10:44:01
Q. In RCTs, is incomplete blinding a risk of bias? 10:44:05 10:44:12
A. Yes, sir. 10:44:13
Q. That being said, there are plenty of medical interventions out there for which perfect blinding is not possible or practical, correct? 10:44:17 10:44:23 10:44:26 10:44:30
A. So, again, plenty is a -- is an indiscriminate term. There are some medical 10:44:30 10:44:43

Page 69

interventions for which masking is difficult, particularly surgical interventions. 10:44:44 10:44:48
Q. Have you ever -- have you ever reviewed the literature on what percentage of RCTs are not blinded? 10:44:51 10:44:57 10:44:59
A. I am not aware of a specific number, sir. 10:45:00 10:45:06
Q. And when you are looking at something that may present a risk of bias in the GRADE guidelines, there is no requirement that you downgrade simply because you have identified that there might be a risk of bias, correct? 10:45:07 10:45:12 10:45:18 10:45:20 10:45:24 10:45:27
MR. CHEEK: Objection. 10:45:27
BY MR. FRAMPTON: 10:45:28
Q. It's a judgment call as to how serious the risk is? 10:45:28 10:45:29
MR. CHEEK: Objection, form. 10:45:30
BY MR. FRAMPTON: 10:45:33
Q. Is that correct? 10:45:33
A. Can you repeat your question just so I have heard it correctly, sir? 10:45:33 10:45:37
Q. Absolutely. Within the GRADE guidelines, if the assessor identifies a potential risk of bias, there is then a 10:45:39 10:45:41 10:45:46

Page 70

judgment call on behalf of the assessor as to whether it is serious enough to warrant downgrading, correct? 10:45:50 10:45:53 10:45:56

A. Yeah. So the GRADE guidelines are not a computer program that you put data in and a -- that there are judgments made by individuals who are rating the quality of the evidence. 10:45:58 10:46:01 10:46:08 10:46:10 10:46:11

Q. So an unblinded RCT is not automatically downgraded, correct? 10:46:12 10:46:16

A. So an unblinded RCT is likely to have a significant risk of bias, which would be downgrading it by 1 to 2 points, so I think it would be highly likely to be downgraded. 10:46:21 10:46:37 10:46:42 10:46:49

Q. Is that your testimony, every unblinded RCT gets downgraded at least one level? 10:46:52 10:46:55 10:46:59

A. So, sir, you have moved from the recommendations of the GRADE guidelines to an empirical claim about how they are applied in practice, and I don't -- again, I am not familiar with a study that has looked at how they have -- a systematic review of how they have been applied in practice. 10:47:00 10:47:09 10:47:15 10:47:18 10:47:24 10:47:30 10:47:32

Q. You would agree that the GRADE 10:47:33

Page 71

guidelines do not rigidly say you must downgrade an unblinded RCT? 10:47:37 10:47:40

A. May I, sir? 10:47:45

Q. Sure. 10:47:47

A. So, sir, I am on page 410 of Exhibit 8. And so it is -- every study addressing a particular outcome will differ to some degree in risk of bias. Review authors and guideline developers must make an overall judgment considering all the evidence, whether quality of evidence for an outcome warrants rating down on the basis of study limitations. 10:48:43 10:48:46 10:48:52 10:48:55 10:48:57 10:49:00 10:49:04 10:49:07

So I take it that, again, this is a general set of recommendations that are -- relied on judgment. So, no, it does not say must, but it would not be clear to me that there are other things that do have the quality of a must within the guidelines. 10:49:14 10:49:18 10:49:22 10:49:32 10:49:34 10:49:38

Q. Have you ever reviewed any literature or any meta-analyses studying blinded versus nonblinded studies of the same intervention to see if the effects are different or see if the results are different? 10:49:42 10:49:46 10:49:55 10:49:59 10:50:02

A. So I am aware that that literature exists. I have not had reason to review 10:50:08 10:50:12

Page 72

particular articles within that body of literature. 10:50:16 10:50:18

Q. And do you -- so you are not aware as we sit here today the extent to which they have found or not found that blinding makes a difference? 10:50:18 10:50:23 10:50:26 10:50:30

A. So I am generally aware that a failure to adequately mask an intervention does have -- make a difference, and that is part of the reason why in general the GRADE guidelines would see that as a potential source of bias and a potential reason to lower the quality of the evidence. 10:50:31 10:50:35 10:50:40 10:50:43 10:50:47 10:50:49 10:50:53

Q. It's not something that you have looked at for purposes of this case? 10:50:53 10:50:57

A. Not to this point in time, sir. 10:51:00

(Thereupon, Exhibit 9, Impact of Blinding on Estimated Treatment Effects in Randomised Clinical Trials: Meta-Epidemiological Study, was marked for purposes of identification.) 10:51:08 10:51:08 10:51:08 10:51:08

BY MR. FRAMPTON: 10:51:08

Q. I show you what I will mark as Exhibit 9. What I am marking as Exhibit 9 is titled Impact of Blinding on Estimated Treatment Effects and Randomized Clinical 10:51:08 10:51:10 10:51:23 10:51:24

Page 73

Trials: Meta-Epidemiological Study. The lead author is Helene Moustgaard. Dr. Antommaria, is this a study that you are familiar with? 10:51:26 10:51:29 10:51:34

A. No, sir, it is not. 10:51:35

Q. Do you recognize any of the authors? 10:51:37 10:51:42

A. No, sir, I do not. 10:51:42

Q. Do you recognize the journal? 10:51:49

A. Yes, sir; I do. 10:51:52

Q. What journal is it? 10:51:54

A. It's published in the BMJ, sir. 10:51:55

Q. Is that a prestigious medical journal? 10:51:58 10:52:00

A. May I look at the article, sir? 10:52:00

Q. Yeah. I am actually not going to ask you substantive questions about the article. So my question is simply whether the BMJ is a reputable article -- I mean, a reputable journal? 10:52:05 10:52:07 10:52:08 10:52:10 10:52:14

A. And all I am distinguishing, sir, is there are a number of different journals within the BMJ publishing group, and I am just ascertaining that this article was published in the BMJ as opposed to another journal within its family of -- 10:52:15 10:52:18 10:52:21 10:52:26 10:52:29 10:52:31

Page 74

Q. Sure. 10:52:32
A. -- journals. So yes, the BMJ is a 10:52:32
high-impact medical journal. 10:52:40
Q. Okay. And, I mean, you don't need 10:52:41
to look at this further. I am just curious, as 10:52:43
a general matter, what is a 10:52:45
meta-epidemiological review? 10:52:47
A. Sir, I am not familiar with that 10:52:49
as a specific term of art. 10:53:00
Q. Okay, fair enough. 10:53:03
(Thereupon, Exhibit 10, GRADE 10:53:09
guidelines: 5. Rating the Quality of Evidence - 10:53:09
Publication Bias, was marked for purposes of 10:53:09
identification.) 10:53:11
BY MR. FRAMPTON: 10:53:11
Q. I show you what I am going to mark 10:53:20
as Defendants' Exhibit 10, still Journal of 10:53:21
Clinical Epidemiology, GRADE Guidelines 5. Is 10:53:37
this, Dr. Antommaria, an article in that same 10:53:40
Journal of Clinical Epidemiology series on the 10:53:42
GRADE guidelines that we were looking at 10:53:45
earlier? 10:53:45
A. Yes, sir. 10:53:46
Q. And are you familiar with this 10:53:48
one? 10:53:49

Page 75

A. I am familiar with this one, sir. 10:53:51
Q. And just tell me in general terms 10:53:56
what publication bias is. 10:54:01
A. Not all studies that are performed 10:54:05
are published in the literature, and so 10:54:07
publication bias would be the difference 10:54:11
between what is published and the entire body 10:54:16
of potential evidence. 10:54:21
Q. And the concern is that positive 10:54:22
results are more likely to be published than 10:54:35
negative results; is that correct? 10:54:37
A. That is one of the concerns, sir. 10:54:39
Q. Are you familiar with the Dutch 10:54:41
studies on people with gender dysphoria? 10:54:57
A. I am familiar with some Dutch 10:55:02
studies on treatment of individuals with gender 10:55:09
dysphoria, sir. 10:55:12
Q. Right. And if I understand, there 10:55:13
is essentially -- it's performed out of Vrije 10:55:16
University; is that correct? 10:55:20
A. I don't recall that particular 10:55:23
name of the university, sir. 10:55:27
Q. The idea is this is a data set of 10:55:30
people who sought care for some form of gender 10:55:32
incongruence at a particular clinic in the 10:55:40

Page 76

Netherlands, right? 10:55:40
A. Yes, it is a particular clinic in 10:55:42
the Netherlands that has an area of expertise 10:55:44
in the treatment of individuals with gender 10:55:47
dysphoria, and they have published a series of 10:55:49
studies based on the patients that they have 10:55:52
seen over time. 10:55:56
Q. And they have been seeing patients 10:55:57
since, like, the '70s; is that correct? 10:56:00
A. I am aware that they have been 10:56:02
seeing patients since at least the '90s. I 10:56:05
can't speak to how much earlier they have 10:56:10
seen -- when it was initially established, sir. 10:56:13
Q. As you said, they have published a 10:56:15
series of observational studies based on the 10:56:17
data from their clinic, correct? 10:56:19
A. They have at least published a 10:56:22
series of observational studies on patients in 10:56:24
their clinics. 10:56:27
Q. And those studies are important 10:56:28
pieces of the literature in the treatment of 10:56:31
gender dysphoria? 10:56:34
A. So, again, sir, you are speaking 10:56:35
in general about some unspecified group of 10:56:40
studies. But yes, a Dutch group has published 10:56:45

Page 77

an important series of observational studies, 10:56:49
particularly on adolescents with gender 10:56:54
dysphoria. 10:56:58
Q. And there is no way of knowing if 10:56:58
the studies that they have published represent 10:57:00
all or a fraction of the studies that they have 10:57:05
conducted, is there? 10:57:07
A. Presumably, there is a way of 10:57:08
knowing. 10:57:11
Q. Are you able to know the answer to 10:57:12
that? 10:57:14
A. I do not know the answer to that, 10:57:14
sir. 10:57:17
(Thereupon, Exhibit 11, GRADE 10:57:32
guidelines 6. Rating the Quality of Evidence - 10:57:32
Imprecision, was marked for purposes of 10:57:32
identification.) 10:57:32
BY MR. FRAMPTON: 10:57:32
Q. I show you what I will mark as 10:57:32
Defendants' Exhibit 11. All right. Exhibit 10:57:35
11, published still in the Journal of Clinical 10:57:46
Epidemiology, titled GRADE Guidelines 6. 10:57:51
Rating the Quality of Evidence - Imprecision. 10:57:53
And, Dr. Antommaria, this is -- this article is 10:57:58
from that same series on the GRADE guidelines 10:58:00

Page 78

from the Journal of Clinical Epidemiology, correct? 10:58:03 10:58:06
A. Correct, sir. 10:58:06
Q. And you are familiar with it? 10:58:07
A. I am aware of it. I am less familiar with it than some other articles in the series, sir. 10:58:08 10:58:13 10:58:16
Q. Are you familiar generally with the concept of imprecision as it is used in the GRADE methodology? 10:58:17 10:58:19 10:58:23
A. Yes, sir. 10:58:24
Q. And imprecision is one of the factors that may warrant downgrading the quality of evidence; is that right? 10:58:26 10:58:29 10:58:33
A. May I refer to one of the other articles, sir? 10:58:34 10:58:41
Q. Yeah. 10:58:42
A. So yes, sir; imprecision is one of the five categories for lowering the rating of the quality of evidence. 10:58:42 10:58:56 10:59:00
Q. And sort of the basic idea is that imprecision is when there is too much variability around the estimated effect of the intervention to be confident in that estimate; is that right? 10:59:00 10:59:06 10:59:09 10:59:12 10:59:16

Page 79

A. I think that's a reasonable summary, sir. 10:59:17 10:59:21
Q. Look on page 1284 in the key points box on the top left-hand corner. 10:59:21 10:59:28
A. I am on 1284, sir. 10:59:38
Q. Thank you. The first bullet reads: GRADE's primary criterion for judging precision is to focus on the 95 percent confidence interval, CI, around the difference in effect between intervention and control for each outcome. Did I read that correctly? 10:59:39 10:59:42 10:59:46 10:59:49 10:59:52 10:59:56
A. Yes, you did, sir. 10:59:58
Q. And you can't calculate a 95 percent confidence interval around the difference in effect between intervention and control without a control, can you? 11:00:05 11:00:09 11:00:11 11:00:13
A. You cannot, sir. 11:00:16
Q. And so we are -- at least as the GRADE methodology uses the term, we are not able to evaluate the risk of imprecision in studies that lack a control, are we? 11:00:18 11:00:26 11:00:28 11:00:32
MR. CHEEK: Objection, form. 11:00:38
THE WITNESS: So I think you are able to evaluate the risk of imprecision in that there is no measure of imprecision and, therefore, there 11:00:39 11:00:41 11:00:45

Page 80

would be a way to adjust the quality of the evidence, given there is not a confidence interval, sir. 11:00:50 11:00:52 11:00:56
BY MR. FRAMPTON: 11:00:57
Q. Right. You would assume that there is at least some risk of imprecision, correct? 11:00:57 11:00:59 11:01:00
A. Yes, sir. 11:01:01
Q. Okay. Let's flip back to that Chen article. What exhibit number is it? 11:01:01 11:01:11
Exhibit 3. I will help you find it. I am sorry, you are going to have a -- you have got a bit of a stack going over there. 11:01:13 11:01:17 11:01:19
A. Okay. So I have Exhibit 3, sir. 11:01:25
Q. Thank you. Take a look through this. This was a study you are familiar with. 11:01:27 11:01:34
There was not a control or comparison group in this study, was there? 11:01:36 11:01:38
A. There was not an explicit control group, although the authors did some additional statistical analysis to potentially address issues of confounding. 11:01:41 11:01:48 11:01:53 11:01:56
Q. And what do you mean by that? 11:02:01
A. So in their methods, they say we also examined how initial levels and rates of 11:02:05 11:02:18

Page 81

change in appearance congruence correlated with those of each psychosocial outcome. So I am on page 240 -- 11:02:21 11:02:24 11:02:39
Q. I see it. 11:02:39
A. -- in the methods in the last sentence, sir. 11:02:40 11:02:41
Q. I see it. So those are rates of change in appearance congruence and psychosocial outcomes are all things they measured for the study participants, correct? 11:02:41 11:02:45 11:02:48 11:02:50
A. Yes, sir. 11:02:52
Q. They weren't comparing that against any kind of comparison or control group, correct? 11:02:54 11:02:57 11:03:01
A. No, sir. 11:03:01
Q. Let's look at page 248. Every document has got page numbers in a different place. These are at the bottom of the page. 11:03:02 11:03:10 11:03:13
A. I am on page 248, sir. 11:03:15
Q. Thank you. And, hey, there is not a lot of text there, so that helps us find where we are going. The first full sentence, do you see where it says: In addition, despite improvement across psychosocial outcomes on average, there was substantial variability 11:03:17 11:03:19 11:03:21 11:03:24 11:03:27 11:03:30

Page 82

around the mean trajectory of change. Some participants continued to report high levels of depression and anxiety and low positive affect in life satisfaction, despite the use of GAH. Did I read that correctly? 11:03:31 11:03:35 11:03:39 11:03:44 11:03:48

A. You did, sir. 11:03:48

Q. Does that sentence suggest a potential imprecision issue to you? 11:03:49 11:03:55

A. So I think that that sentence has implications. I don't know, as you have said, given that a measure of imprecision requires a confidence interval that I would necessarily frame it in the terms of imprecision, but I think that that's a relevant finding of the study. 11:03:57 11:04:16 11:04:22 11:04:26 11:04:29 11:04:32 11:04:36

Q. All right, okay. Would a better term be heterogeneity in outcomes? 11:04:36 11:04:39

A. I think that is an alternative way to describe it, sir. 11:04:43 11:04:48

Q. Let me just sort of back up for a second. The common hormonal intervention for natal males transitioning to female is Estradiol plus anti-androgens; is that correct? 11:04:49 11:04:54 11:05:02 11:05:06

A. Is estrogen frequently accompanied by an anti-androgen, yes, sir. 11:05:11 11:05:16

Page 83

Q. And the common hormonal intervention for natal females transitioning to male is testosterone; is that correct? 11:05:19 11:05:23 11:05:28

A. So I would use the language of individuals' sex assigned at birth, but in general, yes, sir. 11:05:29 11:05:32 11:05:34

Q. Do you understand what I mean if I use the phrase natal male and natal female? 11:05:35 11:05:38

A. I do, sir. 11:05:40

Q. Okay. Those are estrogen plus anti-androgens on the one hand, testosterone on the other hand. Those are different interventions, are they not? 11:05:41 11:05:46 11:05:48 11:05:50

A. They are different pharmacologic agents, sir, yes. 11:05:51 11:05:57

Q. They have different effects on the body? 11:05:58 11:06:00

A. They have some different effects on the body, sir. 11:06:01 11:06:05

Q. One has a masculinizing effect, one has a feminizing effect; is that correct? 11:06:06 11:06:09

A. That is correct. 11:06:11

Q. They have at least some different side effects; is that correct? 11:06:11 11:06:15

A. Some of their side effects are 11:06:16

Page 84

different, yes, sir. 11:06:20

Q. Would you agree that you can't assume the effect of one on psychosocial outcomes is the same as the effect of the other? 11:06:20 11:06:23 11:06:29 11:06:31

MR. CHEEK: Objection, form. 11:06:36

THE WITNESS: I think that it would be a reasonable hypothesis that the effect on one patient population is different than the other, and I think that that was something that Chen and colleagues investigated. 11:06:44 11:06:45 11:06:49 11:06:54 11:06:57

BY MR. FRAMPTON: 11:06:58

Q. Right, and that was sort of part of my question. That is why they separately reported the effects on natal males and the effects on natal females; is that correct? 11:06:58 11:07:02 11:07:04 11:07:09

A. I wouldn't describe it as separately. They reported the results of the cohort and then did subgroup analysis on those two populations. 11:07:11 11:07:12 11:07:16 11:07:22

Q. And are you aware of studies finding an association between positive mental health metrics and -- and -- sort of on one natal sex and not the other? 11:07:24 11:07:27 11:07:31 11:07:41

A. So I believe, in fact, Chen, when 11:07:42

Page 85

they did their subgroup analysis, found that the effects were different in each of the different subgroups. 11:07:54 11:07:58 11:08:03

Q. Was this one -- I am trying to remember, was it positive -- association with positive effects on natal females or natal males, I should have it highlighted somewhere. 11:08:04 11:08:07 11:08:09 11:08:12

A. So I would have to review the study, sir. 11:08:14 11:08:16

Q. Sure. 11:08:16

A. I do recall that that subgroup analysis showed differences in the different subgroups. 11:08:16 11:08:19 11:08:22

Q. Yeah, I'm sorry, I don't know why this wasn't -- look at page 244, if you would, bottom of the page under designated sex at birth. Do you see where it says: Depression and anxiety scores decreased among youth designated female at birth but not among those designated male at birth. Similarly, T scores for life satisfaction increased among youth designated female at birth but not among those designated male at birth? Did I read that correctly? 11:08:22 11:08:36 11:08:43 11:08:46 11:08:54 11:08:57 11:09:00 11:09:02 11:09:05 11:09:08 11:09:11

A. Yes, you did, sir. 11:09:11

Q. And are you aware of any studies finding the association essentially going the other way, positive associations for natal males but not natal females? 11:09:12 11:09:15 11:09:18 11:09:22

A. So it is common for studies to do subgroup analysis on the different outcomes, including the studies by the Dutch team. But I don't recall off the top of my head whether there has been any systematic review that summarizes those results of subgroup analysis across the variety of outcomes. 11:09:24 11:09:31 11:09:35 11:09:44 11:09:46 11:09:51 11:09:54

Q. Sure, all right. 11:09:56

MR. FRAMPTON: Let's go to what I am going to mark as Exhibit -- maybe I am on -- 11:09:56 11:09:56

MR. WILKINSON: 12. 11:09:56

MR. FRAMPTON: -- 12. I was going to get it right. It's still early in the day. 11:09:56 11:09:59

(Thereupon, Exhibit 12, Growing Evidence and Remaining Questions in Adolescent Transgender Care, was marked for purposes of identification.) 11:09:59 11:09:59 11:09:59 11:10:00

BY MR. FRAMPTON: 11:10:00

Q. All right. And what I am handing you, Dr. Antommaria, is a piece titled Growing Evidence and Remaining Questions in Adolescent 11:10:15 11:10:16 11:10:20

Transgender Care. The lead author is Annelou de Vries, published in the New England Journal of Medicine, January 19th, 2023. Do you -- it's a short piece, Dr. Antommaria. Do you recognize it? 11:10:25 11:10:31 11:10:32 11:10:41 11:10:43

A. I do, sir. 11:10:43

Q. You do? You have read this before? 11:10:44 11:10:46

A. I have, sir. 11:10:46

Q. And is this a -- sort of an editorial comment on the Chen paper that we just looked at? 11:10:47 11:10:51 11:10:53

A. As the heading states, it was published as an editorial. And the first sentence of the article is this week in the Journal, a much awaited primary report from Chen, et al. And so yes, it's an editorial on Chen's study. 11:10:53 11:10:57 11:11:01 11:11:04 11:11:07 11:11:11

Q. And are you familiar with these researchers, Drs. de Vries and Hannema? 11:11:11 11:11:15

A. So I am most familiar with Dr. de Vries and less so with Dr. -- if it's pronounced Hannema. 11:11:21 11:11:23 11:11:25

Q. I am guessing, too. What's your familiarity with Dr. de Vries? What do you 11:11:26 11:11:29

know about her? 11:11:32

A. Dr. de Vries is a member of what's colloquially referred to as the Dutch group. 11:11:33 11:11:38

Q. She has been publishing on transgender care for a very long time, right? 11:11:41 11:11:46

Well, for a few decades? 11:11:49

A. For several decades, yes, sir. 11:11:51

Q. Be more precise. Look on page 276 if you would, second full paragraph. Drs. de Vries and Hannema state: Although overall psychological functioning in the study participants improved, there was substantial variation among participants; a considerable number still had depression, anxiety, or both at 24 months, and two died by suicide. Did I read that correctly? 11:11:53 11:12:17 11:12:17 11:12:17 11:12:43 11:12:43 11:12:47 11:12:50 11:12:52

A. You did, sir. 11:12:53

Q. And is that just like we were speaking earlier commenting on the heterogeneity in the data reported by Dr. Chen and her colleagues? 11:12:54 11:12:57 11:13:00 11:13:04

A. In part, sir, yes. 11:13:05

Q. And in other parts? 11:13:07

A. They are not only commenting on the variability, but they state a considerable 11:13:11 11:13:15

number still had depression and anxiety, sir. 11:13:19

Q. Sure. A little further down they say: However, other possible determinants of outcomes were not reported, particularly the extent of mental health care provided throughout GAH treatment. Did I read that correctly? 11:13:21 11:13:30 11:13:38 11:13:39 11:13:42 11:13:47

A. You did, sir. 11:13:47

Q. And help me understand, is there concern that the -- 11:13:48 11:13:52

A. Sir, may I read the full paragraph before you ask your question -- 11:13:57 11:13:59

Q. Oh, of course. 11:14:01

A. -- so I am prepared to answer? 11:14:03

Q. Sure. 11:14:05

A. Thank you, sir. Please go ahead. 11:14:39

Q. Sure. Is the concern that they are expressing that the mental health care provided throughout the GAH treatment could be affecting or confounding the results? 11:14:40 11:14:44 11:14:50 11:14:55

A. So the sentence that you didn't read, sir, was that the correlation between appearance congruence and various psychological-outcome variables suggests an important mediating role of GAH in consequent 11:14:59 11:15:04 11:15:06 11:15:10 11:15:12

Page 90

body changes. So Chen and colleagues, as I had 11:15:17
mentioned previously, did attempt to control 11:15:23
for confounders, and their analysis suggested 11:15:25
that the GAH and consequent body changes are 11:15:29
responsible for the psychological outcomes. 11:15:36
But they do then subsequently go on to 11:15:41
highlight a concern about a lack of information 11:15:43
about the mental health care that the 11:15:49
participants received and the way that that 11:15:53
might influence the outcome. 11:15:56
Q. And the idea is that the mental 11:15:56
health care provided could be confounding the 11:15:59
outcome, correct? 11:16:03
A. That the mental health could be 11:16:03
contributing to the outcome, yes, sir. 11:16:08
Q. Right, it could be responsible for 11:16:09
some of the improvement? 11:16:11
A. Again, the investigators made 11:16:12
efforts to identify whether the GAH was 11:16:19
responsible for the outcomes and provide 11:16:26
evidence that it was responsible for the 11:16:28
outcomes. But yes, they did not control for 11:16:30
the mental health care provided. 11:16:35
Q. And Dr. de Vries is raising that 11:16:38
as a potential confounder, right? 11:16:41

Page 91

A. Dr. De Vries is quote -- is 11:16:44
recommending, quote, future studies that 11:16:52
compare outcomes with different care models are 11:16:54
needed, preferably using similar measures, sir. 11:16:56
Q. My question was she is raising the 11:16:59
provision of mental health care as a potential 11:17:03
confounder, right? 11:17:06
A. I think that that's one potential 11:17:06
interpretation of what she is saying, sir. 11:17:14
Q. Is it how you read it? 11:17:16
A. I think that she is suggesting 11:17:18
that in future studies, methods that compare 11:17:22
outcomes with different care models are needed. 11:17:28
I think that's what she states. She is not 11:17:30
making an explicit claim, sir, about 11:17:33
confounders. 11:17:37
Q. She is calling mental health care 11:17:38
a possible determinant of outcomes, right? 11:17:41
A. Yes, sir. 11:17:43
Q. What do you think she means by 11:17:50
different care models? 11:18:23
MR. CHEEK: Objection, speculation. 11:18:24
BY MR. FRAMPTON: 11:18:25
Q. Or do you know? 11:18:29
A. I am rereading the paragraph, sir, 11:18:29

Page 92

if that's all right. So, sir, it's not clear 11:18:31
to me from the paragraph what she means by 11:19:09
different care models. 11:19:12
(Thereupon, Exhibit 13, GRADE 11:19:12
guidelines: 7. Rating the Quality of Evidence - 11:19:12
Inconsistency, was marked for purposes of 11:19:12
identification.) 11:19:38
BY MR. FRAMPTON: 11:19:38
Q. I show you what I am marking as 11:19:46
Exhibit 13. The Journal of Clinical 11:19:48
Epidemiology, GRADE Guidelines: 7. Rating the 11:20:07
Quality of Evidence - Inconsistency. This 11:20:08
article, Exhibit 13, Dr. Antommaria, is from 11:20:12
that same Journal of Clinical Epidemiology 11:20:16
series on the GRADE guidelines, correct? 11:20:18
A. Correct, sir. 11:20:21
Q. And you are familiar with it? 11:20:22
A. I am, sir. 11:20:23
Q. All right. Inconsistency is one 11:20:24
of the factors one might use to downgrade a 11:20:29
body of evidence under the GRADE guidelines; is 11:20:32
that right? 11:20:34
A. That is correct, sir. 11:20:34
Q. And the basic idea is that studies 11:20:35
within the body of relevant evidence are 11:20:43

Page 93

reporting meaningfully different outcomes, 11:20:46
right? 11:20:48
A. Yes, sir. Whereas uncertainty is 11:20:48
within a individual study, inconsistency is a 11:20:54
cross study. 11:20:59
Q. So the basic idea is if some 11:21:00
studies suggest that a particular intervention 11:21:13
is effective and some suggest that it has no 11:21:15
benefit, that would raise concerns about 11:21:17
inconsistency, right? 11:21:19
A. Can you repeat the question just 11:21:20
so I understand it? 11:21:23
Q. Sure. Some studies suggest that 11:21:24
an intervention has benefit and some suggest it 11:21:26
has no benefit, that would raise concerns about 11:21:30
inconsistency, correct? 11:21:32
A. Correct, sir. 11:21:33
Q. And as we talked about in the way 11:21:34
that studies in the gender medicine area often 11:21:41
do subgroup analyses among birth sex, if you 11:21:47
have got some studies suggesting benefit among 11:21:51
natal males but not females and others 11:21:55
suggesting benefit among natal females but not 11:21:58
males, that would also raise concerns about 11:22:02
inconsistency, would it not? 11:22:04

Page 94

MR. CHEEK: Objection, form. 11:22:06
THE WITNESS: If that were, in fact, 11:22:07
the case, sir. I don't know that that is an 11:22:09
accurate representation of the literature. 11:22:11
BY MR. FRAMPTON: 11:22:13
Q. Right. But if it were, that would 11:22:14
raise inconsistency concerns? 11:22:16
A. If it were, sir, yes, it would. 11:22:18
Q. And have you done a sort of 11:22:21
systematic assessment of the literature to 11:22:23
evaluate whether that is, in fact, what the 11:22:25
literature shows? 11:22:28
MR. CHEEK: Objection, form. 11:22:30
THE WITNESS: I have not conducted a 11:22:32
systematic review of the literature focusing on 11:22:34
that question, sir. 11:22:38
(Thereupon, Exhibit 14, GRADE 11:22:47
guidelines: 8. Rating the Quality of Evidence - 11:22:47
Indirectness, was marked for purposes of 11:22:47
identification.) 11:22:49
BY MR. FRAMPTON: 11:22:49
Q. I hand you what I am marking as 11:22:56
Exhibit 14, still Journal of Clinical 11:22:58
Epidemiology, GRADE Guidelines: 8. Rating the 11:23:03
Quality of Evidence - Indirectness. And, 11:23:05

Page 95

Dr. Antommaria, Exhibit 14 is a article from 11:23:10
the same GRADE guidelines series we have been 11:23:12
looking at in the Journal of Clinical 11:23:15
Epidemiology; is that right? 11:23:18
A. That is correct, sir. 11:23:19
Q. And one of the factors that may 11:23:19
warrant downgrading a body of evidence is 11:23:24
indirectness, correct? 11:23:27
A. Yes, sir. 11:23:31
Q. And one form of indirectness is 11:23:31
differences between the population that you are 11:23:34
interested in and the population that was 11:23:37
studied in the body of evidence, correct? 11:23:42
A. I might say the population that 11:23:44
you are treating as opposed to the -- you are 11:23:51
interested in. But yes, if you are considering 11:23:52
treating a patient, you would be concerned 11:23:56
about differences between that patient's 11:23:59
characteristics and the participants in the 11:24:01
study, sir. 11:24:03
Q. Right. The basic idea being that 11:24:05
you want to be careful about assuming that the 11:24:07
effects of an intervention on one population 11:24:10
will be the same as on a different population, 11:24:12
correct? 11:24:15

Page 96

A. In general, sir. 11:24:15
(Thereupon, Exhibit 15, The Cass 11:24:26
Review, was marked for purposes of 11:24:26
identification.) 11:24:26
BY MR. FRAMPTON: 11:24:26
Q. I am going to hand you what I am 11:24:42
marking as Exhibit 15, with apologies for the 11:24:43
size. You can blame Dr. Cass, not me. What I 11:24:54
am handing you, Dr. Antommaria, is titled the 11:25:03
Cass Review, Independent Review of Gender 11:25:06
Identity Services For Children and Young 11:25:12
People, Interim Report, February 2022. I 11:25:12
assume you are familiar with this document? 11:25:14
A. I am familiar with it, sir. 11:25:16
Q. Okay. What do you know about 11:25:18
Dr. Cass? 11:25:28
A. I generally know that Dr. Cass is 11:25:29
a British pediatrician. 11:25:33
Q. Is it your understanding that she 11:25:35
has been commissioned by the British government 11:25:50
to review the provision of care for children 11:25:56
and young people with gender dysphoria by the 11:26:01
National Health Service? 11:26:04
A. I believe that she chairs a 11:26:05
review -- 11:26:13

Page 97

Q. Right. 11:26:15
A. -- that is reviewing that topic, 11:26:15
sir. 11:26:17
Q. Turn with me if you would -- well, 11:26:19
actually, before we do that, do you in your 11:26:25
clinical practice initiate treatment for 11:26:29
central precocious puberty? 11:26:32
A. No, I do not, sir. 11:26:36
Q. Is that typically done by an 11:26:37
endocrinologist? 11:26:39
A. That would generally be done by an 11:26:40
endocrinologist, sir. 11:26:43
Q. And do you in your clinical 11:26:44
practice make the diagnosis of central 11:26:49
precocious puberty? 11:26:52
A. I might have reason to suspect a 11:26:55
patient has central precocious puberty but 11:26:57
would generally refer to another provider to 11:27:01
confirm that diagnosis and initiate treatment, 11:27:05
sir. 11:27:07
Q. Got it. Would you generally refer 11:27:07
to a pediatric endocrinologist? 11:27:09
A. I would, sir. 11:27:11
Q. Do you know, I am sure you do as a 11:27:12
pediatrician, sort of the typical normal ages 11:27:19

Page 98

for initiation of puberty in natal boys? Is 11:27:23
there a typical age range? 11:27:28
A. I believe that central precocious 11:27:30
puberty would be defined as beginning puberty 11:27:35
before 10 years of age in an individual. So I 11:27:39
would have to look -- it's somewhere between 8 11:27:42
and 10 years of age in individuals who are 11:27:49
assigned male at birth. 11:27:51
Q. So before 8 to 10 years or -- 11:27:52
A. Before 8 to 10 years would be 11:27:56
considered precocious. And I would have to 11:27:59
look to refresh my memory about what specific 11:28:01
age it is, sir. 11:28:05
Q. It would be slightly younger for 11:28:06
natal females? 11:28:09
A. Yes, for -- individuals who are 11:28:09
assigned female at birth typically begin 11:28:11
puberty earlier than individuals assigned male 11:28:15
at birth. 11:28:18
Q. Turn to page 63 of the Cass 11:28:19
Review, if you would. Let's look at the second 11:28:23
sentence in 5.23 where she says, or the 11:28:46
reviewers say: Again, it is important that it 11:28:51
is not assumed that outcomes for, and side 11:28:53
effects -- 11:28:56

Page 99

A. Hang on. 11:28:56
Q. I'm sorry, are we in the wrong 11:28:57
place? 11:28:59
A. No, no, no, you are just not 11:28:59
starting at the beginning, and I needed to find 11:29:01
where you were, sir. 11:29:02
Q. That's fine. 11:29:03
A. Okay, please. 11:29:04
Q. Again, it is important that it is 11:29:04
not assumed that outcomes for, and side effects 11:29:06
in, children treated for central precocious 11:29:09
puberty will necessarily be the same in young 11:29:12
people with gender dysphoria. Did I read that 11:29:15
correctly? 11:29:17
MR. CHEEK: I am going to object. 11:29:18
You did not read that correctly. 11:29:19
MR. FRAMPTON: Oh, I didn't? 11:29:20
MR. CHEEK: Correct. 11:29:21
MR. FRAMPTON: I am going to try it 11:29:22
again. 11:29:23
BY MR. FRAMPTON: 11:29:23
Q. Starting it over. Again, it is 11:29:24
important that it is not assumed that outcomes 11:29:27
for, and side effects in, children treated for 11:29:31
precocious puberty will necessarily be the same 11:29:35

Page 100

in children or young people with gender 11:29:39
dysphoria. Now did I read it correctly? 11:29:42
A. I believe you did, sir. 11:29:45
Q. Do you agree with the authors on 11:29:49
that? 11:29:55
A. May I read the whole paragraph, 11:29:55
sir? 11:29:59
Q. Sure. 11:30:00
A. All right. And then would you 11:31:04
repeat your question, sir? 11:31:05
Q. Do you agree with Dr. -- or the 11:31:07
author's statement that I read into the record? 11:31:09
A. So, again, it's difficult to 11:31:11
interpret a sentence outside of its larger 11:31:20
context. But I would agree that it is 11:31:23
important to be open to the possibility that 11:31:26
outcomes and side effects in one population may 11:31:30
be different than outcomes inside of a 11:31:35
different population. 11:31:38
Q. You would agree that you are 11:31:39
generally not going to initiate puberty 11:31:42
suppression for central precocious puberty in a 11:31:46
12-year-old natal female, correct? 11:31:51
A. So, in general, a 12-year-old who 11:31:58
is not -- would not fulfill the diagnostic 11:32:03

Page 101

criteria for central precocious puberty. 11:32:08
Q. You would potentially, depending 11:32:11
on the assessment and all of that kind of 11:32:15
stuff, initiate puberty suppression in a natal 11:32:17
female at age 12 for gender dysphoria, correct? 11:32:22
A. And, again, would you repeat your 11:32:25
question, sir? 11:32:38
Q. Sure. Provided appropriate 11:32:40
assessments and criteria were fulfilled, you 11:32:42
may initiate puberty suppression in a 11:32:45
12-year-old natal female for gender dysphoria, 11:32:49
correct? 11:32:51
A. You may, sir. 11:32:51
Q. And you would -- in the child with 11:32:53
gender dysphoria, you would continue puberty 11:33:06
suppression until the child either decided to 11:33:08
discontinue or was ready to go to hormonal 11:33:11
interventions, correct? 11:33:17
A. You would not continue them 11:33:18
indefinitely and would need to at some point 11:33:21
reach a decision to discontinue them or to 11:33:24
begin gender affirming hormone therapy, yes. 11:33:27
Q. With central precocious puberty, 11:33:31
you would generally discontinue the treatment 11:33:39
when the child reached an age appropriate for 11:33:42

Page 102

puberty, correct? 11:33:45
A. At an age that was consistent with 11:33:46
statistical population norms, yes. 11:33:51
Q. And I believe what you have said 11:33:54
in other forums is that you would not -- you 11:33:59
would not initiate puberty suppression to treat 11:34:05
gender dysphoria in a child that had not at 11:34:09
least reached Tanner Stage 2, correct? 11:34:11
A. So those are the recommendations 11:34:14
or the clinical practice guidelines for the 11:34:18
field, and I wouldn't have reason to believe 11:34:19
that I contradicted them in some other forum. 11:34:25
Q. Sure. And Tanner Stage 2 means 11:34:29
the child has actually started puberty, 11:34:31
correct? 11:34:32
A. Correct. 11:34:33
Q. Let's stick with Dr. Cass for a 11:34:33
minute. Move to page 32, if you would. 11:34:56
A. Yes, sir. 11:35:07
Q. Looking at 3.10: In the last few 11:35:07
years, there has been a significant change in 11:35:20
the numbers and case-mix of children and young 11:35:22
people being referred to GIDS. From a baseline 11:35:24
of approximately 50 referrals per annum in 11:35:28
2009, there was a steep increase from 2014-15, 11:35:32

Page 103

and it all -- and at the time of the CQC 11:35:37
inspection of the Tavistock and Portman NHS 11:35:41
Foundation Trust in October 2020 there were 11:35:45
2,500 children and young people being referred 11:35:48
per annum, 4,600 children and young people on 11:35:51
the waiting list, and a waiting time of over 11:35:54
two years to first appointment. Did I read 11:35:55
that correctly? 11:35:59
A. You did, sir. 11:35:59
Q. Has it also been your experience 11:36:00
that there has been a substantial increase in 11:36:08
the number of patients, children and young 11:36:12
people presenting with potential gender 11:36:16
dysphoria? 11:36:20
A. I believe that the literature 11:36:20
shows, sir, increasing numbers of individuals 11:36:24
presenting to clinics that treat gender 11:36:28
dysphoria, yes. 11:36:33
Q. And we don't know why, do we? 11:36:34
A. I think there are a variety of 11:36:36
potential reasons why, sir. 11:36:43
Q. Any that have been rigorously 11:36:45
studied and established? 11:36:49
A. So, again, part of the question 11:36:51
would be what rigorously studied means, but not 11:37:01

Page 104

established, sir. But I don't think that 11:37:11
that's fundamentally different than some of the 11:37:12
changes in the epidemiology of other 11:37:15
conditions, such as autism or Type 1 diabetes. 11:37:18
Q. And we don't know why those are 11:37:21
increasing, either, do we? 11:37:32
A. We do not, sir. 11:37:33
Q. And that raises indirectness 11:37:34
issues, does it not, if we have got an 11:37:36
increase, a new population, we don't really 11:37:37
understand why? 11:37:40
A. I don't believe, sir, that it 11:37:41
necessarily -- that an increasing population 11:37:44
necessarily raises indirectness issues, sir. 11:37:47
Q. You think we can just assume that 11:37:51
this increased population will have the same 11:37:55
outcomes as the prior much smaller population? 11:37:58
MR. CHEEK: Objection, form. 11:38:02
THE WITNESS: So it depends on the 11:38:04
characteristics of the population, sir. If the 11:38:05
population has the same demographic and clinical 11:38:09
characteristics but there is simply a larger 11:38:14
number of them, there would be no indirectness 11:38:16
concerns. 11:38:19
BY MR. FRAMPTON: 11:38:19

Page 105

Q. You don't think that the etiology 11:38:20
of the increase matters at all to that 11:38:24
analysis? 11:38:26
MR. CHEEK: Objection, form. 11:38:28
THE WITNESS: So, sir, my 11:38:31
understanding of the issue of directness is the 11:38:32
characteristics of the population in the study are 11:38:37
whether they are the same or different from the 11:38:43
characteristics of the individuals who you are 11:38:46
considering treating. Many of the individuals who 11:38:50
are presenting to clinics would have met the 11:38:56
criteria for inclusion in the Dutch studies. And, 11:38:59
therefore, I would say that I don't think that on 11:39:05
the face of it, it necessarily raises indirectness 11:39:08
questions. 11:39:12
BY MR. FRAMPTON: 11:39:12
Q. The case-mix has also changed, has 11:39:21
it not? 11:39:25
MR. CHEEK: Can you repeat that 11:39:26
question? 11:39:27
BY MR. FRAMPTON: 11:39:27
Q. I said the case-mix has also 11:39:27
changed, has it not? 11:39:29
MR. CHEEK: Objection, form. 11:39:30
THE WITNESS: And by case-mix you 11:39:31

mean what, sir? 11:39:33
BY MR. FRAMPTON: 11:39:33
Q. Well, let's see what Dr. -- let's 11:39:35
just read what Dr. Cass said about that, still 11:39:37
on page 32. 11:39:39
A. I am on 32, sir. 11:39:48
Q. All right, 3.11. This increase in 11:39:50
referrals has been accompanied by a change in 11:39:52
the case-mix from predominantly 11:39:54
birth-registered males presenting with gender 11:39:57
incongruence from an early age, to 11:40:00
predominantly birth-registered females 11:40:02
presenting with later onset of reported gender 11:40:04
incongruence in the early teen years. In 11:40:07
addition, approximately one-third of children 11:40:10
and young people referred to GIDS have autism 11:40:11
or other types of neurodiversity. There is 11:40:16
also an over-representation percentage wise 11:40:19
compared to the national percentage of looked 11:40:20
after children. Did I read that paragraph 11:40:21
correctly? 11:40:23
A. You did, sir. 11:40:23
Q. Does this accurately reflect your 11:40:25
understanding of the US experience as well in 11:40:32
terms of the changing population? 11:40:36

A. So I think that looked after 11:40:39
children is likely to be a British 11:40:46
colloquialism that I am not clear -- 11:40:49
Q. Put that one aside. 11:40:49
A. -- what it's referring to. 11:40:51
Q. Put that one aside, rest of the 11:40:52
paragraph. Well, let's just do them in turn. 11:40:53
A. Okay. 11:40:58
Q. Predominantly birth-registered 11:40:58
males presenting with gender incongruence from 11:41:00
an early age to predominantly birth-registered 11:41:02
females presenting with later onset of reported 11:41:06
gender incongruence in early teen years. Is 11:41:08
that consistent with the US experience? 11:41:12
A. So my sense is that there is some 11:41:14
heterogenous data about those potential changes 11:41:27
but that some individuals have reported similar 11:41:34
changes in the United States. 11:41:38
Q. And what about the increase in 11:41:38
children with autism or other types of 11:41:50
neurodiversity? 11:41:53
MR. CHEEK: Objection, form. 11:41:54
THE WITNESS: So I don't read 11:41:56
Dr. Cass's reporting that as a change. I take it 11:41:58
that she says, in addition, approximately 11:42:03

one-third of children and young people referred to 11:42:05
GIDS have autism or other types of neurodiversity. 11:42:08
I don't believe that at least in this sentence she 11:42:12
is representing that that proportion has changed 11:42:14
over time. 11:42:16
BY MR. FRAMPTON: 11:42:17
Q. Does that sound about right for 11:42:21
the US, about a third? 11:42:22
A. I apologize -- 11:42:24
Q. Or do you know? 11:42:31
A. -- I do not know the specific 11:42:32
numbers. 11:42:34
Q. Look at page 19. 11:42:34
A. Sir, recognizing this is a very 11:42:48
big exhibit, when you reach a point in your 11:42:50
line of questioning, can we take another break? 11:42:54
Q. Yes, we will be there very, very 11:42:57
shortly, I promise. 11:43:00
A. Thank you. 11:43:01
Q. All right, 1.28. Much of the 11:43:01
existing literature about natural history and 11:43:13
treatment outcomes for gender dysphoria in 11:43:15
childhood is based on a case-mix of 11:43:17
predominantly birth-registered males presenting 11:43:19
in early childhood. There is much less data on 11:43:22

the more recent case-mix of predominantly 11:43:25
birth-registered females presenting in early 11:43:27
teens, particularly in relation to treatment 11:43:29
and outcomes. Did I read that correctly? 11:43:31
A. You did, sir. 11:43:33
Q. Do you agree with her statement 11:43:34
about the state of the statements with regard 11:43:40
to the state of the literature? 11:43:42
A. So if I recall the Dutch studies 11:43:49
correctly, there were a reasonable number of 11:43:53
individuals assigned female at birth in their 11:43:58
data. I would agree that there is potentially 11:44:01
less data about individuals with a shorter 11:44:09
duration of gender dysphoria. 11:44:17
Q. A later onset of gender dysphoria? 11:44:18
A. I think it's complicated to figure 11:44:20
out when gender dysphoria has its onset, but 11:44:36
potentially later presentation to clinical 11:44:39
care. 11:44:43
Q. When you say the Dutch studies had 11:44:45
a reasonable number of what you are calling 11:44:47
birth-assigned females, natal females, what do 11:44:52
you mean by a reasonable number? 11:44:56
A. So, again, I would have to refresh 11:44:57
my memory looking at the -- at the studies. 11:44:58

But, for example, I don't believe that there were only 5 percent of participants were female assigned at birth. 11:45:04 11:45:05 11:45:09

Q. So you just -- you disagree with Dr. -- with this review when it says the case-mix was predominantly birth-registered males and that there is much less data on the more recent case-mix? 11:45:09 11:45:12 11:45:14 11:45:17 11:45:20

A. So all I am -- so when you -- when I read this, sir, Dr. -- the authors of this report are contrasting both sex assigned at birth and age of presentation, and I would put more emphasis than the authors of the report on the age of presentation than I would on the sex assigned at birth. 11:45:21 11:45:31 11:45:44 11:45:53 11:46:01 11:46:06 11:46:09

Q. Are you aware of any study as to whether responses and long-term outcomes from puberty blockers or cross-sex hormones are different for children on the autistic spectrum, aware of any studies that have looked at that? 11:46:10 11:46:16 11:46:19 11:46:23 11:46:26 11:46:29

A. I cannot recall a study that does -- that focused exclusively on that population or did subgroup analysis on that population. 11:46:29 11:46:32 11:46:35 11:46:38

MR. FRAMPTON: All right. Then we will take a break. 11:46:39 11:46:39

THE WITNESS: Thank you. 11:46:40

(Recess taken.) 11:46:41

MR. FRAMPTON: Let's go back on. 11:53:52

(Thereupon, Exhibit 16, GRADE guidelines: 11. Making An Overall Rating of Confidence in Effect Estimates For a Single Outcome and All Outcomes, was marked for purposes of identification.) 11:53:54 11:53:54 11:53:54 11:53:54 11:53:55

BY MR. FRAMPTON: 11:53:55

Q. Dr. Antommaria, I am going to show you what I am marking as Exhibit 16. And this is still Journal of Clinical Epidemiology, GRADE Guidelines 11. Dr. Antommaria, is this an article in the same Journal of Clinical Epidemiology GRADE Guidelines series we have been looking at? 11:53:55 11:53:56 11:54:09 11:54:12 11:54:16 11:54:21 11:54:21

A. It is, sir. 11:54:22

Q. You are familiar with it? 11:54:23

A. I am, sir. 11:54:26

Q. All right, turn to page 152. Let's look at the key points in the upper left-hand corner. So if you are applying the GRADE methodology, you assign a rating of 11:54:26 11:54:28 11:54:31 11:54:41

confidence in effect estimates, or quality of evidence, to each outcome that you are studying, correct? 11:54:48 11:54:52 11:54:53

A. Yes, sir. 11:54:54

Q. And that presumably should be the patient important outcomes that we looked at before, right? 11:54:56 11:55:00 11:55:03

A. Yes, sir. 11:55:03

Q. And to do that, you simultaneously consider all eight sort of upgrade and downgrade domains, correct? 11:55:05 11:55:13 11:55:15

A. Yes, sir. 11:55:17

Q. And one way at least of presenting the application of the GRADE methodology is an evidence profile, like we see in Table 1 on the next page, correct? 11:55:17 11:55:24 11:55:28 11:55:32

A. Yes, sir. 11:55:32

Q. And this sort of presents the number and type of studies the authors considered, correct? 11:55:55 11:55:58 11:56:01

A. That the individual performing the evaluation considered, yes. 11:56:01 11:56:09

Q. Yes, I'm sorry. I will say evaluator from here forward so we are saying the same thing. And it gives you the 11:56:10 11:56:12 11:56:14

evaluator's conclusion as to each of the upgrade or downgrade domains, right, or at least as to the downgrade domains? 11:56:17 11:56:20 11:56:29

A. Yes, I only see five of the eight listed in the table, sir. 11:56:30 11:56:33

Q. And it's the five downgrade domains that you see, right? 11:56:34 11:56:35

A. Yes, sir. 11:56:36

Q. Okay. And then they have given you at least some explanation when they downgraded as to why? 11:56:38 11:56:41 11:56:43

A. So there is comments under each of the columns. I don't see necessarily that they have assigned a minus 1 or minus 2. But in the quality concluding, they give a reason for the final conclusion, sir. 11:56:48 11:57:01 11:57:04 11:57:08 11:57:14

Q. They give a reason that's grounded in the five downgrade domains, correct? 11:57:15 11:57:18

A. Yes, sir. 11:57:21

Q. Go to the next -- I'm sorry, page 155, if you would. 11:57:24 11:57:29

A. I am on 155, sir. 11:57:37

Q. Okay. The second full paragraph on the left-hand column says: Despite the limitations of breaking continua into discrete 11:57:39 11:57:43 11:57:48

categories, treating each domain for rating 11:57:52
confidence up or down as a discrete category 11:57:55
enhances transparency. Indeed, the example 11:57:58
highlights once again that the great merit of 11:58:02
GRADE is not that it necessarily ensures 11:58:05
reproducible judgments, observers will 11:58:07
inevitably differ in close-call situations when 11:58:11
rating up or down for individual domains or for 11:58:14
the overall confidence per outcome, but that it 11:58:16
achieves explicit and transparent judgment. 11:58:19
Did I read that correctly? 11:58:22
A. You did, sir. 11:58:22
Q. Do you agree that one of the -- 11:58:23
one of the great merits of the GRADE system is 11:58:28
that done correctly, there should be a high 11:58:31
level of transparency as to why the evaluator 11:58:34
rated the evidence quality the way that he or 11:58:39
she did? 11:58:42
A. Yes, one of the benefits of the 11:58:44
GRADE methodology is its emphasis on 11:58:49
transparency. 11:58:53
Q. So that even if you don't agree 11:58:54
with the evaluator, you at least know why a 11:58:55
particular quality rating was assigned, right? 11:58:58
A. That would be one of the 11:59:01

components of the transparency, sir. 11:59:04
Q. And you know what studies went 11:59:06
into that conclusion, right? 11:59:08
A. Yes, that is part of a systematic 11:59:10
review, that they list the studies that they 11:59:20
evaluated. 11:59:26
Q. When you read a systematic review 11:59:29
that has followed the GRADE methodology, you 11:59:35
should come away with it with a clear 11:59:36
understanding of the evaluator's judgment calls 11:59:39
on the quality of evidence and why he or she 11:59:43
made those calls, correct? 11:59:46
A. Ideally, that would be the way the 11:59:47
GRADE methodology is applied. 11:59:53
Q. All right. Let's go to -- let's 11:59:54
go to what I am going to mark as Exhibit 17.
(Thereupon, Exhibit 17, Endocrine
Treatment of Gender-Dysphoric/Gender-Incongruent
Persons: An Endocrine Society Clinical Practice
Guideline, was marked for purposes of
identification.) 12:00:15
BY MR. FRAMPTON: 12:00:15
Q. This document is entitled 12:00:27
Endocrine Treatment of Gender Dysphoric/Gender 12:00:30
Incongruent Persons, an Endocrine Society 12:00:33

Clinical Practice Guideline. Dr. Antommaria, 12:00:38
you are familiar with this document, correct? 12:00:40
A. I am. 12:00:42
Q. And this is a set of clinical 12:00:44
practice guidelines published by the Endocrine 12:00:45
Society in 2017 for treating people with gender 12:00:49
dysphoria or gender incongruence, correct? 12:00:53
A. It is a clinical practice 12:00:58
guideline, yes. 12:01:00
Q. I'm sorry if I used a different 12:01:00
article. It is a clinical practice guideline 12:01:02
published by the Endocrine Society, correct? 12:01:05
A. Correct. 12:01:08
Q. And it is their most recent 12:01:08
clinical practice guideline, is it not? 12:01:10
A. It's their most recent clinical 12:01:12
practice guideline on this particular topic, 12:01:13
yes. 12:01:16
Q. Yes, okay. And the evaluators 12:01:16
used -- claim to have used the GRADE 12:01:23
methodology, correct? 12:01:29
A. Yes, the authors of this guideline 12:01:29
report that they used the GRADE methodology. 12:01:33
Q. And you have not conducted your 12:01:34
own systematic review of this evidence, 12:01:39

correct? 12:01:42
A. No, sir, I have not. 12:01:42
Q. You have not conducted your own 12:01:44
sort of application of the GRADE methodology to 12:01:47
this evidence, correct? 12:01:49
A. No, sir, I have not. 12:01:50
Q. Let's go to page -- 12:01:53
A. I think it would be -- I think it 12:01:57
would be exceptionally difficult for a single 12:02:00
individual to do either of those things, sir. 12:02:02
Q. All right. Let's go to page 37 -- 12:02:04
I'm sorry, 3873. 12:02:11
MR. CHEEK: Counsel, can you say it 12:02:18
again, 38? 12:02:19
MR. FRAMPTON: 3873. 12:02:21
MR. CHEEK: Thank you. 12:02:22
MR. FRAMPTON: We have got a lot of 12:02:22
four-digit page numbers in this one. 12:02:24
THE WITNESS: I am on that page, sir. 12:02:26
BY MR. FRAMPTON: 12:02:27
Q. Okay. Are you familiar with what 12:02:27
systematic reviews the authors commissioned for 12:02:33
this set of clinical practice guidelines? 12:02:37
A. I believe that the authors 12:02:39
commissioned two systematic reviews for this 12:02:42

Page 118

guideline, sir. 12:02:45
Q. Okay. And what were they on? 12:02:45
A. So one was on the effect of sex 12:02:47
steroid use in transgender individuals on 12:02:55
lipids and cardiovascular outcomes, and the 12:02:58
second was on the effect of sex steroids on 12:03:03
bone health in transgender individuals. 12:03:08
Q. They did not commission any 12:03:12
systematic reviews on psychosocial outcomes, 12:03:14
did they? 12:03:18
A. They did not, sir. 12:03:18
Q. Or effects on brain development? 12:03:23
A. They did not, sir. 12:03:28
Q. Fertility? 12:03:33
A. So, again, I think that -- so I 12:03:34
would say that I think that their commissioning 12:03:40
of systematic reviews would be unlikely that 12:03:43
they would be able to commission systematic 12:03:45
reviews on all of the patient relevant outcomes 12:03:48
because of the way in which professional 12:03:52
societies are resourced and that the systematic 12:03:53
reviews that were commissioned for this 12:04:01
clinical practice guideline are comparable to 12:04:03
the type -- the number of systematic reviews 12:04:06
commissioned for other clinical practice 12:04:08

Page 119

guidelines. 12:04:10
Q. There is no systematic review on 12:04:10
the efficacy of these interventions in 12:04:18
improving mental health, is there? 12:04:21
A. There is not, sir. 12:04:23
Q. Let's go to page 3883. 12:04:24
A. Yes, sir. 12:04:37
Q. All right. 2.4 is a strong 12:04:37
recommendation for the use of sex hormone 12:04:50
treatment based on what they have assessed as 12:04:55
low quality evidence; is that -- am I reading 12:04:59
that correctly? 12:05:03
A. Yes, that's what the No. 1 and the 12:05:04
two circles with plus signs in them indicate. 12:05:08
Q. Okay. Turn to the next page, if 12:05:10
you would. And I just -- structurally in this 12:05:15
guideline, they follow that recommendation with 12:05:19
the evidence, the values and preferences, and 12:05:25
the remarks on that recommendation, correct? 12:05:29
A. Yes, sir. You have reviewed 12:05:31
extensively the components of the GRADE 12:05:40
guidelines relative to the rating of quality of 12:05:44
the evidence. There are a number of papers 12:05:46
about making recommendations. But yes, as part 12:05:48
of making the recommendations, they describe 12:05:53

Page 120

the values and preferences as part of being 12:05:55
transparent about their methods. 12:06:00
Q. They do not give us how they 12:06:06
evaluated any of the downgrade domains for this 12:06:14
body of evidence, do they? 12:06:19
A. So they do not provide a table 12:06:20
similar to the one that we just reviewed, sir. 12:06:28
Q. Nor do they explain in the 12:06:31
evidence section how they applied any of the 12:06:34
downgrade or upgrade factors, do they? 12:06:39
A. So, again, so I would have to read 12:06:41
the evidence statement related to each of the 12:06:47
individual recommendations to know whether they 12:06:50
mention any of those factors or not. 12:06:52
Q. I am asking about 2.4. 12:06:54
A. Then please let me read the 12:06:57
evidence statement. 12:07:00
Q. Sure. 12:07:00
A. So, sir, on page 3885, the end of 12:09:31
the first incomplete paragraph, the authors 12:09:38
state: However, only minimal data support 12:09:42
earlier use of gender-affirming hormones in 12:09:45
transgender adolescents currently exist. So I 12:09:48
take it that that is a reference to 12:09:54
indirectness, which would be potentially a 12:09:58

Page 121

reason for downgrading the evidence. 12:10:01
Q. We don't know whether they did or 12:10:03
did not downgrade the evidence based on 12:10:06
indirectness, do we? 12:10:09
A. They do not explicitly state that 12:10:10
the reason why they graded the evidence to be 12:10:21
of low quality was as a result of indirectness, 12:10:24
no. 12:10:26
Q. Well, all of the studies are 12:10:26
observational, right, or do we know? 12:10:30
A. They would in general be 12:10:35
observational. 12:10:37
Q. Which would start us at low 12:10:38
quality, right? 12:10:40
A. Yes, sir. 12:10:41
Q. So we don't know if it's just that 12:10:41
they left them at low quality or if they 12:10:47
upgraded and downgraded, or we don't know how 12:10:50
they planted it low, do we? 12:10:54
A. No, we do not, sir. 12:10:56
Q. And it doesn't tell us how many 12:10:58
studies went into this quality assessment, does 12:11:05
it? 12:11:09
A. So indirectly, sir, so, for 12:11:09
example, currently available data from 12:11:21

Page 122

transgender -- I am on page -- 12:11:24
Q. I see it. 12:11:27
A. -- 84. Currently available data 12:11:28
from transgender adolescent support treatment 12:11:33
with sex hormones starting at age 16, and they 12:11:35
provide two references. We need to look at 12:11:38
those references to see if they are to studies 12:11:41
or summaries of studies or reviews. But they 12:11:44
do reference the recommendations, sir, so there 12:11:50
would be a way to determine in some way how 12:11:53
many studies they are basing their 12:11:57
recommendations on. 12:11:58
Q. You would have to piece together 12:11:59
the footnotes and figure out -- or the end 12:12:00
notes and figure out what they seem to be 12:12:03
using, right? They have not compiled it for us 12:12:05
and presented it? 12:12:07
A. Again, as I said, they don't 12:12:08
provide a table similar to the table that we 12:12:10
reviewed in Exhibit 16. 12:12:12
Q. And we don't know if these studies 12:12:14
were selected via systematic review. In fact, 12:12:17
it appears they were not, correct? 12:12:21
A. That would be a reasonable 12:12:24
conjecture. 12:12:26

Page 123

Q. Let's look at this endnote 63 that 12:12:27
you just referenced. So the statement 12:12:31
currently available data from transgender 12:12:43
adolescents support treatment with sex hormones 12:12:47
starting at age 16 years is citing to a paper 12:12:48
lead author de Vries published in Pediatrics in 12:12:56
2014, correct? 12:13:00
A. Correct, sir. 12:13:00
Q. And that is a -- that's not a 12:13:02
systematic review or anything, that's a single 12:13:05
study, is it not? 12:13:07
A. Yes, sir. 12:13:08
Q. And then they are also citing to 12:13:08
122, which is an NHS document, correct? 12:13:12
A. The author of that document is the 12:13:16
NHS, sir. 12:13:29
Q. And do you know if that's a study 12:13:30
or review or what it is? 12:13:33
A. I do not, sir. 12:13:35
Q. And assuming if it is not a study 12:13:41
itself, do you have any idea what studies it 12:13:44
cites to? 12:13:47
A. I would have to reference the 12:13:48
document, sir. 12:13:49
Q. Fair enough. Do you -- can you 12:13:50

Page 124

tell me in what situations the GRADE guidelines 12:14:03
permit making a strong recommendation based on 12:14:09
low quality evidence? 12:14:13
A. So there are specific situations 12:14:15
in which they report that that is acceptable. 12:14:21
I would need to refer to the appropriate 12:14:24
article in the series to identify those. I 12:14:27
believe that there are approximately five 12:14:31
situations in which they state that that is an 12:14:34
inappropriate thing to do. 12:14:40
Q. Did the Endocrine Society in its 12:14:41
2017 guidelines tell us which of those 12:14:43
situations they were relying upon to make a 12:14:46
strong recommendation based on low quality 12:14:50
evidence? 12:14:52
A. They did not. The thing that I 12:14:53
would state, sir, is that the GRADE guidelines 12:14:59
are an ideal process and that this guideline is 12:15:02
comparable to many other clinical practice 12:15:10
guidelines in medicine that clinicians rely on, 12:15:12
and in some ways you may be holding the 12:15:20
guidelines up to unrealistic standards in 12:15:25
practice. 12:15:29
Q. Have you independently determined 12:15:30
which of the situations for making a strong 12:15:34

Page 125

recommendation based on low quality evidence 12:15:38
would apply here? 12:15:40
A. I have not, sir. 12:15:41
Q. All right. Let's look at 12:15:43
something else. 12:15:47
A. But not having done so does not 12:15:48
mean that one of those situations does not, in 12:15:50
fact, apply. 12:15:52
Q. I am trying to understand your 12:15:53
testimony. You in preparing your expert report 12:15:54
did not opine as to which one applies, correct? 12:15:57
A. I have not formed an opinion on 12:16:00
that matter, sir. 12:16:03
Q. Understood. 12:16:04
(Thereupon, Exhibit 18, Standards of 12:16:05
Care for the Health of Transgender and Gender 12:16:05
Diverse People, Version 8, was marked for purposes 12:16:05
of identification.) 12:16:05
BY MR. FRAMPTON: 12:16:05
Q. All right. Dr. Antommaria, I am 12:16:23
handing you what I am marking as Exhibit 18. 12:16:24
Hopefully, it's excerpts from WPATH's SOC8. 12:16:31
That's what it's supposed to be. Tell me if 12:16:37
that's what it appears to be. 12:16:39
A. Yes, it appears to be portions but 12:16:59

not the entirety of WPATH's SOC8. 12:17:01
Q. That's right. It should have the 12:17:07
entirety of the adolescent chapter, which is 12:17:09
probably all we are going to look at. So 12:17:14
flip -- let's see, I don't even have it in 12:17:20
front of me. Let's go to the adolescent 12:17:24
chapter, which I believe begins on page 43, 12:17:56
S43. I don't know why there is an S in front 12:18:11
of it, but it's S43. 12:18:13
MR. CHEEK: Counsel, just sort of 12:18:15
flipping through this, there are -- like it goes 12:18:17
from page S13, S14, and then jumps to S43. 12:18:24
MR. FRAMPTON: Yeah. 12:18:32
MR. CHEEK: Okay, okay. 12:18:33
MR. FRAMPTON: No, that's correct. I 12:18:34
mean, that's -- you can see there is a table of 12:18:35
contents on S4. I eliminated a bunch of chapters 12:18:37
I wasn't going to ask him about. 12:18:41
MR. CHEEK: Understood. Thank you 12:18:42
for the clarity. 12:18:43
BY MR. FRAMPTON: 12:18:44
Q. Dr. Antommaria, I -- 12:18:47
MR. CHEEK: I'm sorry, which page are 12:18:48
you on? 12:18:49
MR. FRAMPTON: I am on S43. 12:18:49

MR. CHEEK: Thank you. 12:18:51
BY MR. FRAMPTON: 12:18:51
Q. Doctor, are you also on -- 12:18:51
A. I am on S43. 12:18:51
Q. Thank you, sir. Are you familiar 12:18:54
generally with this chapter 6 on adolescents of 12:19:00
SOC8? 12:19:04
A. I am, sir. 12:19:05
Q. And I'm sorry, did you answer my 12:19:06
question? We are, in fact, looking at WPATH 12:19:08
SOC8, correct? 12:19:11
A. Yes, I agreed that this exhibit 12:19:12
was parts of WPATH's SOC8. 12:19:14
Q. Great. Do you agree that the 12:19:19
recommendations in the adolescent chapter are 12:19:27
not based on a systematic review of the 12:19:29
evidence? 12:19:31
A. That is correct, sir. 12:19:31
Q. And as a result, there are no 12:19:35
GRADE type assessments of the quality of the 12:19:43
evidence, correct? 12:19:46
A. As a result of that and a number 12:19:47
of additional factors, yes. 12:19:51
Q. We will just read it. On S46, in 12:19:54
that first not full paragraph in the upper 12:20:09

left-hand corner, the authors provide what they 12:20:17
call a short narrative review instead of a 12:20:19
systematic review; is that correct? 12:20:23
A. That's what they state. 12:20:24
Q. Okay. And their claim is that the 12:20:26
number of studies is too small to allow for a 12:20:29
systematic review; is that right? 12:20:33
A. The low number of studies is one 12:20:36
of the reasons that they provide for not 12:20:52
performing the systematic review or that a 12:20:55
systematic review was not possible. Are we 12:20:57
moving to another document, sir? 12:21:20
Q. We are moving to another document. 12:21:22
(Thereupon, Exhibit 19, Gender 12:21:22
Dysphoria In Young People Is Rising - And So Is 12:21:22
Professional Disagreement, was marked for purposes 12:21:22
of identification.) 12:21:22
BY MR. FRAMPTON: 12:22:15
Q. All right. Do you have the new 12:22:15
exhibit? Oh, I see it there. All right. What 12:22:18
I have marked as Exhibit 19 is an article 12:22:20
entitled Gender Dysphoria In Young People Is 12:22:26
Rising - And So is Professional Disagreement, 12:22:29
Jennifer Block and the BMJ; is that correct? 12:22:31
A. If by article you mean a news 12:22:34

article, yes, sir. 12:22:41
Q. Yes, I understand this is not a 12:22:44
peer-reviewed article, correct? Correct? 12:22:45
A. Correct. 12:22:49
Q. Sorry, she has to have a verbal 12:22:49
response or she can't -- 12:22:52
A. I apologize. 12:22:53
Q. Have you seen this before? 12:22:54
A. I am familiar with it, sir. 12:22:57
Q. Have you read it? 12:22:59
A. I have, sir. 12:23:07
Q. Go to page 2, the second page. 12:23:16
The very bottom of the page, that paragraph 12:23:30
that starts and spills over reads: Guyatt, who 12:23:31
co-developed GRADE, found, quote, serious 12:23:34
problems, unquote, with the -- 12:23:37
A. Oh, I'm sorry. 12:23:38
Q. Are you in the wrong place? 12:23:39
A. No, I just want to -- so we are on 12:23:40
2 of 10, sir? 12:23:44
Q. You are not looking -- no, we need 12:23:45
the other set of copies. I'm sorry, I am going 12:23:52
to remark this. I made a better copy of that 12:23:55
exhibit. 12:23:57
MR. CHEEK: Do you want to just mark 12:24:05

Page 130

that as 20? 12:24:07
MR. FRAMPTON: Sure. 12:24:09
(Thereupon, Exhibit 20, Gender 12:24:09
Dysphoria In Young People Is Rising - And So is 12:24:09
Professional Disagreement, was marked for purposes 12:24:09
of identification.) 12:24:10
BY MR. FRAMPTON: 12:24:10
Q. This is a whole lot easier to 12:24:10
read. 12:24:12
A. The PDF as opposed to the web 12:24:12
page, right? 12:24:15
Q. Yes. 12:24:15
A. Thank you. 12:24:16
Q. All right. Do we appear to be 12:24:26
looking at the same document, just a better 12:24:27
copy? 12:24:30
A. We now appear to be viewing the 12:24:30
PDF of that article. 12:24:31
Q. Great, all right. Bottom of page 12:24:33
2. 12:24:37
A. Yes, sir. 12:24:37
Q. All right. It says: Guyatt, who 12:24:38
co-developed GRADE, found, quote, serious 12:24:42
problems with the Endocrine Society guidelines, 12:24:44
noting that the systematic reviews didn't look 12:24:47

Page 131

at the effect of the interventions on gender 12:24:50
dysphoria itself, arguably, quote, the most 12:24:52
important outcome, unquote. We'll stop there 12:24:56
for now. Did I read that correctly? 12:25:01
A. You did, sir. 12:25:02
Q. Do you think a reasonable 12:25:03
scientist could agree with Dr. Guyatt's 12:25:15
concerns expressed in that sentence? 12:25:19
A. So I think that part of the 12:25:22
difficulty, sir, is knowing what Dr. Guyatt's 12:25:26
concerns are or are not in that this is not an 12:25:30
article that is published by Dr. Guyatt. This 12:25:34
is a newspaper. It is a news article in which 12:25:38
a reporter is characterizing statements by 12:25:42
Dr. Guyatt and, in part, selectively quoting 12:25:46
him and running partial quotes into a sentence. 12:25:52
So it's difficult for me to know what 12:25:56
Dr. Guyatt's concerns are or are not because of 12:26:00
the nature of this material, sir. 12:26:04
Q. Have you ever -- have you seen 12:26:05
anything, any medium in which Dr. Guyatt 12:26:09
disagreed with the way that he was 12:26:12
characterized in this piece? 12:26:15
A. I don't, but I would imagine that 12:26:17
there are many people who believe that they 12:26:26

Page 132

have been mischaracterized in news reports who 12:26:29
don't publicly affirm their belief. 12:26:33
Q. Other than your general view that 12:26:39
news reports might mischaracterize someone, do 12:26:41
you have any specific reason to believe that 12:26:44
Dr. Guyatt's comments here were 12:26:47
mischaracterized or taken out of context? 12:26:49
A. I don't have specific reason to 12:26:51
believe that. I am just marking for you, sir, 12:26:56
that a news article is very different than a 12:26:58
peer-reviewed article that Dr. Guyatt has 12:27:02
written on the subject. 12:27:04
Q. Assuming the sentence that I read 12:27:05
you -- well, it doesn't even -- we don't even 12:27:08
have to make that assumption. Could a 12:27:12
reasonable scientist share the concerns 12:27:16
expressed in the sentence that I read you, 12:27:18
regardless of whether they were or were not 12:27:20
expressed by Dr. Guyatt? 12:27:22
A. So the sentence reads that he 12:27:24
found serious problems with the Endocrine 12:27:47
Society guidelines, noting the systematic 12:27:50
reviews didn't look at the effects of 12:27:51
interventions on gender dysphoria itself. The 12:27:53
systematic reviews weren't intended to look at 12:27:59

Page 133

the effect on gender dysphoria. They looked at 12:28:12
other factors. And the study does cite 12:28:14
articles which did look at the effect on gender 12:28:21
dysphoria and other mental health outcomes. 12:28:25
Q. Sorry, my question was could a 12:28:31
reasonable scientist share the concern 12:28:36
expressed in the sentence I read you that the 12:28:39
Endocrine Society didn't look at the effective 12:28:43
interventions on gender dysphoria itself? 12:28:46
A. So, again, sir, it's difficult for 12:28:47
me to answer your question because it's hard 12:28:51
for me to understand the concern that is being 12:28:54
expressed in this sentence. We have discussed 12:28:58
the systematic reviews that were conducted. 12:29:01
The systematic reviews for the guideline 12:29:05
addressed other important outcomes, and the 12:29:09
Endocrine Society guidelines does cite studies 12:29:16
which looked at the effect of interventions on 12:29:19
gender dysphoria. 12:29:21
Q. Could a reasonable scientist be 12:29:24
concerned that they didn't systematically look 12:29:26
at the effect of interventions on gender 12:29:30
dysphoria? 12:29:32
A. That might be a reasonable 12:29:43
concern. 12:29:46

Page 134

Q. All right. Further down the page, 12:29:46
bottom, it says, last partial paragraph. 12:29:50
A. So I'm sorry, page 3 now, sir? 12:29:55
Q. I'm sorry, yes, you're right. We 12:29:58
turned the page. I did not flag that for you. 12:29:59
Page 3, left-hand column, bottom of the page. 12:30:02
For minors, WPATH contends that the evidence is 12:30:06
so limited that, quote, a systematic review 12:30:09
regarding outcomes of treatment in adolescents 12:30:12
is not possible, unquote. But Guyatt counters 12:30:15
that, quote, systematic reviews are always 12:30:17
possible, unquote, even if few or no studies 12:30:19
meet the eligibility criteria. If an entity 12:30:23
has made a recommendation without one, he says, 12:30:27
quote, they would be violating standards of 12:30:30
trustworthy guidelines, end quote. Did I read 12:30:32
that correctly? 12:30:35
A. You did, sir. 12:30:35
Q. Could a reasonable scientist share 12:30:36
the concerns expressed in the portion that I 12:30:38
read? 12:30:43
A. So I take it that the portion that 12:30:43
you read articulates at least two separate 12:30:46
concerns. I would agree with the statement 12:30:52
that a systematic review is always possible if 12:30:57

Page 135

the -- even if the results of that systematic 12:31:01
review identified few, if any -- the language 12:31:04
here is few, if no, studies. The additional 12:31:09
concern that is expressed is if an entity has 12:31:13
made a recommendation without one, and I take 12:31:17
it a systematic review, they would be violating 12:31:20
the standards of the trustworthy guidelines. 12:31:23
And I would say that given the 12:31:26
practical limitations of being able to do a 12:31:30
systematic review for every single 12:31:34
recommendation in the guideline that a 12:31:36
guideline might be -- still be trustworthy and 12:31:40
important in relevant ways without having 12:31:46
conducted a systematic review for every single 12:31:48
recommendation that it makes. 12:31:52
Q. Would you agree that the 12:31:58
importance of conducting a systematic review 12:31:59
turns at least in part on the importance of the 12:32:02
outcome to be reviewed? 12:32:06
MR. CHEEK: Objection, form. 12:32:10
THE WITNESS: Just so I understand 12:32:17
your question, can you rephrase it? 12:32:18
BY MR. FRAMPTON: 12:32:20
Q. Absolutely. So, for example -- if 12:32:21
I am understanding your comment correctly, for 12:32:27

Page 136

example, if a -- if a guideline committee 12:32:29
decided to forego doing a systematic review on 12:32:36
a relatively unimportant outcome, presumably, 12:32:43
that would be more acceptable than neglecting a 12:32:47
systematic review on a critically important 12:32:51
outcome, correct? 12:32:53
MR. CHEEK: Objection, form. 12:32:54
THE WITNESS: So the relative 12:33:01
importance of an outcome might be one of multiple 12:33:03
factors that was taken in consideration in 12:33:06
prioritizing potential systematic reviews in 12:33:12
preparation for writing the guideline. 12:33:16
BY MR. FRAMPTON: 12:33:16
Q. It's something that should be 12:33:16
taken into consideration, right? 12:33:17
A. I believe that I said that it was 12:33:19
one of the -- one of the factors that should be 12:33:21
considered. 12:33:24
Q. There are systematic reviews out 12:33:24
there on the efficacy of puberty suppression 12:33:51
and cross-sex hormones on psychosocial outcomes 12:33:57
in adolescents, are there not? 12:34:00
MR. CHEEK: Objection, form. 12:34:02
THE WITNESS: There are systematic 12:34:04
reviews of those topics. 12:34:05

Page 137

BY MR. FRAMPTON: 12:34:06
Q. Since 2017, correct? 12:34:15
A. And there may be systematic 12:34:15
reviews predating 2017. One of the factors 12:34:22
that goes into whether you would perform a 12:34:27
systematic review might be a consideration as 12:34:30
to whether or not you think that there is 12:34:33
significant evidence of which you are already 12:34:35
not aware. 12:34:38
Q. The systematic reviews on 12:34:38
psychosocial outcomes of puberty suppression or 12:34:47
cross-sex hormones in adolescents that you can 12:34:51
think of post date 2017, do they not? 12:34:53
MR. CHEEK: Objection, form. 12:34:58
THE WITNESS: So I don't recall the 12:35:01
publication dates of the systematic reviews that I 12:35:02
can think of. So without referring -- 12:35:06
BY MR. FRAMPTON: 12:35:10
Q. Which ones can you think of? 12:35:10
A. So there are the two reviews which 12:35:11
have been performed as part of the Cass Review. 12:35:17
But there is an older systematic review that 12:35:20
was published in Pediatrics, which is 12:35:23
pre-pandemic. And so I don't recall from the 12:35:29
top of my head whether that was published 12:35:33

Page 138

before or after 2017, I apologize. 12:35:36
Q. Is that the Chew article; is that 12:35:38
the lead author? 12:35:43
A. I don't -- 12:35:44
Q. Let's find Chew. 12:35:45
A. I don't recall -- 12:35:47
Q. Let's see if it's the right one. 12:35:47
A. -- the first author of that 12:35:49
systematic review, sir. 12:35:52
Q. Maybe we'll get there, maybe we 12:36:57
won't. All right. Are you aware of any 12:36:59
clinical practice guidelines that recommend 12:37:19
puberty suppression or cross-sex hormones for 12:37:23
treating adolescents with gender dysphoria that 12:37:25
are based on a systematic review of the 12:37:28
efficacy of puberty blockers or cross-sex 12:37:31
hormones? 12:37:33
A. Can you repeat your question just 12:37:34
so I am clear, sir? 12:37:42
Q. I am going to try. Are you aware 12:37:44
of any clinical practice guidelines that 12:37:48
recommend puberty suppression or cross-sex 12:37:51
hormones for adolescents with gender dysphoria 12:37:54
that are based on a systematic review of the 12:37:57
efficacy of either puberty blockers or 12:38:01

Page 139

cross-sex hormones? 12:38:04
A. I am not, sir. Again, though, I 12:38:04
think that that is consistent with clinical 12:38:21
practice guidelines in many other areas in 12:38:22
health care, in medicine, including pediatrics. 12:38:26
Will we be coming back to these, 12:39:09
sir? 12:39:12
Q. We might. We'll come back to at 12:39:12
least some of them. 12:39:15
A. May I set them here? 12:39:16
Q. That's fine. 12:39:17
(Thereupon, Exhibit 21, Congenital 12:39:22
Adrenal Hyperplasia Due to Steroid 21-Hydroxylase 12:39:22
Deficiency: An Endocrine Society Clinical 12:39:22
Practice Guideline, was marked for purposes of 12:39:22
identification.) 12:39:22
BY MR. FRAMPTON: 12:39:22
Q. Handing you what I marked as 12:39:43
Exhibit 21. All right. And this is a document 12:39:44
entitled Congenital Adrenal Hyperplasia Due to 12:39:57
Steroid 21-Hydroxylase Deficiency, An Endocrine 12:40:01
Society Clinical Practice Guideline. I would 12:40:06
never have read this but for you, 12:40:08
Dr. Antommaria. Do you recognize this 12:40:10
document? 12:40:11

Page 140

A. I do, sir. 12:40:11
Q. What is it? 12:40:12
A. As the title suggests, it's a 12:40:14
clinical practice guideline prepared by the 12:40:20
Endocrine Society for a clinical condition 12:40:22
called congenital adrenal hyperplasia. 12:40:27
Q. And is that a condition that you 12:40:29
are responsible for making the initial 12:40:33
diagnosis of? 12:40:38
A. No, sir, it is not. 12:40:38
Q. Is it a condition for which you 12:40:41
are responsible for initiating treatment? 12:40:45
A. No, sir, it is not. 12:40:47
Q. Would those two things generally 12:40:50
be done by an endocrinologist? 12:40:53
A. In clinical settings where an 12:40:55
endocrinologist was available, yes. There may 12:41:06
be clinical settings in which a pediatric 12:41:10
endocrinologist was not available, and someone 12:41:13
else might make that diagnosis and initiate 12:41:16
that treatment. 12:41:21
Q. Tell us -- tell me generally what 12:41:21
the condition is. Describe it for me, please. 12:41:25
A. So it is a condition in which 12:41:30
individuals are lacking a enzyme, that enzyme 12:41:35

Page 141

being 21-Hydroxylase. And as a result, the 12:41:42
individuals produce an excess of I believe 12:41:48
cortisol, sir, which then has a variety of 12:41:53
effects on the individual. 12:41:59
Q. The typical treatment is 12:42:00
corticosteroids; is that correct? 12:42:06
A. It is, sir. 12:42:07
Q. And what happens if it's not 12:42:10
treated? 12:42:14
A. It depends on the type of 12:42:15
congenital adrenal hyperplasia the individual 12:42:21
has. But in the -- what's referred to as the 12:42:24
salt wasting form, individuals potentially can 12:42:28
die as a result of a lack of treatment. 12:42:34
Q. Flip to 4044, if you would. And 12:42:35
just as sort of a backup, clinical practice 12:42:51
guidelines -- 12:42:55
A. Hold on a second, sir. 12:42:55
Q. Yeah. Well, this question 12:42:56
actually doesn't -- 12:42:57
A. No, that's -- 12:42:58
Q. I appreciate you finding it. 12:42:59
Clinical practice guidelines like this will 12:43:01
often have -- they will often address more than 12:43:03
just therapy for the condition, correct? 12:43:07

Page 142

A. Yes, sir. They will address 12:43:10
features such as diagnosis. 12:43:19
Q. Screening, potentially? 12:43:22
A. If screening is relevant to -- 12:43:24
Q. Right. 12:43:32
A. -- the -- to the diagnosis. In 12:43:34
many conditions, screening would be irrelevant. 12:43:35
Q. Right. Look at the section on 12:43:39
4044 entitled Treatment of Classic Congenital 12:43:47
Adrenal Hyperplasia. Do you see that, 4.1 12:43:52
through 4.6? 12:43:56
A. I do, sir. 12:43:57
Q. Are any of those strong 12:43:58
recommendations based on low quality evidence 12:44:02
in that section? 12:44:06
A. All of the recommendations are 12:44:07
based on moderate quality evidence, sir. 12:44:08
Q. Let's look then at the stress 12:44:12
dosing section, 4.7 to 4.11. Again, are all of 12:44:15
those based on at least moderate quality 12:44:27
evidence? 12:44:29
A. No, sir. 12:44:29
Q. Which one did I -- oh, there we 12:44:32
go. Are there any strong recommendations in 12:44:37
favor of pharmacological intervention based on 12:44:44

Page 143

low quality evidence? 12:44:47
A. Can you -- so I am reading the 12:44:48
recommendation that's based on low quality 12:45:08
evidence. Can you repeat your question, sir? 12:45:10
Q. Is there a strong recommendation 12:45:13
in favor of pharmacological intervention based 12:45:15
on low quality evidence? 12:45:18
A. There is a strong recommendation 12:45:20
against pharmacological treatment based on low 12:45:33
quality evidence, sir. 12:45:35
Q. Right. My question was is there a 12:45:36
strong recommendation in favor of 12:45:39
pharmacological intervention based on low 12:45:41
quality evidence? 12:45:43
A. So the answer to your question is 12:45:44
no, sir. But I don't understand the import of 12:46:01
your question, given that within the GRADE 12:46:04
approach, recommendations for and 12:46:08
recommendations against are treated as 12:46:10
symmetric. 12:46:15
Q. In the -- when the GRADE 12:46:16
guidelines go through the situations in which a 12:46:20
strong recommendation may be based on low 12:46:24
quality evidence, is it your testimony that 12:46:27
they are symmetric as to whether the 12:46:31

Page 144

recommendation is for or against intervention, 12:46:33
or do you know? 12:46:35
MR. CHEEK: Objection, form. 12:46:37
THE WITNESS: So as I previously 12:46:42
stated, sir, I don't recall all of those criteria 12:46:43
at this point in time, so I don't know. But I 12:46:51
would say that in general, the GRADE approach 12:46:53
treats strong recommendations for and strong 12:46:57
recommendations against similarly. 12:46:59
BY MR. FRAMPTON: 12:47:03
Q. Look at -- go to the next -- are 12:47:13
you on 4045 now? 12:47:15
A. I am on 4044, sir. 12:47:17
Q. All right, go to 4045. All right. 12:47:19
And I am just going to do one more set of 12:47:21
these. Treatment of Nonclassic Congenital 12:47:23
Adrenal Hyperplasia, 5.1 through 5.6. Any 12:47:26
strong recommendations in favor of 12:47:31
pharmacological intervention based on low 12:47:34
quality evidence? 12:47:36
A. No, sir. But we skipped the 12:47:36
section on monitoring therapy. 12:47:50
Q. Okay. All right, we are going to 12:47:51
move to another document. 12:48:22
(Thereupon, Exhibit 22, Pediatric 12:48:22

Page 145

Obesity - Assessment, Treatment, and Prevention: 12:48:22
An Endocrine Society Clinical Practice Guideline, 12:48:22
was marked for purposes of identification.) 12:48:52
BY MR. FRAMPTON: 12:48:52
Q. I show you what I am marking as 12:48:52
Exhibit 22. It's entitled Pediatric Obesity - 12:48:54
Assessment, Treatment, and Prevention: An 12:48:54
Endocrine Society Clinical Practice Guideline. 12:49:03
Dr. Antommaria, do you recognize this document? 12:49:05
A. I do, sir. 12:49:08
Q. Is this the Endocrine Society's 12:49:09
clinical practice guidelines for pediatric 12:49:12
obesity? 12:49:14
A. It is, sir. 12:49:16
Q. All right, a couple of very quick 12:49:16
things on this document. Go to page 710, 12:49:20
please. 12:49:24
A. Yes, sir. 12:49:24
Q. Do you see in 3.2 a strong 12:49:24
recommendation in favor of -- well, I'll just 12:49:30
read it. We recommend that clinicians 12:49:36
prescribe and support healthy eating habits 12:49:39
such as avoiding the consumption of 12:49:42
calorie-dense, nutrient-poor foods. Did I read 12:49:44
it correctly so far? 12:49:47

Page 146

A. Yes, sir, you did. 12:49:48
Q. And then they also encourage the 12:49:49
consumption of whole fruits rather than fruit 12:49:52
juices; is that correct? 12:49:55
A. Omitting a parenthetical phrase, 12:49:55
yes, sir. 12:50:01
Q. Yeah, I didn't feel like we needed 12:50:01
to read all of the various forms of junk food 12:50:02
there. And that's a strong recommendation 12:50:06
based on low quality evidence, correct? 12:50:08
A. It is, sir. 12:50:09
Q. Can you identify any risks 12:50:10
associated with avoiding the consumption of 12:50:15
calorie-dense, nutrient-poor foods? 12:50:19
A. Sir, I think that many people 12:50:28
derive enjoyment and pleasure from eating 12:50:31
calorie-dense, nutrient-poor foods. 12:50:35
Q. Can you -- can you identify any 12:50:37
medical risks? 12:50:43
A. I think that, unfortunately, 12:50:52
individuals who live in food deserts may have 12:50:56
limited access to other sources of nutrition, 12:51:02
and foregoing alternative sources of nutrition 12:51:06
might result in medical risks, sir. 12:51:11
Q. If they just don't eat; is that 12:51:12

Page 147

what you are saying? 12:51:17
A. Yes, because of lack of access to 12:51:18
alternative forms of food. 12:51:21
Q. Any others? 12:51:23
A. Not that I can think of at this 12:51:28
time, sir. 12:51:30
Q. And you don't imagine a reasonable 12:51:31
pediatrician would ever recommend that a child 12:51:33
not eat rather than eating nutrient-poor foods 12:51:35
that are available to him or her? 12:51:40
MR. CHEEK: Objection, form. 12:51:42
BY MR. FRAMPTON: 12:51:47
Q. Do you? 12:51:47
A. I would think that a reasonable 12:51:47
pediatrician would have other alternatives than 12:51:53
making that recommendation, sir. 12:51:56
Q. Flip one more page. 4.3 is: We 12:51:57
recommend that clinicians prescribe and support 12:52:09
the reduction of inactivity and also a minimum 12:52:10
of 20 minutes of moderate to vigorous physical 12:52:13
activity daily, with a goal of 60 minutes, all 12:52:16
in the context of a calorie controlled diet. 12:52:19
Did I read that correctly? 12:52:22
A. You did, sir. 12:52:23
Q. Do you agree that a normal healthy 12:52:25

Page 148

child can comply with this recommendation with 12:52:28
minimal risk? 12:52:30
A. Depending on the type of moderate 12:52:31
to vigorous physical activity they are 12:52:53
performing and where that is performed, yes. 12:52:55
(Thereupon, Exhibit 23, Part 4: 12:52:55
Pediatric Basic and Advanced Life Support, was 12:52:55
marked for purposes of identification.) 12:53:03
BY MR. FRAMPTON: 12:53:03
Q. I will represent to you what I 12:53:21
have done here. So these are pediatric basic 12:53:22
and advanced life support. Do you recall 12:53:26
citing the document that I am about showing 12:53:28
you? I am about to hand it to you. 12:53:32
A. I cited pediatric and advanced 12:53:34
life support. I don't know that I have cited 12:53:36
what you are about to hand to me until I see 12:53:38
it. 12:53:40
Q. Fair enough, and I'll tell you 12:53:40
what I have done. There was a table in here 12:53:41
that I just had to pull out and print 12:53:43
separately because it wouldn't print within the 12:53:45
document. That's what I have done. 12:53:47
MR. CHEEK: Just for the record, 12:53:52
counsel is attaching that table to the tail end 12:53:54

Page 149

of -- 12:53:54
MR. FRAMPTON: In the back, yeah. 12:53:54
MR. CHEEK: The tail end of the 12:53:54
exhibit, yeah. 12:54:01
BY MR. FRAMPTON: 12:54:01
Q. Handing you what I am marking as 12:54:01
Exhibit 23. Dr. Antommaria, does this appear 12:54:03
to be a set of clinical practice guidelines 12:54:39
published by the American Heart Association on 12:54:41
pediatric basic and advanced life support? 12:54:43
A. It does, sir. 12:54:48
Q. And you recall citing this in your 12:54:49
expert report, right? 12:54:52
A. I do, sir. 12:54:52
Q. And look at the back at this 12:54:53
table. Yeah, you can detach it for now and 12:54:57
just put it back when we finish. The table at 12:55:04
the back is the recommendation and rating 12:55:13
system that they use instead of the GRADE 12:55:16
methodology, correct? 12:55:21
A. Yes, sir. 12:55:21
Q. Okay. And would you agree if you 12:55:22
look on the right-hand column, level quality of 12:55:30
evidence, that level C-LD most closely aligns 12:55:33
to what GRADE would call low quality evidence? 12:55:42

Page 150

A. With certain exceptions, sir. I 12:55:46
don't believe that GRADE includes physiological 12:56:14
and mechanistic studies in human subjects 12:56:20
within its categorization of low quality 12:56:22
evidence. 12:56:24
Q. And on the left-hand side, they 12:56:25
have got a class of recommendation that's 12:56:26
called a strong recommendation, correct? 12:56:28
A. They have two classes of 12:56:30
recommendations that are called strong 12:56:35
recommendations, sir. 12:56:38
Q. I am seeing strong and moderate. 12:56:39
What am I missing? 12:56:44
A. So Class I is strong. And Class 12:56:45
III, the Roman numeral III at the bottom of 12:56:49
column one, is also a strong recommendation. 12:56:52
Q. Oh, okay. And one -- Class I is 12:56:53
strongly recommend that the benefit is greater 12:57:02
than the risk. Class III is strong that the 12:57:04
risk is greater than the benefit, correct? 12:57:07
A. Yes. In the GRADE 12:57:09
recommendations, there are strong 12:57:13
recommendations for and against, as we 12:57:15
previously discussed. And I would take these 12:57:19
to be strong recommendations for and against. 12:57:21

Page 151

Q. Okay. These clinical practice 12:57:23
guidelines are for dealing with pediatric 12:57:29
cardiac arrest, correct? 12:57:31
A. That's the core issue, sir. 12:57:37
Q. Yeah. That's a medical emergency, 12:57:40
is it not? 12:57:43
A. Yes, sir. 12:57:43
Q. Okay. Left untreated, what's the 12:57:46
mortality rate? 12:57:50
A. Of someone in full arrest? 12:57:51
Q. Yes, sir. 12:57:56
A. Exceptionally high, sir. 12:57:58
Q. Approaching a hundred percent? 12:58:00
A. Not a hundred percent, but 12:58:02
exceptionally close to a hundred percent. 12:58:05
Q. Got it. So as a general matter, 12:58:06
medical intervention is required to avoid 12:58:09
imminent death, right? 12:58:11
A. Some intervention, including 12:58:15
bystander CPR, is necessary to prevent that, 12:58:20
yes. 12:58:22
Q. Okay. Go to page 9 of the 12:58:22
document. 12:58:27
A. Yes, sir. 12:58:42
Q. All right. So we have got a -- in 12:58:43

Page 152

5.1, we have got lay rescuers should begin CPR 12:58:44
for any victim who is unresponsive, not 12:58:48
breathing normally, and does not have signs of 12:58:51
life; do not check for a pulse. Did I read 12:58:53
that correctly? 12:58:56
A. That is the first recommendation, 12:58:57
sir. 12:59:01
Q. And that's a strong 12:59:01
recommendation, correct? 12:59:03
A. Yes, sir. 12:59:03
MR. CHEEK: I just want to make clear 12:59:07
for the record, we are also looking at the table 12:59:09
as opposed to the recommendation-specific 12:59:11
supportive text below. 12:59:15
MR. FRAMPTON: Sure. 12:59:16
BY MR. FRAMPTON: 12:59:17
Q. And the level of evidence is 12:59:17
classified as C-LD, correct? 12:59:19
A. That is correct, sir. 12:59:22
Q. And if you look at the specific 12:59:28
supportive text, that's based on evidence that 12:59:29
lay rescuers are not able to reliably determine 12:59:32
if people have a pulse, right? 12:59:35
A. I would need to read the text to 12:59:36
confirm that, sir. Would you like me to? 12:59:39

Page 153

Q. Actually, no. In the absence 12:59:46
of -- if you don't have medical equipment 12:59:52
readily available, would you agree that CPR is 12:59:58
the only intervention known to decrease 13:00:00
mortality for someone who is in cardiac arrest? 13:00:02
A. Can you repeat your question, sir? 13:00:06
Q. Sure. If there is no medical 13:00:14
equipment readily available, would you agree 13:00:18
that CPR is the only intervention known to 13:00:21
decrease mortality in someone with cardiac 13:00:25
arrest? 13:00:27
A. I am having difficulty with your 13:00:27
formulation of your question because I don't 13:00:40
quite understand how not having medical 13:00:43
equipment available relates to performing CPR 13:00:47
in that there are components of CPR that can be 13:00:55
performed without medical equipment and 13:00:59
components of CPR that require medical 13:01:01
equipment. So I am just having trouble 13:01:03
understanding the formulation of your question, 13:01:04
sir. 13:01:09
Q. What medical equipment do you need 13:01:09
to perform CPR? 13:01:11
A. So CPR is a very broad term. 13:01:13
There are different forms of CPR. Potentially, 13:01:19

performing CPR entails establishing a reliable airway, which might include intubation. And so, again, as a doctor and you being a lawyer, there's reasons why I am having trouble understanding your question because of -- it's conflating things that I wouldn't necessarily --

Q. Let me try again.

A. Please.

Q. For a lay rescuer, is there anything they can do for someone in cardiac arrest that increases mortality other than CPR?

MR. CHEEK: Objection, form.

BY MR. FRAMPTON:

Q. I'm sorry, that decreases mortality.

A. That decreases mortality. So it's not my intention to be pedantic, sir. But yes, they could activate 9-1-1 if they didn't know how to perform CPR or alert other individuals who might know how to perform CPR in order to decrease mortality.

Q. Anything else?

A. That would be the primary alternative, sir.

Q. Is that all you can think of sitting here today?

A. That are aside from performing CPR that a lay bystander could do to decrease mortality in somebody with cardiac arrest, sir?

Q. Yes. You said call 9-1-1, perform CPR, or alert someone who can perform CPR. Anything else?

A. I think that sitting here today, those would be the primary options that I would think of, sir.

Q. You cited in your expert report the three non-gender dysphoria systematic reviews that we have just looked at, correct?

A. Can you repeat that, sir?

Q. Sure. I am just -- you -- we have just now looked at three clinical practice guidelines that you cited in your expert report, correct?

A. Yes, I cite each of these clinical practice guidelines in my expert report.

Q. And how did you select those to cite?

A. I selected the two other Endocrine Society guidelines because they are two -- the

only other Endocrine Society guidelines that are specific to the pediatric population. And I picked CPR as a important non-Endocrine Society guideline.

Q. Okay. Why CPR?

A. Because of its view of its potential importance and it being potentially salient to nonphysician readers in a way that congenital adrenal -- I'm sorry, CAH would not be salient.

Q. Did you look at any clinical practice guidelines in trying to decide which ones to include that you did not end up citing in your report?

A. No, sir; I did not.

Q. You just picked out these three?

A. Yes.

MR. FRAMPTON: I think we can break for lunch.

(Lunch recess taken.)

MR. FRAMPTON: Let's go on the record.

(Thereupon, Exhibit 24, Hormonal Treatment in Young People With Gender Dysphoria: A Systematic Review, was marked for purposes of

identification.)

BY MR. FRAMPTON:

Q. Doctor, I am handing you what I marked as Exhibit 24, which is titled Hormonal Treatment in Young People With Gender Dysphoria, a Systematic Review. Lead author, Denise Chew, published in Pediatrics in 2018. And my question as you look at it is simply going to be is that the systematic review that you believe you were referencing in your testimony this morning that you believed you had seen?

A. Yes, sir. You could appreciate distinguishing 2017 and 2018.

Q. Obviously. No, I just -- why we wanted to show it to you, all right. Tell me if I am correctly stating -- well, let me back up and lay a foundation. You are familiar with the principle of clinical equipoise, correct?

A. I am, sir.

Q. Tell me if I am stating it correctly, the idea being that there is clinical equipoise when there is genuine uncertainty within the community of experts as to which arm of a trial is more beneficial.

Page 158

A. That's a reasonable summary, sir. 13:42:00
(Thereupon, Exhibit 25, Consensus 13:42:37
Parameter: Research Methodologies to Evaluate 13:42:37
Neurodevelopmental Effects of Pubertal Suppression 13:42:37
in Transgender Youth, was marked for purposes of 13:42:37
identification.) 13:42:37
BY MR. FRAMPTON: 13:42:37
Q. Dr. Antommaria, I am handing you 13:42:37
what I have marked as Exhibit 25. It is titled 13:42:38
Consensus Parameter: Research Methodologies to 13:42:43
Evaluate Neurodevelopmental Effects of Pubertal 13:42:45
Suppression in Transgender Youth. The lead 13:42:50
author, Diane Chen. And, Dr. Antommaria, is 13:42:51
this a paper that you are familiar with? 13:43:04
A. One minute, sir. 13:43:06
Q. I don't think you cited it in your 13:43:18
expert report. I am just curious if you are 13:43:21
familiar with it. 13:43:24
A. It is not an article with which I 13:43:25
am familiar, sir. 13:43:28
Q. That's fine. You can put it aside 13:43:30
then. Do you believe -- do you believe it 13:43:32
would be ethical to conduct a cohort study in 13:43:45
which you are comparing -- again, cohort study, 13:43:50
not RCT, cohort study in which you are 13:43:54

Page 159

comparing adolescents receiving cross-sex 13:43:58
hormones to transgender adolescents who for 13:44:02
whatever reason are not receiving cross-sex 13:44:04
hormones? 13:44:07
A. So whether a study is ethical 13:44:07
relies on a variety of different factors. In 13:44:27
part, it would rely on the importance of the 13:44:31
question and what the participants were 13:44:36
anticipated to do. So in your general 13:44:41
description, it's hard to know what the 13:44:45
relevant outcome is. 13:44:46
And the way in which individuals 13:44:49
who are and are not receiving treatment might 13:44:52
differ from one another. So if there were 13:44:59
greater specificity provided about a variety of 13:45:05
different factors, that might potentially be 13:45:10
ethical. But it's hard to answer your question 13:45:12
at the level of abstraction that you have posed 13:45:14
it. 13:45:17
Q. You can't say sitting here today 13:45:17
that it would unequivocally be unethical? 13:45:19
MR. CHEEK: Objection, form. 13:45:24
THE WITNESS: No, sir, I could not. 13:45:29
BY MR. FRAMPTON: 13:45:30
Q. And the same thing, a cohort study 13:45:30

Page 160

comparing transgender youth who did not take 13:45:33
puberty-suppressing medication to transgender 13:45:36
youth who do take puberty-suppressing 13:45:40
medication, can you say unequivocally sitting 13:45:43
here today such a study would be unethical? 13:45:45
A. No, sir, I cannot. 13:45:48
(Thereupon, Exhibit 26, Evidence 13:46:04
Review: Gonadotropin Releasing Hormone Analogues 13:46:04
for Children and Adolescents With Gender 13:46:04
Dysphoria, was marked for purposes of 13:46:04
identification.) 13:46:05
BY MR. FRAMPTON: 13:46:05
Q. We are going to go across the 13:46:11
Atlantic. Not physically, unfortunately, that 13:46:12
would be more fun, but in our minds. I hand 13:46:15
you what I am marking as Exhibit 26, a document 13:46:24
entitled Evidence Review: Gonadotropin 13:46:33
Releasing Hormone Analogues For Children and 13:46:38
Adolescents With Gender Dysphoria, prepared by 13:46:39
NICE in October of 2020. Dr. Antommaria, are 13:46:42
you familiar with that document? 13:46:55
A. I am, sir. 13:46:56
Q. Do you understand it to be a 13:46:56
systematic review conducted by NICE on puberty 13:46:59
suppression for children and adolescents with 13:47:03

Page 161

gender dysphoria? 13:47:05
A. Yes, sir. 13:47:06
Q. Just as a general matter, I am 13:47:15
presuming you don't view the British medical 13:47:17
establishment as less technically sophisticated 13:47:20
than the medical establishment in the United 13:47:22
States, or do you? 13:47:24
A. That high level of abstraction, 13:47:25
no, sir, I don't consider them less 13:47:32
sophisticated. 13:47:34
Q. And in the community of medical 13:47:35
experts on gender dysphoria, you regularly 13:47:38
review and rely upon studies conducted in 13:47:46
Europe, do you not? 13:47:49
MR. CHEEK: Objection, form. 13:47:51
THE WITNESS: Can you repeat the 13:47:58
question just so I answer it correctly? 13:47:58
BY MR. FRAMPTON: 13:48:00
Q. Sure. In the community of medical 13:48:00
experts who deal with gender dysphoria, would 13:48:02
you agree that you regularly review and rely 13:48:07
upon studies conducted in Europe? 13:48:10
A. I think that's a fair 13:48:13
characterization, sir. 13:48:17
Q. Sure. Go to page 14 of this 13:48:17

document, if you would. 13:48:25
A. I am on page 14, sir. 13:48:34
Q. Thank you. All right. They have 13:48:35
got under review process -- well, let me just 13:48:42
ask you this: Have you undertaken a close 13:48:51
review of the search methodology that the 13:48:53
authors of this systematic review undertook? 13:48:57
A. Again, I apologize for asking. 13:49:01
Can you repeat the question? 13:49:10
Q. Sure. Have you undertaken a close 13:49:11
review of the search methodology employed by 13:49:12
the authors of this systematic review? 13:49:14
A. And search methodology, meaning 13:49:16
the specific search strategies -- 13:49:24
Q. Yes. 13:49:28
A. -- that were implemented in the 13:49:29
various databases that they searched? 13:49:31
Q. Yes, sir. 13:49:33
A. No, I have not, sir. 13:49:34
Q. So sitting here today, you don't 13:49:35
have any criticisms of that process? 13:49:37
A. As I have said, I haven't reviewed 13:49:45
it, so I don't currently have any criticisms. 13:49:46
Q. Let's look at the review 13:49:49
questions. We are still on page 14. Review 13:49:57

question 1: For children and adolescents with 13:50:01
gender dysphoria, what is the clinical 13:50:04
effectiveness of treatment with GnRH analogs 13:50:07
compared with one or a combination of 13:50:12
psychological support, social transitioning to 13:50:15
the desired gender, or no intervention. Did I 13:50:18
read that correctly? 13:50:21
A. You did, sir. 13:50:21
Q. Do you agree that's an important 13:50:22
question for a systematic review to look at? 13:50:26
A. So it's been awhile since I have 13:50:28
looked at this report, sir. It's unclear how 13:50:37
they are distinguishing children and 13:50:40
adolescents. Given that GnRH analogs are only 13:50:43
used in individuals who are adolescents, I 13:50:48
don't quite understand the children and 13:50:55
component of the question. But in terms of the 13:50:57
remainder of the question, yes, I think that 13:51:00
that's an important question, sir. 13:51:11
Q. Question 2 is: For children and 13:51:12
adolescents with gender dysphoria, what is the 13:51:17
short-term and long-term safety of GnRH analogs 13:51:21
compared with one or a combination of 13:51:24
psychological support, social transitioning to 13:51:25
the desired gender, or no intervention. And 13:51:28

putting aside your concern about what they mean 13:51:30
by children, do you agree that is also an 13:51:33
important question? 13:51:36
A. Yes, also evaluating the safety as 13:51:36
well as the efficacy is important. 13:51:41
Q. Looking on page 15, so one more 13:51:43
page. Would you agree that in Table 1, they 13:51:54
appear at least to have provided a summary of 13:52:00
all of the included studies? 13:52:09
A. That is the title of the table, 13:52:14
sir. 13:52:27
Q. And you don't have any reason to 13:52:27
doubt that they did that, correct? 13:52:30
A. I do not, sir. 13:52:31
Q. Let's go to page 4. 13:52:32
A. I'm sorry, page number what? 13:52:41
Q. 4, sorry. I let my voice drop. 13:52:42
A. I am on page 4, sir. 13:52:50
Q. Would you agree that on page 4, 13:52:51
they have identified the critical outcomes that 13:52:59
they have examined in this systematic review? 13:53:07
A. So, sir, on page 4, I see the 13:53:10
first question about clinical effectiveness. I 13:53:18
see that they are providing greater specificity 13:53:24
as to which aspects of clinical effectiveness 13:53:29

they considered and that they appear to be 13:53:35
distinguishing critical and important outcomes. 13:53:41
Q. And they then provide the studies 13:53:51
that they were able to identify and examine for 13:53:54
each of those outcomes, correct? 13:53:57
A. Yes, sir. 13:53:59
Q. Go to page 76, if you would. 13:54:06
A. I am on page 76, sir. 13:54:41
Q. And on page 76, Appendix E, which 13:54:43
is a set of evidence tables further discussing 13:54:46
the included studies, correct? 13:54:49
A. That's what it appears to be, sir. 13:54:51
Q. Are you familiar with the 13:55:08
Newcastle-Ottawa tool for cohort studies? 13:55:10
A. Not at a high level of detail, 13:55:14
sir. 13:55:23
Q. Well, do you have any 13:55:23
understanding of what that is? 13:55:24
A. It appears to be a tool that they 13:55:25
are utilizing to appraise the quality of the 13:55:29
evidence that appears to offer domains that are 13:55:32
not identical with the domains utilized by the 13:55:40
GRADE approach, sir. 13:55:45
Q. Okay. Have you studied what the 13:55:46
Newcastle-Ottawa tool is? 13:55:54

Page 166

A. No, sir, I have not. 13:55:58
Q. Do you recognize it as a tool that 13:56:00
is sometimes cited in the literature? 13:56:05
A. I do, sir. 13:56:06
Q. And then if we -- go to page 99, 13:56:07
if you would. 13:56:14
A. I am on page 99, sir. 13:56:21
Q. All right. And here, they have 13:56:22
given us GRADE profiles for the various studies 13:56:24
included, correct? 13:56:30
A. So, again, sir, I haven't looked 13:56:32
at this recently. It's in a different format 13:56:52
in terms of, like, Table 2 only includes a 13:56:58
single study instead of all of the studies, 13:57:02
sir. 13:57:06
Q. Well, do you know how many studies 13:57:06
they identified as included for that particular 13:57:11
question? 13:57:15
A. No, sir, I don't. I am just -- in 13:57:15
looking at this briefly at this time, I am just 13:57:26
noting that the format of the table is 13:57:29
significantly different than the evidence 13:57:34
tables presented in Appendix E. 13:57:37
Q. Right. But in Appendix G, they 13:57:41
have given an evaluation of risk of bias, 13:57:52

Page 167

indirectness, inconsistency, and imprecision 13:57:57
for each of the studies, correct? 13:58:00
A. They do, sir. There would be a 13:58:01
fifth category, if I recall correctly. And 13:58:17
it's not clear to me, again, not having 13:58:21
reviewed this recently why that fifth category 13:58:26
isn't included. 13:58:29
Q. Right. We don't see publication 13:58:29
bias, correct? 13:58:31
A. I would have to double-check and 13:58:31
see which one is the one that is omitted. 13:58:33
Q. And then they provide a certainty 13:58:36
rating, correct? 13:58:40
A. They do, sir. 13:58:40
Q. So they are telling you, for 13:58:48
example, in Table 2, study one, they are 13:58:59
telling you that this study -- this is a cohort 13:59:03
study, and it was downgraded one level because 13:59:08
of high risk of bias, correct? Is that what 13:59:13
they are reflecting here? 13:59:18
A. So, again, sir, it's been awhile 13:59:19
since I have looked at this. I am unclear as 13:59:24
to why they are listing a certainty category as 13:59:26
opposed to a grade of efficacy category. And 13:59:31
you represented this as having been downgraded 13:59:34

Page 168

a level, but I don't -- you know, I don't 13:59:43
necessarily see a comprehensive list of 13:59:47
upgrades and downgrades and the specific reason 13:59:49
listed. So it would take me more time to 13:59:54
refamiliarize myself with the table. 13:59:58
Q. Footnote 2 does say downgraded one 13:59:59
level. The cohort study by de Vries, et al., 14:00:04
2011, was assessed as at high risk of bias, 14:00:08
poor quality overall, lack of blinding, and no 14:00:10
control group, correct? 14:00:13
A. Yes, sir. 14:00:16
Q. Okay. And if you downgraded an 14:00:16
observational -- let me back up. Observational 14:00:21
studies start out at low quality under the 14:00:24
GRADE methodology, right? 14:00:27
A. Yes, that's the initial category 14:00:28
to which they are assigned. 14:00:32
Q. And if it was downgraded one 14:00:32
level, that would take it to very low, correct? 14:00:34
A. Correct. 14:00:36
Q. And that appears to be what they 14:00:37
are reflecting in this table of the de Vries 14:00:40
study, correct? 14:00:47
A. Oh, and as I said, I am just 14:00:47
unclear as to why the far right column is 14:00:51

Page 169

labeled as certainty as opposed to grade of the 14:00:53
evidence. 14:00:56
Q. All right. Go to page 74. 14:00:56
A. Yes, sir. 14:01:21
Q. This appears to be a table of 14:01:21
excluded studies; is that correct? 14:01:24
A. Yes, sir. 14:01:26
Q. So they have listed the 14:01:29
potentially relevant studies that they 14:01:32
excluded, and then they have given reasons for 14:01:35
the exclusion, right? 14:01:37
A. One moment, sir. 14:01:38
Q. Sure. 14:01:42
A. So these appear to be the studies 14:01:57
that pass the level of screening for titles and 14:01:59
abstracts but were excluded at the level of 14:02:05
reviewing the full article, and they have 14:02:07
listed them, these 16 articles and the reasons 14:02:12
for exclusion. 14:02:15
Q. And that's good practice if you 14:02:16
are doing a systematic review, is it not? 14:02:17
A. Yes, sir. 14:02:19
Q. That way, if you are a researcher 14:02:21
in the field and you think, well, why didn't 14:02:26
they include X, Y, or Z study, you know you can 14:02:29

Page 170

look at this table and have some idea as to 14:02:33
what their reasons were, correct? 14:02:35
A. Correct, sir. 14:02:37
Q. All right. Let's flip back to 14:02:37
page 4. 14:02:40
A. I am on page 4, sir. 14:02:47
Q. Thank you. Directly under 14:02:48
critical outcomes, it says: The critical 14:02:49
outcomes for decision making are the impact on 14:02:53
gender dysphoria, mental health, and quality of 14:02:56
life. The quality of evidence for these 14:02:58
outcomes was assessed as very low certainty 14:03:01
using modified GRADE. Did I read that 14:03:04
correctly? 14:03:06
A. You did, sir. 14:03:07
Q. So they do claim to be using some 14:03:07
form of the GRADE methodology, correct? 14:03:11
A. Yes, sir. 14:03:13
Q. And have you done any research on 14:03:14
NICE to understand how that particular 14:03:18
organization might modify the GRADE 14:03:21
methodology? 14:03:26
A. So, sir, I am not sure whether the 14:03:26
reference to modify GRADE is a modification 14:03:32
that NICE made or it is one of the various 14:03:35

Page 171

updated versions of the GRADE methodology. 14:03:39
Q. Fair enough. That assessment of 14:03:41
very low certainty would appear to match up 14:04:06
with that GRADE evidence table we looked at, 14:04:12
correct, where they called it certainty? 14:04:15
A. It would appear to, sir. 14:04:17
Q. Okay. You don't have any 14:04:18
criticisms of the thoroughness of the NICE 14:04:25
review that we are looking at right now, do 14:04:29
you? 14:04:31
A. Not at this time, sir. 14:04:31
(Thereupon, Exhibit 27, Evidence 14:04:31
Review: Gender-Affirming Hormones For Children and 14:04:31
Adolescents With Gender Dysphoria, was marked for 14:04:31
purposes of identification.) 14:05:00
BY MR. FRAMPTON: 14:05:00
Q. Dr. Antommaria, I am going to hand 14:05:00
you what I am marking as Exhibit 27, which is 14:05:01
titled Evidence Review: Gender-Affirming 14:05:07
Hormones For Children and Adolescents With 14:05:10
Gender Dysphoria. Dr. Antommaria, do you 14:05:12
recognize this as the other NICE 2020 14:05:17
systematic review of evidence? 14:05:22
A. Yes, sir. 14:05:24
Q. And you have reviewed this before, 14:05:26

Page 172

right? 14:05:28
A. I have, sir. 14:05:28
Q. And similar to the last one we 14:05:29
looked at, you don't have any criticisms of 14:05:36
their search strategy or methodology in 14:05:40
conducting this systematic review, do you? 14:05:43
A. Not at this time, sir. 14:05:45
Q. Okay. Let's go to page 14. So 14:05:46
review question 1: For children and 14:06:07
adolescents with gender dysphoria, what is the 14:06:12
clinical effectiveness -- 14:06:14
A. I'm sorry. 14:06:15
Q. I am in the -- are we in the wrong 14:06:16
place? I'm sorry. 14:06:19
A. I am on page 14. I don't see 14:06:20
review questions. 14:06:21
Q. I think it's at the very bottom. 14:06:22
A. Oh, thank you so much. 14:06:25
Q. No worries. It's cut off, which 14:06:26
makes it a little bit more difficult. All 14:06:29
right. So No. 1: For children and adolescents 14:06:31
with gender dysphoria, what is the clinical 14:06:35
effectiveness of treatment with 14:06:38
gender-affirming hormones compared with one or 14:06:41
a combination of psychological support, social 14:06:44

Page 173

transitioning to the desired gender, or no 14:06:47
intervention. And, Dr. Antommaria, presumably 14:06:51
putting aside again your concern about how they 14:06:55
are using the word children, do you agree this 14:06:58
is an important question? 14:07:02
A. I do, sir. 14:07:02
Q. No. 2: For children and 14:07:03
adolescents with gender dysphoria, what is the 14:07:08
short-term and long-term safety of 14:07:09
gender-affirming hormones compared with one or 14:07:12
a combination of psychological support, social 14:07:14
transitioning to the desired gender, or no 14:07:17
intervention. Did I read that correctly? 14:07:20
A. You did, sir. 14:07:22
Q. And putting aside your concern 14:07:23
about how they are using the word children, you 14:07:25
agree this is also an important question, 14:07:28
correct? 14:07:30
A. I do, sir. 14:07:30
Q. Let's go to page 70, please. 14:07:33
A. Seven zero, sir? 14:07:43
Q. Seven zero, yes. 14:07:45
A. I am on page 70, sir. 14:07:54
Q. And this one also has a list of 14:07:55
excluded studies; is that correct? 14:07:57

Page 174

A. It does, sir. 14:07:59
Q. Okay. And on page 72, does it 14:07:59
appear that one of the excluded studies is the 14:08:13
de Vries 2014 study in Pediatrics? 14:08:18
A. It does, sir. 14:08:23
Q. Okay. And they have provided the 14:08:26
reasons why they excluded that study, correct? 14:08:28
A. I am just reading the reasons, 14:08:30
sir. 14:08:42
Q. Sure. 14:08:42
A. Yes, they provide reasons for 14:08:42
excluding the study, sir. 14:08:45
Q. And that was the study the 14:08:46
Endocrine Society cited to support its 14:08:51
recommendation for the use of cross-sex 14:08:58
hormones, correct? 14:09:00
A. It was one of the studies, sir. 14:09:01
Q. And the other was an NHS document; 14:09:05
is that right? 14:09:09
A. For that single sentence, yes. 14:09:09
Q. Go to page 4, please. 14:09:22
MR. CHEEK: Which page? 14:09:32
MR. FRAMPTON: 4. Sorry, I let my 14:09:33
voice drop again. 14:09:35
THE WITNESS: I am on page 4, sir. 14:09:37

Page 175

BY MR. FRAMPTON: 14:09:38
Q. All right. And it looks like in 14:09:38
this review as well they have identified their 14:09:44
critical outcomes and listed the studies that 14:09:49
were relevant to each of their critical 14:09:52
outcomes, correct? 14:09:54
A. Yes, sir. 14:09:54
Q. And you have not reviewed these to 14:10:06
determine whether you agree that they picked 14:10:09
out the most pertinent studies for each 14:10:11
outcome, have you? 14:10:14
A. I have not reviewed it for that 14:10:14
purpose, sir. 14:10:18
Q. And would the same be true for the 14:10:49
studies listed for the important outcomes? 14:10:51
A. Would the same what be true, sir? 14:10:55
Q. Let me just ask it again. With 14:11:00
respect to the studies they have listed 14:11:01
concerning what they have identified as 14:11:03
important outcomes, you have not gone and 14:11:05
determined if you agree or disagree with their 14:11:08
list of included studies? 14:11:11
A. No, sir, I haven't had to a reason 14:11:15
to do that. 14:11:17
Q. Got it. 14:11:17

Page 176

(Pause in proceedings.) 14:11:17
MR. FRAMPTON: All right. Let's go 14:15:27
back on the record. 14:15:27
BY MR. FRAMPTON: 14:15:27
Q. All right. Dr. Antommaria, would 14:15:27
you go to page 6, please? 14:15:27
A. I am on page 6, sir. 14:15:27
Q. Great. At the top of that page, 14:15:27
do you see a discussion of a study by Kuper, et 14:15:27
al., published in 2020? 14:15:27
A. Yes, sir. 14:15:27
Q. Is that a study you are familiar 14:15:27
with? 14:15:28
A. Sir, do you know where the full 14:15:28
reference to that article is? 14:15:28
Q. Yeah. Go to the very last page, 14:15:28
it's at the top. 14:15:28
A. I would need to look at the 14:15:28
article itself. 14:15:28
(Thereupon, Exhibit 28, Body 14:15:40
Dissatisfaction and Mental Health Outcomes of 14:15:40
Youth on Gender-Affirming Hormone Therapy, was 14:15:40
marked for purposes of identification.) 14:15:52
BY MR. FRAMPTON: 14:15:52
Q. I hand you what I am marking as 14:15:56

Page 177

Exhibit 28. It's a study entitled 14:15:57
Testicular -- wait a minute, that's the wrong 14:16:03
one. What did I hand you? 14:16:08
A. You handed me the Kuper study, 14:16:10
sir. 14:16:12
Q. That's what I meant to hand you. 14:16:12
I was looking at the wrong tab. All right. I 14:16:13
handed you a study called Body Dissatisfaction 14:16:16
and Mental Health Outcomes of Youth on 14:16:18
Gender-Affirming Hormone Therapy, correct? 14:16:21
A. You did, sir. 14:16:22
Q. All right. It appears to be 14:16:24
the -- you are calling -- do we pronounce her 14:16:30
name Kuper? Is that your understanding, or do 14:16:35
you know? 14:16:38
A. I don't know, sir. 14:16:38
Q. All right. In any event -- 14:16:39
A. I am happy to refer to it as the 14:16:44
Kuper study, sir. 14:16:46
Q. I don't know, either, so we will 14:16:47
do our best. The question was this is the 14:16:48
study that we just looked at that was cited in 14:16:51
the NICE review on cross-sex hormone therapy, 14:16:54
correct? 14:17:00
A. Yes, on gender-affirming hormone 14:17:00

Page 178

therapy. 14:17:04
Q. Yes, okay. You asked to see the 14:17:04
whole thing. Is this a study that you are 14:17:08
familiar with? 14:17:10
A. I may have seen it in the past. I 14:17:10
am not particularly familiar with it, sir. 14:17:14
Q. All right. We won't mess with it 14:17:16
then, that's fine. Put it aside. All right. 14:17:18
Go back to the NICE review, the 14:17:32
Gender-Affirming Hormones For Children and 14:17:37
Adolescents With Gender Dysphoria. 14:17:40
MR. CHEEK: So you are referring to 14:17:42
Defendants' Exhibit 27? 14:17:44
MR. FRAMPTON: Yes. 14:17:46
MR. CHEEK: Thank you. 14:17:47
BY MR. FRAMPTON: 14:17:48
Q. Go to page 13, if you would. I 14:17:59
don't know if I already told you that or not. 14:18:02
A. I am on page 13, sir. 14:18:08
Q. Great. The second paragraph under 14:18:10
discussion: All the studies included in the 14:18:12
evidence review are uncontrolled observational 14:18:15
studies which are subject to bias and 14:18:18
confounding and were a very low certainty using 14:18:21
modified GRADE. A fundamental limitation of 14:18:23

Page 179

all the controlled studies included in this 14:18:26
review is that any changes in scores from 14:18:28
baseline to follow-up could be attributed to a 14:18:30
regression to the mean. Did I read that 14:18:33
correctly? 14:18:37
A. Yes, you did, sir. 14:18:37
Q. Do you agree that a reasonable 14:18:40
scientist could share that concern about the 14:18:41
uncontrolled observational studies? 14:18:47
A. That is a possible explanation for 14:18:49
the results, sir. 14:18:54
Q. Go to page 14. I'm sorry, let's 14:18:55
go to 13 again. I was wrong. Let's just read 14:19:29
the next paragraph there. The included studies 14:19:33
have relatively short follow-up, with an 14:19:37
average duration of treatment with 14:19:39
gender-affirming hormones between around 1 year 14:19:40
and 5.8 years. Further studies with a longer 14:19:43
follow-up are needed to determine the long-term 14:19:47
effect of gender-affirming hormones for 14:19:50
children and adolescents with gender dysphoria. 14:19:52
Did I read that correctly? 14:19:56
A. You did, sir. 14:19:57
Q. Do you agree that some of the 14:19:58
risks associated with these hormonal 14:20:02

Page 180

interventions are more long-term risks, risks 14:20:08
that don't necessarily manifest in 1 to 5.8 14:20:13
years? 14:20:18
MR. CHEEK: Objection, form. 14:20:18
THE WITNESS: There may be risks that 14:20:24
become apparent after 5.8 years that weren't 14:20:26
apparent prior to that time. 14:20:30
BY MR. FRAMPTON: 14:20:31
Q. Well, 5.8 years is not typically 14:20:32
long enough for the cardiovascular risks to 14:20:36
result in someone having a heart attack or 14:20:39
stroke or something like that; is that correct? 14:20:42
A. There would be cardiovascular 14:20:44
risks which appeared later. There are also to 14:20:54
the best of my knowledge adult studies with a 14:21:01
longer period of follow-up to look at those 14:21:03
risks in adult individuals, sir. 14:21:05
Q. And they found increased 14:21:06
mortality, have they not, or do you know? 14:21:12
A. I believe that some of them have 14:21:16
found increased mortality, sir, although not 14:21:20
necessarily primarily or solely associated with 14:21:26
cardiovascular risks. 14:21:31
Q. Some have found increased 14:21:34
mortality associated with cardiovascular risks, 14:21:39

Page 181

have they not? Do you know? 14:21:42
A. So my specific recall is that some 14:21:43
of the studies that have looked at long-term 14:21:51
mortality attributed a significant component of 14:21:54
long-term mortality to things such as HIV. And 14:21:59
so I would need to look at the specific 14:22:06
contribution that cardiovascular risk made to 14:22:11
long-term mortality. 14:22:14
Q. And that wasn't something you 14:22:15
dealt with in your report, correct? 14:22:18
A. So in my report, I discuss the 14:22:20
relative risks and benefits of gender-affirming 14:22:27
health care and opine that the potential 14:22:30
benefits may outweigh the potential risks, sir. 14:22:34
And so that would be one of the considerations 14:22:37
of the potential risks. 14:22:39
Q. Let's go to the next paragraph on 14:22:40
page 13. Most studies included in this review 14:22:45
did not report comorbidities, physical or 14:22:52
mental health, and no study reported 14:22:55
concomitant treatments in detail. Because of 14:22:58
this, it is not clear whether any changes seen 14:23:01
were due to gender-affirming hormones or other 14:23:04
treatments the participants may have received. 14:23:08
Did I read that correctly? 14:23:12

Page 182

A. You did, sir. 14:23:13
Q. And other treatments the 14:23:14
participants may have received could include 14:23:17
psychiatric medication, could it not? 14:23:20
A. That is one of the possible other 14:23:22
treatments, sir. 14:23:26
Q. Another possible treatment could 14:23:27
be some form of mental health therapy; is that 14:23:29
correct? 14:23:32
A. Yes, sir. 14:23:32
Q. Go back to page 4. 14:23:34
A. I am on page 4, sir. 14:23:55
Q. Under critical outcomes, using 14:23:57
modified GRADE, this review rated the quality 14:23:59
of evidence on clinical effectiveness as very 14:24:03
low certainty, correct? 14:24:13
A. Yes, sir. 14:24:14
Q. And in the GRADE methodology, 14:24:24
there is a qualitative difference between low 14:24:27
and very low quality evidence, correct? 14:24:34
A. That is why they have two 14:24:37
different categories, sir. 14:24:41
Q. I assumed so, that's why I asked 14:24:41
the question. And so when you are formulating 14:24:43
a treatment recommendation, it matters whether 14:24:47

Page 183

the evidence base is low or very low quality, 14:24:54
correct? 14:24:57
A. The quality of the evidence is one 14:24:57
of the factors that is considered in making 14:25:02
recommendations, sir. 14:25:06
Q. Would you agree that there is 14:25:07
discordance between the Endocrine Society's 14:25:13
assessment of the evidence on gender-affirming 14:25:17
hormones and the NICE's assessment? 14:25:23
A. May I, sir? 14:25:28
Q. Yeah. And what I am getting at is 14:25:32
one assessed the quality of evidence as low, 14:25:37
and the other assessed it as very low. 14:25:39
A. Again, it would be helpful to 14:25:49
refer specifically to the guideline and to 14:25:51
specific recommendations that we discussed 14:25:53
earlier today. May I? 14:25:57
Q. Sure. 14:25:59
A. So, sir, the Endocrine Society 14:26:39
makes six recommendations relative to the 14:26:41
treatment of adolescents. They evaluate the 14:26:43
quality of evidence for five of those 14:26:46
recommendations as being of low quality and of 14:26:47
one of those recommendations as being very low 14:26:51
quality. 14:26:54

Page 184

Q. And at least with respect to the 14:26:54
critical outcomes, the NICE review rated the 14:27:00
quality of evidence as very low, correct? 14:27:04
A. For -- we have just reviewed the 14:27:06
efficacy, we haven't looked at the safety. But 14:27:14
yes, relative to the efficacy of 14:27:18
gender-affirming hormones and the efficacy and 14:27:21
I believe safety of GnRH agonist, yes, it was 14:27:25
very low. 14:27:31
Q. So would you agree there is at 14:27:32
least some degree of discordance there? 14:27:33
A. They rated the quality of the 14:27:35
evidence differently, sir. 14:27:39
Q. And would you take the position 14:27:41
that no reasonable scientist could agree with 14:27:47
the NICE reviews on that point and disagree 14:27:52
with the Endocrine Society? 14:27:55
A. So, sir, I thought that part of 14:28:00
our conversation earlier today is that these 14:28:04
were matters of judgment and that it would be a 14:28:09
matter of judgment as to whether the evidence 14:28:16
is of low or very low quality. 14:28:20
Q. All right. Go back to Exhibit 15, 14:28:22
which is the Cass Review. 14:28:29
A. One moment, sir. I have it, sir. 14:28:54

Page 185

Q. All right. Let's look at page -- 14:29:01
I mean, I'm sorry, paragraph 4.15. 14:29:13
Clinicians -- 14:29:19
A. Can you tell me what page number 14:29:19
that is? 14:29:21
Q. I'm sorry, 47. 14:29:21
A. 4.15, sir? 14:29:30
Q. Yes, sir. 14:29:31
A. All right. 14:29:31
Q. Clinicians and associated 14:29:32
professionals we have spoken to have 14:29:34
highlighted the lack of an agreed consensus on 14:29:36
the different possible implications of 14:29:39
gender-related stress, whether it may be an 14:29:42
indication that the child or young person is 14:29:44
likely to grow up to be a transgender adult and 14:29:46
would benefit from physical intervention or 14:29:49
whether it may be a manifestation of other 14:29:51
causes of distress. Following directly from 14:29:54
this is a spectrum of opinion about the correct 14:29:56
clinical approach ranging broadly between those 14:29:58
two take a more gender-affirmative approach to 14:30:01
those who take a more cautious development and 14:30:05
informed approach. Did I read that correctly? 14:30:08
A. You did, sir. 14:30:09

Page 186

Q. And do you have any doubt that the authors conducting the Cass Review found a lack of consensus among the relevant clinicians?
A. So I am not aware of the specific methodology that they utilized in order to ascertain that conclusion. But given the general credibility of Dr. Cass and the British medical profession, I would not have a prima facie reason to think that this is inaccurate.
Q. Fair enough. All right. Go to page 63.
A. Yes, sir.
Q. 5.21. The lack of available high level evidence was reflected in the recent NICE review into the use of puberty blockers and feminizing/masculinizing hormones commissioned by NHS England with the evidence being too inconclusive to form the basis of a policy position. Did I read that correctly?
A. You did, sir.
Q. Would you agree that she is saying -- well, this interim review based on what they deemed to be too inconclusive in evidence did not make specific treatment recommendations, correct?

Page 187

A. My understanding of the interim report is that the Cass Review does not make specific recommendations relative to the use of so-called puberty blockers or gender-affirming hormone therapy for adolescents.
Q. They believed in this interim report that the evidence was too inconclusive to form the basis of a policy position; is that correct?
A. So that's what the sentence that you read states, sir.
Q. Would you interpret that as them saying that there is uncertainty as to what the proper policy should be?
MR. CHEEK: Objection, speculation.
THE WITNESS: So, sir, we have spent a considerable amount of time discussing the GRADE approach to rating the quality of the evidence. We haven't discussed the GRADE approach to making recommendations. It's not clear to me at this point that the Cass Review has under -- has undertaken the necessary steps to formulate a policy position. So I am somewhat agnostic to the meaning of this sentence and its implications.
BY MR. FRAMPTON:

Page 188

Q. They did not promote a policy position, correct?
A. So this is a -- at the point of issuing an interim report, the interim report does not contain a policy position relative to the use of puberty blockers and gender-affirming hormone therapy. It makes other recommendations for the organization of services to individuals with gender dysphoria, but it does not make recommendations either for or against the use of puberty blockers or gender-affirming hormone therapy.
Q. And they tell us the reason for that is inconclusive evidence, correct?
A. So that's what this sentence says. I don't -- one might still be able to take a policy position relative to there being inconclusive evidence. That's why I am having difficulty interpreting this statement. We frequently in medicine make -- have to make medical judgments and decisions on the available evidence.
Q. Making a judgment for a particular patient is different from making a clinical practice guideline recommendation, correct,

Page 189

that would apply to many patients?
A. They are distinct but related, sir.
Q. All right. Let's go --
A. May I set this aside, sir?
Q. Yes.
(Thereupon, Exhibit 29, Care of Children and Adolescents With Gender Dysphoria, was marked for purposes of identification.)
BY MR. FRAMPTON:
Q. I show you what I am marking as Defendants' Exhibit 29, a document entitled Care of Children and Adolescents With Gender Dysphoria. And, Dr. Antommaria, are you familiar with this document?
A. I am, sir.
Q. And what do you understand it to be?
A. I understand it to be an official English language translation of the summary of the Swedish National Board of Health and Welfare's report on the care of adolescents and children with gender dysphoria, sir.
Q. Okay. Turn to page 3, please.
A. Yes, sir.

Page 190

Q. The last paragraph begins: A systematic review published in 2022 by the Swedish Agency For Health Technology Assessment and Assessment of Social Services, endnote 2, shows that the state of knowledge largely remains unchanged compared to 2015. Did I read that correctly?
A. You did, sir.
Q. All right. So they are purporting -- they purport to be citing to a systematic review published in 2022, correct?
A. Yes, sir.
Q. Let me show you your expert report, which oddly enough this far into our deposition I have not yet marked, but we will do that.
(Thereupon, Exhibit 30, Expert Declaration of Armand H. Antommaria, M.D., Ph.D., FAAP, HEC-C, was marked for purposes of identification.)
BY MR. FRAMPTON:
Q. I show you what I am marking as Exhibit 30. And, Dr. Antommaria, is Exhibit 30 your expert report in this case?
A. One moment, sir.

Page 191

Q. Yeah.
A. It appears to be, sir.
MR. CHEEK: Hal, this is -- let me just -- can you look and make sure that the one we are entering as Defendants' Exhibit 30 is a complete copy? That was your intention, right?
MR. FRAMPTON: Yes.
THE WITNESS: So the part where it becomes unstapled looks like it has the relevant pages.
MR. CHEEK: But it's a complete copy of your expert report? The reason I am asking is we have got an extra page here.
THE WITNESS: What is the page titled, 50 what? It's like double printed.
MR. CHEEK: I don't know.
THE WITNESS: So that page is in here.
MR. FRAMPTON: So it was in one of yours.
BY MR. FRAMPTON:
Q. All right. Dr. Antommaria, flip to page 19. And I am looking at the footnote --
A. So I apologize, the page numbers

Page 192

are double printed. Can you give me the paragraph number, sir?
Q. Yeah, I am looking at footnote -- looking at footnote 41, but the second page of footnote 41.
A. So I'm sorry, the copy of the report that you gave me has the references included in the paragraph and not footnotes.
Q. Let me see it. We will mark a new one.
MR. CHEEK: For clarity, Defense Exhibit No. 30 is Dr. Antommaria's declaration from the PI hearing?
MR. FRAMPTON: Correct.
MR. CHEEK: Okay.
(Thereupon, Exhibit 31, PLaintiff-Intervenor United States' Disclosure of Expert Testimony of Armand H. Matheny Antommaria, M.D., Ph.D., FAAP, HEC-C, was marked for purposes of identification.)
BY MR. FRAMPTON:
Q. All right. 31 is your expert report. And hopefully, now you can turn to page 19.
A. All right. I am on page 19, sir.

Page 193

Q. Great. Do you see in that footnote, it's one, two, three, four lines down -- I'm sorry, yeah, three lines down: Note the Swedish Agency for Health Technology Assessment and Assessment of Social Services, SBU, gender dysphoria in children and adolescents, an inventory of the literature, and then there is a citation, is a scoping review. Do you see that language?
A. Yes, sir.
Q. And what is the date of that scoping review document?
A. Here, it's reported as 2019, sir.
Q. Okay. Go back to the Swedish English language summary.
A. Yes, sir.
Q. And go to endnote 2, which is the systematic review that they appear to be citing.
A. Yes, sir.
Q. And what is the date on that document?
A. 2022, sir.
Q. Is it possible, Dr. Antommaria, that the Swedish government commissioned a

Page 194

scoping review in 2019 and a systematic review in 2022? 14:42:39 14:42:42
A. That is a possibility, sir. 14:42:43
Q. Do you know one way or the other? 14:42:46
A. Not at the present moment, sir. 14:42:52
Q. And do you know whether the 2022 systematic review assessed the quality of evidence based on the GRADE methodology? 14:42:57 14:43:10 14:43:13
A. I do not, sir. You will note that even in this English language translation of the summary, the title of that document is given in Swedish. And so one of the difficulties of assessing this literature is not all of the material is available in official English translation. 14:43:15 14:43:35 14:43:39 14:43:42 14:43:48 14:43:52 14:43:55
Q. And have you made an effort to obtain an English translation of the document reflected in endnote 2 of the Swedish language summary? 14:43:57 14:44:04 14:44:08 14:44:14
A. I have made an effort to ascertain all of the relevant European literature. I have not independently commissioned English translations of any of the literature, sir. 14:44:14 14:44:21 14:44:27 14:44:32
Q. Have you run any of them through Google Translate? 14:44:35 14:44:37

Page 195

A. No, sir. I have colleagues who conduct research in regard to patients with what might be referred to as low health literacy, and there is good evidence in the literature that Google Translate is not a reliable source of translation of medical documentation. 14:44:42 14:44:45 14:44:50 14:44:54 14:44:56 14:44:59 14:45:02
Q. So it is possible this Swedish recommendation is based on a systematic review of the evidence rather than just a scoping review? 14:45:02 14:45:10 14:45:12 14:45:15
A. That is a possibility, sir. 14:45:16
Q. And it's also possible that systematic review may rate the quality of evidence using the GRADE methodology? 14:45:21 14:45:24 14:45:27
A. So, sir, this document makes a variety of recommendations. In its making of recommendations, it neither grades the quality of the evidence nor the strength of the recommendations. If it was relying on a document that graded the quality of the evidence, I would have thought that that would be reflected in this document. So, no, I don't know for certain, but I would have good reason to believe that that's not the case. 14:45:33 14:45:39 14:45:44 14:45:46 14:45:48 14:45:51 14:45:55 14:45:58 14:46:01 14:46:05

Page 196

Q. Flip to page 4, please. 14:46:06
MR. CHEEK: And we are still on -- 14:46:57
MR. FRAMPTON: We are on the Swedish -- 14:46:59 14:47:00
MR. CHEEK: 29, right? 14:47:01
MR. FRAMPTON: Yes. 14:47:02
THE WITNESS: I am on page 4, sir. 14:47:03
BY MR. FRAMPTON: 14:47:05
Q. All right. Do you see about halfway down the page, it says: To ensure that new knowledge is gathered, the NBHW further deems that treatment with GnRH analogs and sex hormones for young people should be provided within a research context which does not necessarily imply the use of randomized control trials, RCTs. Did I read that correctly? 14:47:10 14:47:12 14:47:16 14:47:19 14:47:23 14:47:24 14:47:26 14:47:30
A. You did, sir. 14:47:33
Q. So the Swedish government is concluding that going forward, puberty blockers and cross-sex hormones should be provided only within a research context; is that correct? 14:47:34 14:47:38 14:47:41 14:47:43
A. That is correct, sir. 14:47:45
Q. And you don't consider that recommendation unethical, do you? 14:47:48 14:47:52
A. One minute, I am just reading the 14:47:55

Page 197

paragraphs. 14:48:05
Q. Sure. 14:48:06
A. So, in general, I don't, sir. I will note that later in the paragraph, it does state until the research study is in place that NBHW deems that relevant treatment with GnRH analogs and sex hormones may be given in exceptional cases in accordance with the updated recommendations and criteria described in this guideline. So I take it that they considered that treatment is sufficiently important that it should go on prior to research studies being in place. 14:48:42 14:48:46 14:48:48 14:48:53 14:48:59 14:49:01 14:49:03 14:49:07 14:49:10 14:49:12 14:49:18
Q. As soon as they get a research protocol, everything is going to be in the context of research, correct? 14:49:21 14:49:23 14:49:24
A. That's their recommendation, sir. 14:49:26
Q. Back on page 3. 14:49:29
A. Yes, sir. 14:49:38
Q. Recommendations and criteria for hormonal treatment. So they say: For adolescents with gender incongruence, the NBHW deems that the risks of puberty-suppressing treatment with GnRH analogs and gender-affirming hormonal treatment currently 14:49:38 14:49:44 14:49:45 14:49:50 14:49:51 14:49:54

Page 198

outweigh the possible benefits and that the treatment should be offered only in exceptional cases. Did I read that correctly? 14:49:57 14:50:00 14:50:02

A. You did, sir. 14:50:03

Q. And does that suggest that they believe there is significant uncertainty as to the benefits and risks of these treatments? 14:50:04 14:50:10 14:50:13

MR. CHEEK: Objection, speculation. 14:50:19

THE WITNESS: So, sir, the difficulty with this document is that this is a six-page summary of a substantially longer document which presumably would go into greater detail about that judgment. But because that is not currently available in an official English translation, it's hard to fully assess the justification for the statement, sir. 14:50:21 14:50:22 14:50:29 14:50:33 14:50:40 14:50:48 14:50:51 14:50:54

BY MR. FRAMPTON: 14:50:55

Q. The statement certainly suggests they believe there is uncertainty -- 14:50:56 14:50:58

MR. CHEEK: Objection. 14:51:00

BY MR. FRAMPTON: 14:51:01

Q. -- as to the risks and benefits, correct? 14:51:01 14:51:02

MR. CHEEK: Objection, speculation. 14:51:03

THE WITNESS: So in reading that 14:51:13

Page 199

statement, sir, they don't make reference to uncertainty. 14:51:15 14:51:20

BY MR. FRAMPTON: 14:51:20

Q. They make reference to their judgment being that the benefits generally outweigh the risks -- I mean, I'm sorry, that the risks generally outweigh the benefits, correct? 14:51:23 14:51:24 14:51:28 14:51:30 14:51:32

A. Correct, sir. 14:51:32

(Thereupon, Exhibit 32, Bilaga 3. Inkluderade Studier Appendix 3. Characteristics of Included Studies: Extracted data, was marked for purposes of identification.) 14:51:39 14:51:39 14:51:39 14:51:39

BY MR. FRAMPTON: 14:51:39

Q. I hand you what I am marking as Defendants' Exhibit 32. And my question, Dr. Antommaria, have you -- the document is marked Characteristics of Included Studies: Extracted Data. Does this document appear to be available in English? 14:51:39 14:51:42 14:51:58 14:52:03 14:52:06 14:52:12

A. May I look at the document, sir? 14:52:13

Q. Yeah, of course. 14:52:16

A. So this document, which I am not certain what the nature of the document is, is in English, sir. 14:52:42 14:52:44 14:52:48

Page 200

Q. In reviewing what was available in English from the Swedish report, did you not come across this document? 14:52:49 14:52:59 14:53:04

A. No, I did not, sir. 14:53:06

Q. It appears to be a table of evidence of included studies; is that at least what it appears to be? 14:53:08 14:53:17 14:53:22

A. Sir, I can't read the -- may I? 14:53:23

Q. Uh-huh. 14:53:47

A. So, sir, it's hard for me to know what this is. I am looking at Reference 2, which you pointed to earlier. That title in Swedish is different than the title in the top right-hand corner of this. So -- so it's hard for -- although this is dated 2002, it's hard for me to -- at this point, not knowing from where this was downloaded or other information, it's hard for me to know what it is, sir. 14:54:11 14:54:14 14:54:17 14:54:22 14:54:24 14:54:34 14:54:38 14:54:40 14:54:43

Q. The title -- were you looking at endnote 2? 14:54:45 14:54:50

A. I am looking at -- I am going to go to Exhibit 29. 14:54:51 14:54:55

Q. Yes. 14:54:56

A. Reference 2, I believe that was a reference that you pointed me to earlier, sir? 14:54:58 14:55:01

Page 201

Q. Right. And do you see in that title Hormonbehandling vid könsdysfori? 14:55:04 14:55:06

A. So, again, sir, I don't read Swedish. There is a sentence -- a first sentence, then I do see a second sentence which appears to have some similarity, but I don't -- so I will -- I don't know what the top title is, and that top title doesn't correspond to the first sentence. So, again, it would be hard for me to form an opinion about -- 14:55:19 14:55:22 14:55:27 14:55:32 14:55:36 14:55:41 14:55:44 14:55:46

Q. Sure. 14:55:50

A. -- what this is. 14:55:52

Q. Okay. It's just not something you have come across in your review of the Swedish documents? 14:55:52 14:55:55 14:55:58

A. It is not, sir. 14:55:58

Q. Okay. 14:55:59

(Thereupon, Exhibit 33, Bilaga till rapport, was marked for purposes of identification.) 14:56:03 14:56:03 14:56:03

BY MR. FRAMPTON: 14:56:03

Q. I hand you what I am marking as Exhibit 33. And is this also not something you came across in your review of the Swedish literature? 14:56:04 14:56:07 14:56:40 14:56:42

Page 202

A. So this is not something that I am familiar with, sir. 14:56:43 14:56:45
Q. All right, then I won't ask you about that. What's lupus nephritis? 14:56:46 14:56:58
A. So nephritis would be an inflammation of the kidneys, and lupus is a rheumatologic condition. So it would be a inflammation of the kidneys caused by a specific rheumatologic condition. 14:57:04 14:57:09 14:57:12 14:57:15 14:57:17
Q. Is that -- would treating that condition normally be the province of a nephrologist? 14:57:20 14:57:23 14:57:28
A. A nephrologist or a rheumatologist, sir. 14:57:29 14:57:31
Q. You typically would not initiate treatment for that condition? 14:57:31 14:57:35
A. No, sir; I am neither a rheumatologist nor a nephrologist. 14:57:36 14:57:40
Q. Do you have an understanding of what happens if that condition is left untreated? 14:57:42 14:57:53 14:57:55
A. A general understanding, sir. 14:57:55
Q. And what is that? 14:57:57
A. My general understanding is that if it is left untreated, the individual might 14:57:58 14:58:04

Page 203

progress to chronic renal failure and require dialysis or a kidney transplant for their renal failure. 14:58:08 14:58:12 14:58:17
Q. Okay. Chronic kidney disease is a life-threatening disease, is it not? 14:58:17 14:58:25
A. Untreated it can be life-threatening, sir. 14:58:26 14:58:30
Q. Do you have -- do you have any knowledge of the quality of evidence supporting the efficacy of cyclophosphamide to treat lupus nephritis? 14:58:31 14:58:36 14:58:40 14:58:45
MR. CHEEK: Objection, foundation. 14:58:46
THE WITNESS: No, sir, I do not. 14:58:49
BY MR. FRAMPTON: 14:58:50
Q. When we call -- just generally in the medical literature, when we call a condition refractory, what does that generally mean? 14:58:57 14:59:00 14:59:02 14:59:06
A. It would generally mean that it has not responded to treatment. 14:59:06 14:59:12
Q. What -- could you treat multiple sclerosis in your practice? 14:59:15 14:59:25
A. I do not, sir. So in my practice as a pediatric hospitalist, I do not treat multiple sclerosis. 14:59:26 14:59:36 14:59:39

Page 204

Q. Do you know the quality of evidence supporting the efficacy of any particular treatment on progressive or refractory MS? 14:59:41 14:59:45 14:59:48 14:59:51
A. At a high level of generality, I do, sir. 14:59:52 14:59:59
Q. Okay. What about therapy that can be gonadotoxic? 14:59:59 15:00:06
MR. CHEEK: Objection, form. 15:00:10
THE WITNESS: Do I know the level of evidence that supports gonado -- potentially gonadotoxic therapy for MS? 15:00:13 15:00:14 15:00:21
BY MR. FRAMPTON: 15:00:21
Q. Yes. 15:00:21
A. No, sir, I do not. 15:00:22
Q. What is familial adenomatous polyposis? Did I even say that right? 15:00:22 15:00:29
A. You are close enough that I understand what you are asking me, sir. 15:00:31 15:00:33
Q. That's all I'm going for. 15:00:34
A. It is a genetic condition that results in polyps in the intestinal tract which can progress to be cancerous. 15:00:38 15:00:41 15:00:46
Q. Without surgical intervention, is a person with that condition's likelihood of 15:00:50 15:00:58

Page 205

developing cancer at a young age pretty high? 15:01:01
A. Without appropriate screening and intervention, yes, sir. 15:01:04 15:01:08
Q. What are endometriomas? 15:01:10
A. An endometrioma would be a proliferation of the endometrium, which is the lining of the uterus, sir. 15:01:16 15:01:20 15:01:21
Q. And can -- if they are large enough, can they impair fertility? 15:01:22 15:01:25
A. They can, sir. 15:01:27
Q. Do you know the quality of evidence supporting the efficacy of surgical intervention to treat large endometriomas? 15:01:28 15:01:36 15:01:38
A. I do not, sir. 15:01:44
Q. What is ulcerative colitis? 15:01:45
A. Ulcerative colitis is an inflammatory process of the intestinal tract, sir. 15:01:56 15:02:00 15:02:05
Q. And surgery is not generally the first line treatment for that condition, is it? 15:02:05 15:02:07
A. No, there would be other interventions that would be utilized to try to prevent the need for surgery, sir. 15:02:08 15:02:10 15:02:13
Q. And surgery generally would only be done if there is no other way of controlling 15:02:17 15:02:20

Page 206

the condition, correct? 15:02:23
A. If medical therapy was 15:02:23
unsuccessful, surgery might be considered, sir. 15:02:28
Q. And you can have with that 15:02:30
condition emergency situations that require 15:02:34
surgery, correct, like a bleed or perforation, 15:02:36
if you know? 15:02:42
A. I don't know that surgery would be 15:02:44
necessarily the primary intervention for 15:02:46
bleeding, but for perforation, yes, sir. 15:02:48
Q. Because if a perforation is left 15:02:52
untreated, that can cause death presumably, 15:02:54
right? 15:02:57
A. It can cause peritonitis, which 15:02:58
would be an infection in the abdominal cavity 15:03:01
which if left untreated could result in death, 15:03:06
sir. 15:03:08
Q. For a natal male at Tanner Stage 2 15:03:09
seeking to begin puberty blockers, what are the 15:03:22
options for preserving that child's fertility? 15:03:26
A. The primary option for preserving 15:03:29
fertility in that case would be delaying the 15:03:38
use of puberty blockers, sir. 15:03:41
Q. So you wouldn't actually start 15:03:43
them at Tanner 2 if you were trying to preserve 15:03:45

Page 207

fertility? 15:03:48
MR. CHEEK: Objection, foundation. 15:03:48
THE WITNESS: If that was your 15:03:50
exclusive or predominant goal, there would be a 15:03:56
reason to delay utilizing puberty blockers. There 15:04:00
might be other ways later in the future that by 15:04:05
discontinuing gender-affirming medical care 15:04:13
fertility could be reestablished. 15:04:16
BY MR. FRAMPTON: 15:04:20
Q. Have you seen any studies showing 15:04:22
the success of that process? 15:04:23
A. I am aware of studies that show 15:04:28
the resumption of fertility in individuals who 15:04:34
have discontinued gender-affirming hormone 15:04:37
therapy, sir. 15:04:41
Q. Aware of any studies dealing with 15:04:41
individuals who started puberty suppression at 15:04:44
Tanner Stage 2? 15:04:47
MR. CHEEK: Objection, form. 15:04:48
THE WITNESS: Not specifically of 15:04:50
that population, sir. 15:04:53
BY MR. FRAMPTON: 15:04:54
Q. Just as a general matter, if a 15:04:54
natal male starts puberty suppression at Tanner 15:04:57
Stage 2, continues seamlessly into estrogen and 15:05:01

Page 208

anti-androgen therapy, that person will never 15:05:06
develop fertility, correct, without stopping 15:05:10
treatment? 15:05:14
A. So, in general, the expectation 15:05:14
would be if that individual continued 15:05:19
treatment, that is correct that they would not 15:05:23
be fertile. 15:05:25
Q. And, likewise, with a natal female 15:05:26
who begins puberty suppression at Tanner Stage 15:05:30
2 and progresses seamlessly to testosterone 15:05:34
therapy, that individual would not develop 15:05:38
fertility, correct? 15:05:41
A. If they continued on treatment, 15:05:43
they would not be anticipated to have 15:05:51
biologically related children. It is to say 15:05:53
that for some individuals the benefit of 15:05:56
treatment would outweigh that risk, but that 15:05:59
risk would exist. 15:06:01
Q. And it wouldn't be a risk, it 15:06:02
would be they are not going to have fertility 15:06:12
without discontinuing treatment, correct? 15:06:15
MR. CHEEK: Objection, form. 15:06:20
THE WITNESS: I'm sorry, I don't 15:06:21
understand the distinction that you are making, 15:06:22
sir. 15:06:24

Page 209

BY MR. FRAMPTON: 15:06:24
Q. Well, I think you were 15:06:25
characterizing it as a risk of infertility, and 15:06:26
I was distinguishing it's really -- without 15:06:30
discontinuing treatment, it's a certainty of 15:06:33
infertility, is it not? 15:06:36
A. So when -- as an emphasis, when I 15:06:37
would refer to a risk, I wouldn't say that 15:06:40
risks involve both a magnitude and a 15:06:42
probability. So while colloquially risk might 15:06:44
have implications about probability, I don't 15:06:48
know that in the way an ethicist uses a risk 15:06:52
that it necessarily has those similar 15:06:57
implications. 15:07:04
Q. But you would agree, again, for 15:07:06
the natal female starting puberty suppression 15:07:08
at Tanner Stage 2 continuing seamlessly through 15:07:10
to testosterone therapy that that person -- you 15:07:13
would not have any expectation that person 15:07:16
would develop fertility with that course of 15:07:18
treatment, correct? 15:07:22
A. So given the currently available 15:07:22
resources for fertility preservation, no. 15:07:34
Q. Are you aware of any studies that 15:07:37
document healthy conception and birth by a 15:08:02

Page 210

natal female after an extended period of years 15:08:06
on cross-sex hormones? By that, I mean at 15:08:09
least five years. 15:08:11
A. So as I have said, I am aware of 15:08:17
literature that shows that individuals have 15:08:19
fertility after discontinuing gender-affirming 15:08:26
hormone therapy for a period of time. I would 15:08:31
have to look at those specific studies to see 15:08:32
whether individual -- whether individuals are 15:08:36
assigned female at birth in those studies had 15:08:39
been on gender-affirming hormone therapy for 15:08:42
more than or less than five years. 15:08:45
Q. Okay. Sitting here today, can you 15:08:47
name any studies we should look at for that 15:08:50
proposition? 15:08:52
A. I thought they might be referenced 15:08:53
in my report, sir, but they are not. 15:11:33
Q. Okay. Let me -- let me show you 15:11:34
what I am going to mark as Defendants' 15:11:43
Exhibit 34. 15:11:46
(Thereupon, Exhibit 34, Considering 15:11:46
Sex as a Biological Variable in Basic and Clinical 15:11:46
Studies: An Endocrine Society Scientific 15:11:46
Statement, was marked for purposes of 15:11:46
identification.) 15:11:47

Page 211

BY MR. FRAMPTON: 15:11:47
Q. 34 is an exhibit entitled 15:12:01
Considering Sex As a Biological Variable in 15:12:03
Basic and Clinical Studies, an Endocrine 15:12:06
Society Scientific Statement. And I am 15:12:09
curious, Dr. Antommaria, if you are familiar 15:12:11
with this scientific statement from the 15:12:14
Endocrine Society? 15:12:16
A. I am not, sir. 15:12:19
Q. I have got one thing I am going to 15:12:20
ask you about in it, and I simply want to see 15:12:22
if their delineation of what a DSD is aligns 15:12:26
with your understanding. So flip to page 225, 15:12:31
please. 15:12:34
A. Yes, sir. 15:12:41
Q. Under Biological Basis of 15:12:42
Diversity in Sexual/Gender Development and 15:12:48
Orientation, do you see that heading? 15:12:51
A. I do, sir. 15:12:53
Q. There it says: Given the 15:12:53
complexities of the biology of sexual 15:12:55
determination and differentiation, it is not 15:12:58
surprising that there are dozens of examples of 15:12:59
variations or errors in these pathways 15:13:02
associated with genetic mutations that are now 15:13:05

Page 212

well-known to endocrinologists and geneticists. 15:13:08
In medicine, these situations are generally 15:13:12
termed disorders of sexual development, DSD, or 15:13:14
differences in sexual development. DSD 15:13:18
includes genetic disorders in the sexual 15:13:22
determination pathway, disorders of 15:13:25
steroidogenesis, disorders of steroid hormone 15:13:30
action, especially androgen insensitivity 15:13:33
syndrome, and less well-defined, quote, 15:13:36
developmental field defects, unquote, such as 15:13:38
Mayer-Rokitansky-Küster-Hauser syndrome. Did I 15:13:45
read that correctly? 15:13:48
A. Yes, sir. 15:13:48
Q. That's amazing. Is that a 15:13:49
reasonable sort of explanation of what a DSD is 15:13:51
to your understanding, or do you have a 15:13:58
different understanding? 15:14:00
A. May I reread it, sir? 15:14:00
Q. Of course. 15:14:03
A. So I would say that it has a 15:14:58
relative slant toward endocrinological causes 15:15:02
of DSDs but that the general description is 15:15:07
accurate, sir. 15:15:13
Q. Do you agree that most transgender 15:15:13
people do not have a DSD? 15:15:17

Page 213

A. I believe that that's an accurate 15:15:20
statement, sir. 15:15:31
Q. What is complete androgen and 15:15:32
sensitivity syndrome? 15:15:48
A. It is a disorder in which an 15:15:51
individual has a variant in androgen receptor. 15:15:57
And so although they make testosterone, their 15:16:04
body does not respond to testosterone or other 15:16:10
androgens. 15:16:15
Q. They are chromosomally male; is 15:16:15
that correct? 15:16:20
A. They have XY chromosomes. 15:16:20
Q. But they will not experience 15:16:26
endogenous male puberty, correct? 15:16:34
A. If by -- if by male puberty you 15:16:36
mean puberty in the technical sense of the 15:16:49
development, enlargement of testes and other 15:16:54
features of a typically masculinizing puberty, 15:16:58
no, they will not. 15:17:02
Q. And there is no medical 15:17:03
intervention that will cause them to experience 15:17:07
male puberty, correct? 15:17:10
A. There is no current intervention 15:17:11
that's capable of producing those phenotypic 15:17:17
changes. 15:17:21

Page 214

Q. And they nearly always identify as 15:17:22
female, according to the literature, correct? 15:17:26
A. Yes, individuals with complete 15:17:28
androgen sensitivity generally have female 15:17:33
gender identities. 15:17:37
Q. And the only -- the only 15:17:39
experience of puberty that they can have just 15:17:48
physically is female puberty, correct? 15:17:51
A. As I have said, they are unable to 15:17:55
develop a so-called masculine phenotype. And, 15:18:09
yes, they are capable of developing 15:18:16
effeminate -- so-called effeminate or female 15:18:21
phenotype. 15:18:22
Q. For a natal male with gender 15:18:23
dysphoria who does not have a DSD, okay? 15:18:33
A. Okay. 15:18:39
Q. Without medical intervention, that 15:18:40
individual will experience endogenous male 15:18:44
puberty, assuming they progress to that point 15:18:48
in their life? 15:18:51
A. Well, so there might be multiple 15:18:52
other reasons why somebody assigned male at 15:19:02
birth doesn't have an endogenous male puberty, 15:19:05
aside from a DSD such as a physical injury to 15:19:11
their testes so that there would be multiple 15:19:15

Page 215

reasons why they might not experience 15:19:19
masculinizing puberty, sir. 15:19:22
Q. So barring some other medical 15:19:25
condition or injury, no DSD, no other medical 15:19:27
condition or injury other than gender 15:19:31
dysphoria, they will experience endogenous 15:19:33
puberty, correct? 15:19:39
A. Yes, aside from injury, infection, 15:19:40
or other illness, yes. 15:19:47
Q. And, again, we are assuming no 15:19:48
other medical conditions, injuries, infections, 15:20:03
illness. During endogenous puberty, they will 15:20:07
develop secondary sex characteristics typical 15:20:10
of their native sex, correct? 15:20:13
A. Yes, typical of their sex assigned 15:20:14
at birth. 15:20:16
If you are reaching the end of a 15:20:29
section, sir, can we take another brief break? 15:20:30
MR. FRAMPTON: Let's do it. 15:20:32
(Recess taken.) 15:20:33
MR. FRAMPTON: Back on the record. 15:34:01
BY MR. FRAMPTON: 15:34:01
Q. Dr. Antommaria, could you pull out 15:34:18
Exhibit 17 of your -- my apologies for your 15:34:20
ridiculous stack there. It's all good stuff, 15:34:25

Page 216

though. All right. You are looking at the 15:34:29
Endocrine Society guidelines from 2017, 15:34:34
correct? 15:34:36
A. I am, sir. 15:34:36
Q. All right. Go to page 3879. 15:34:37
A. Yes, sir. 15:34:47
Q. All right. And you have 15:34:47
already -- you said you believe that these 15:34:53
guidelines were developed through a rigorous 15:34:56
method, correct? 15:34:58
A. Yes, sir. 15:34:59
Q. All right. Under 3879 under 15:35:05
evidence it says: In most children -- 15:35:10
A. So I'm sorry, just so we are in 15:35:13
the same place, that's under 1.3 and 1.4, sir? 15:35:15
Q. That's right. 15:35:20
A. Okay. 15:35:21
Q. It says: In most children 15:35:21
diagnosed with GD/gender incongruence, it did 15:35:23
not persist into adolescence. The percentages 15:35:28
differed among studies, probably dependent on 15:35:31
which version of the DSM clinicians used, the 15:35:33
patient's age, the recruitment criteria, and 15:35:37
perhaps cultural factors. However, the large 15:35:39
majority, about 85 percent, of prepubertal 15:35:42

Page 217

children with a childhood diagnosis did not 15:35:46
remain GD/gender incongruent in adolescence. 15:35:49
Did I read that correct? 15:35:54
A. You did, sir. 15:35:55
Q. And that was the Endocrine Society 15:35:55
author's view of the evidence, correct? 15:36:03
A. That is their summary of the 15:36:05
evidence, sir. 15:36:10
Q. Okay. And they are basing it -- 15:36:10
and if you need to look at endnote 20, go 15:36:14
ahead. They are basing it on primarily Dutch 15:36:17
studies, correct? 15:36:19
A. So there is a single reference to 15:36:20
Reference 20, which is a study by the Dutch 15:36:32
group, yes. 15:36:37
Q. Okay. And in the Dutch group 15:36:37
studies on persistence and desistance, they did 15:36:44
not measure the point at which someone stopped 15:36:49
experiencing gender dysphoria, correct? 15:36:56
A. Correct, sir. I believe my 15:36:58
general understanding of this study design was 15:37:05
to look at individuals' gender identity at two 15:37:08
different points in time. 15:37:14
Q. And no understanding of where 15:37:15
between those points in time their experience 15:37:17

Page 218

of gender dysphoria changed, right? 15:37:21
A. So presumably, the clinicians may 15:37:23
have a sense of when that changed, but the 15:37:30
studies did not report data about that. 15:37:34
(Thereupon, Exhibit 35, A Critical 15:37:55
Commentary on Follow-up Studies and Desistance 15:37:55
Theories About Transgender and 15:37:55
Gender-nonconforming Children, was marked for 15:37:55
purposes of identification.) 15:37:55
BY MR. FRAMPTON: 15:37:55
Q. I show you what I am marking as 15:37:59
Exhibit 35. It is a document that I have got 15:38:01
to switch notebooks for. All better. It is a 15:38:07
document entitled Critical Commentary on 15:38:20
Follow-up Studies and Desistance Theories About 15:38:23
Transgender and Gender Nonconforming Children. 15:38:26
The lead author is Julia Temple Newhook. All 15:38:29
right. You are -- I imagine you are familiar 15:38:43
with this paper, correct, sir? 15:38:46
A. Yes, sir. 15:38:48
Q. All right. And it comments on 15:38:50
four studies related to -- that it believes are 15:38:58
related to desistance rates, correct? 15:39:04
A. Without reviewing the study again, 15:39:09
I don't know if it's forcer, but it does 15:39:15

Page 219

analyze studies about so-called desistance. 15:39:18
Q. Well, let me nail that down. Go 15:39:23
to page 1. We have got somewhat normal page 15:39:27
numbers. 15:39:34
A. I am on what I take to be the 15:39:37
first page, sir. 15:39:39
Q. That's my understanding as well, 15:39:39
you are with me. The second sentence in the 15:39:43
main text: This statement largely draws on 15:39:48
estimates from four follow-up studies conducted 15:39:51
with samples of gender-nonconforming children 15:39:54
in one of two clinics in Canada or the 15:39:58
Netherlands, and then it contains a citation to 15:40:03
four studies; is that correct? 15:40:05
A. Oh, I'm sorry, I was reading that 15:40:06
in the abstract, not in the text. Let me look 15:40:08
in the text, sir. 15:40:11
Q. Okay. 15:40:12
A. You read that correctly, sir. 15:40:20
Q. And then it says: This article 15:40:21
outlines methodological, theoretical, ethical, 15:40:25
and interpretive concerns regarding these 15:40:28
studies, correct? 15:40:31
A. Correct, sir. 15:40:31
Q. So would you agree that the author 15:40:32

Page 220

is reporting that she is -- that they are going 15:40:36
to review these four particular studies 15:40:38
concerning desistance? 15:40:42
A. In part, sir. 15:40:45
Q. What do you mean in part? 15:40:49
A. Well, they say this statement 15:40:50
largely draws on. So I take it that they are 15:40:52
also drawing on other sources than the four 15:40:55
studies that are -- that are subsequently 15:40:59
listed in the reference. 15:41:01
Q. Is this -- this paper is not a 15:41:02
systematic review of the literature on 15:41:14
desistance rates, is it? 15:41:16
A. No, it's not, sir. 15:41:18
Q. And you would agree that there are 15:41:21
more than four studies out there measuring 15:41:25
desistance rates, correct? 15:41:28
A. Yes, sir. 15:41:31
Q. Okay. And we don't know if these 15:41:33
authors -- well, strike that. The only studies 15:41:37
these authors call out are the four listed 15:41:44
there on page 1, right? 15:41:49
A. So, again, sir, I would have to 15:41:50
reread relevant portions of the article. At 15:41:58
the beginning of the article, yes, they 15:42:01

Page 221

identify them. Their article is focusing on 15:42:02
these four articles. 15:42:06
Q. They certainly -- because it's not 15:42:07
a systematic review, they are not purporting to 15:42:14
provide any kind of comprehensive analysis of 15:42:19
the literature on desistance rates, correct? 15:42:22
A. They are not purporting to have 15:42:25
conducted a systematic review. 15:42:29
Q. Did -- to your awareness, did any 15:42:30
of the authors of the four studies they did 15:42:42
call out publish any kind of response to this 15:42:46
article? 15:42:50
A. It's my understanding that 15:42:50
Professor Zucker published an article that he 15:42:59
in part comments on this one, sir. 15:43:03
Q. Is he the only one? 15:43:05
A. Others may have commented on it in 15:43:09
passing, so that's a possibility. I don't 15:43:20
recall. 15:43:29
Q. You are not aware of Dr. Steensma 15:43:29
publishing a response to this article? 15:43:32
A. So I know that Dr. Steensma has 15:43:34
published articles about desistance. It's hard 15:43:39
for me to recall whether I would characterize 15:43:49
any of those articles as a response to this 15:43:52

Page 222

article, as opposed to he references this 15:43:53
article among other articles. My sense was 15:43:57
that Professor Zucker's article is much more a 15:44:05
response, sir. 15:44:07
(Thereupon, Exhibit 36, A Critical 15:44:10
Commentary on A Critical Commentary on Follow-up 15:44:10
Studies and Desistance Theories About Transgender 15:44:10
and Gender Nonconforming Children, was marked for 15:44:10
purposes of identification.) 15:44:11
BY MR. FRAMPTON: 15:44:11
Q. I show you what I am marking as 15:44:43
Defendants' Exhibit 36. The document I am 15:44:45
handing you is titled A Critical Commentary on 15:44:56
a Critical Commentary on Follow-up Studies and 15:44:59
Desistance Theories About Transgender and 15:45:04
Gender Nonconforming Children. The lead author 15:45:09
is Thomas Steensma. Is that the document I 15:45:10
have handed you, Dr. Antommaria? 15:45:12
A. It is. I appreciate -- 15:45:14
Q. Have you seen this one before? 15:45:14
A. I appreciate you having such a 15:45:15
comprehensive collection of articles, sir. 15:45:17
Q. I have got a lot. Have you seen 15:45:19
this one before? 15:45:21
A. I believe I -- I believe I have, 15:45:22

Page 223

sir. 15:45:27
Q. Would you not -- you would 15:45:27
characterize this as a response to the Temple 15:45:28
Newhook article we just looked at, would you 15:45:34
not? 15:45:36
A. So seeing it again, sir, yes, it's 15:45:36
a commentary on the commentary. 15:45:41
Q. Is there some reason you didn't 15:45:44
cite either Professor Zucker's or Professor 15:45:51
Steensma's responses in your expert report? 15:45:54
A. Sir, I don't understand my expert 15:45:57
report to be a systematic review of the 15:46:05
literature. There are lots of articles that I 15:46:09
don't cite in my expert report. 15:46:12
Q. Sure. You didn't think it 15:46:13
relevant to cite Professor Steensma and Zucker 15:46:15
critically responding to Professor Temple 15:46:22
Newhook's article? 15:46:27
A. May I look at my report, sir? 15:46:28
Q. Sure. 15:46:32
A. So, sir, I am trying to find where 15:47:49
I cite -- 15:47:50
Q. Temple Newhook? 15:47:55
A. -- Temple Newhook. But I would 15:47:56
say in the process of looking at that, I would 15:47:59

Page 224

say that Reference 52 does cite Zucker on the 15:48:02
natural history of gender identity disorder in 15:48:06
children in Zucker debate Different Strokes For 15:48:09
Different Folks, which -- you know, I would 15:48:13
have to look at those articles. But I believe 15:48:17
one of those is his quote, response, or 15:48:22
commentary on Temple Newhook, or at least 15:48:25
references that. 15:48:29
Q. So the reference to Temple Newhook 15:48:29
is -- I'll find it for you. This is going to 15:48:42
be on page 22. 15:48:50
MR. CHEEK: And just so we are clear, 15:48:51
this is Defendants' Exhibit 31? 15:48:52
MR. FRAMPTON: Yes, you are right. 15:48:53
BY MR. FRAMPTON: 15:48:53
Q. Middle of the page, the studies to 15:48:56
which the legislation refers have substantial 15:48:58
limitations. For example, many include 15:49:01
children who would not fulfill the current 15:49:03
diagnostic criteria for gender dysphoria. Do 15:49:05
you see that? 15:49:09
THE WITNESS: Yes. So I'm sorry that 15:49:09
I don't understand your question, sir. So I 15:49:21
believe that Newhook's paper does provide support 15:49:24
for that claim and is an appropriate reference to 15:49:28

Page 225

support that claim. 15:49:34
Q. Okay. And you didn't think it 15:49:35
appropriate to cite Steensma or Zucker 15:49:37
responding to the claim of methodological 15:49:42
deficiencies? 15:49:51
A. No, sir. I believe that the 15:49:52
Newhook paper does identify limitations in the 15:50:01
studies that she analyzes and that the Steensma 15:50:06
article and the Zucker article do not 15:50:12
comprehensively refute her identification of 15:50:15
some of the limitations of those studies. 15:50:19
Q. They do disagree with some of her 15:50:22
methodological concerns, do they not, or do you 15:50:33
recall? 15:50:36
MR. CHEEK: Objection, form. 15:50:36
THE WITNESS: They do, sir. But, 15:50:43
again, my report is not intended to be a 15:50:44
comprehensive review of the literature. I have 15:50:48
cited a reference that provides appropriate 15:50:51
justification for the opinion that I have offered. 15:50:57
(Thereupon, Exhibit 37, The Amsterdam 15:51:16
Cohort of Gender Dysphoria Study (1972-2015): 15:51:16
Trends in Prevalence, Treatment, and Regrets, was 15:51:16
marked for purposes of identification.) 15:51:17
BY MR. FRAMPTON: 15:51:17

Page 226

Q. I show you what I am marking as 15:51:17
Exhibit 37, a document titled The Amsterdam 15:51:19
Cohort of Gender Dysphoria Study (1972-2015): 15:51:28
Trends in Prevalence, Treatment, and Regrets. 15:51:33
The lead author is Dr. Wiepjes. That's my best 15:51:36
Dutch pronunciation for today. Does that 15:51:43
appear to be what I have handed you, sir? 15:51:46
A. It does, sir. 15:51:48
Q. Are you familiar with this one? 15:51:49
A. I am, sir. 15:51:51
Q. All right. So let's look at what 15:51:52
this study did. All right. So if you look at 15:51:58
the bottom of the first column on page 583, are 15:52:15
you there? 15:52:22
A. The left-hand column, sir? 15:52:22
Q. Yes. 15:52:24
A. Yes. 15:52:26
Q. It says: In the present study we 15:52:26
included the complete population seen at the 15:52:29
gender identity clinic of the VUmc from 1972 15:52:31
through December 2015 to assess the current 15:52:35
prevalence of transgender people who received 15:52:38
medical treatment, the frequency of specific 15:52:41
medical treatments performed, and the numbers 15:52:44
of people who received HT in line with their 15:52:46

Page 227

sex assigned at birth because they regretted 15:52:50
undergoing gonadectomy. Did I read that 15:52:56
correctly? 15:52:59
A. Yes, sir. 15:52:59
Q. So if I understand that sentence, 15:53:01
they are reporting -- they are measuring 15:53:07
essentially three things, how many of their 15:53:09
patients received specific medical treatments, 15:53:15
that's one, right, they are measuring that? 15:53:18
A. Well, I believe the first thing 15:53:20
that they list, sir, is, yes, the prevalence of 15:53:24
transgender people who received medical 15:53:31
treatment. 15:53:32
Q. And by prevalence, they are 15:53:33
counting their own patients as to how many of 15:53:36
them received particular medical treatments, 15:53:38
right? 15:53:41
A. Correct. 15:53:41
Q. All right. And second, they are 15:53:42
measuring the frequency within their patient 15:53:49
population of specific medical treatments, 15:53:53
right? 15:53:57
A. Correct. 15:53:58
Q. And then, third, how many of their 15:53:58
patients had a gonadectomy but then came back 15:54:02

Page 228

to them asking for hormones consistent with 15:54:07
their birth sex, right? 15:54:12
A. Yes, they analyzed regret, or what 15:54:15
they characterize as regret. 15:54:22
Q. Yeah, well, that's what I am 15:54:24
trying to get at is they are characterizing 15:54:24
regret as a patient who had a gonadectomy but 15:54:28
then came back to them asking for hormones 15:54:33
consistent with their birth sex, correct? 15:54:37
A. Yes, sir. 15:54:40
Q. Okay. And those are the only 15:54:40
people that they are characterizing as 15:54:50
regretting, correct? 15:54:51
A. I'm sorry, I am reviewing their 15:54:52
methods. 15:54:59
Q. Understood. 15:54:59
A. So I am reading, sir, at the top 15:55:35
of page 584. Some people regretted the 15:55:37
interventions they had undergone. Trans women 15:55:40
who started testosterone treatment after a 15:55:42
vaginoplasty or trans men who started estrogen 15:55:45
treatment after oophorectomy and expressed 15:55:49
regret were categorized as those who 15:55:51
experienced regret. So it appears that there 15:55:54
were two criteria; that it was both initiating 15:55:58

Page 229

hormone therapy consistent with the sex 15:56:03
assigned at birth and an expression of regret. 15:56:05
Q. Okay. But they are only people 15:56:08
who underwent a gonadectomy and then came back 15:56:13
and sought hormones consist with their birth 15:56:17
sex, correct? 15:56:21
A. I think that's roughly analogous 15:56:21
to what they are saying, sir. 15:56:29
Q. Okay. They did not measure 15:56:30
satisfaction with any particular therapy, did 15:56:35
they? 15:56:38
A. May I look at the methods? 15:56:38
Q. Of course. 15:56:42
A. So it appears that they did 15:57:15
abstract reasons for regret from the patients' 15:57:17
medical records, but they did not appear to 15:57:24
have administered a measure of patient 15:57:26
satisfaction, sir. 15:57:29
Q. But, again, Doctor, that is only 15:57:31
people who underwent a gonadectomy and then 15:57:33
came back to them requesting hormones consist 15:57:36
with their birth sex, right? 15:57:38
A. So I don't -- I don't know -- so, 15:57:40
again, I would have to read this more closely 15:57:44
to know whether they reviewed all of the 15:57:46

patients' records for expressions of regret or just that subpopulation of patients' records for expressions of regret. But you had asked about satisfaction, and they did not administer a measure of satisfaction to the patient population. 15:57:49 15:57:55 15:57:59 15:58:05 15:58:08 15:58:12

Q. They did not measure how long patients continued a particular therapy? 15:58:12 15:58:19

A. Please let me look. So your question again, sir? 15:58:26 15:59:20

Q. They did not measure how long patients continued a particular therapy? 15:59:21 15:59:23

A. So I am looking at Table 1, and it provides data about individuals starting what I would believe to be puberty suppression and stopping puberty suppression. So there may be data potentially about the duration of therapy, but I don't -- again, in this -- and, again, in Table 4 there is information about the characteristics of people who regret, and they report ages and times. 15:59:25 15:59:45 15:59:49 15:59:51 16:00:02 16:00:05 16:00:21 16:00:22 16:00:29

So there does appear to be some data in the report about duration of some treatments for some patient populations. So, again, I would have to reread the article to 16:00:30 16:00:32 16:00:35 16:00:39

give you more detail about what that looks like. 16:00:42 16:00:44

Q. In Table 4, everyone that they characterize as having regret, all of them had a gonadectomy, did they not? You have got a year listed for all of them, right? 16:00:44 16:00:48 16:00:50 16:00:53

A. So your question again, sir? 16:00:55

Q. Everyone they characterize as having regret had a gonadectomy, correct? 16:01:07 16:01:08

A. Yes, sir. 16:01:11

Q. Go to page 589. 16:01:13

A. Yes, sir. 16:01:22

Q. All right. First full paragraph towards the bottom: Our findings could be an underestimation of people with -- 16:01:22 16:01:25 16:01:29

A. Oh, I'm sorry. Sir, are you -- which paragraph are you in, sir? 16:01:30 16:01:32

Q. First full paragraph on the left-hand side, page 589. And I am towards the bottom of that paragraph. 16:01:34 16:01:35 16:01:39

A. All right. 16:01:40

Q. Our findings could be an underestimation of people with regret after gonadectomy because some might choose to go elsewhere for reversal therapy or might 16:01:41 16:01:44 16:01:49 16:01:51

experience regret without pursuing reversal surgery or hormone therapy, HT. Regret might not always result in a desire for reversal therapy, as it may be hidden from others. In addition, in our population the average time to regret was 130 months, so it might be too early to examine regret rates in people who started with HT in the past 10 years. Do you see that? 16:01:54 16:01:58 16:01:59 16:02:02 16:02:04 16:02:07 16:02:10 16:02:12

A. I do, sir. 16:02:16

Q. So they seem to be saying they were not counting people who chose not to seek reversal therapy, correct? 16:02:16 16:02:20 16:02:22

A. So your question again, sir, is? 16:02:23

Q. The authors are noting that they are not counting people who regret the gonadectomy but did not pursue reversal therapy, correct? 16:03:03 16:03:05 16:03:09 16:03:12

A. Reversal surgery or hormone therapy, yes, sir. It's common for authors at the conclusion of a study to discuss potential limitations, and I take it that that's what they are doing. 16:03:12 16:03:20 16:03:29 16:03:32 16:03:36

Q. Sure. Go to page 587. 16:03:36

A. Yes, sir. 16:03:47

Q. Bottom of the page: An 16:03:48

interesting finding is the percentage of children who were referred in childhood before 12 years of age and who started PS when the GD persisted and the eligibility criteria were fulfilled. This 40 percent of children who started PS is almost identical to the 39 percent of persistence of childhood GD reported in a previous Dutch study using a smaller cohort of children. Did I read that correctly? 16:03:54 16:03:56 16:03:59 16:04:03 16:04:07 16:04:10 16:04:13 16:04:17 16:04:22

A. You did, sir. 16:04:23

Q. So in this study, they are claiming that they are reporting essentially a 40 percent persistence rate for childhood gender dysphoria; is that right? 16:04:24 16:04:30 16:04:32 16:04:35

A. Yes, in the population that they are referring to, yes, sir. 16:04:37 16:04:44

(Thereupon, Exhibit 38, A Follow-Up Study of Boys With Gender Identity Disorder, was marked for purposes of identification.) 16:05:19 16:05:19 16:05:20

BY MR. FRAMPTON: 16:05:20

Q. I show you what I am marking as Defendants' Exhibit 38. This is a study titled A Follow-Up Study of Boys With Gender Identity Disorder. The lead author is Devita Singh. 16:05:21 16:05:22 16:05:26 16:05:30

Dr. Antommaria, are you familiar with this 16:05:53

Page 234

study? 16:05:55
A. I have read this study previously. 16:05:55
Q. And have you evaluated the 16:05:58
desistance rates calculated in this study? 16:06:21
A. What do you mean by evaluated, 16:06:26
sir? 16:06:27
Q. Are you familiar with them? 16:06:28
A. To the extent that I have 16:06:30
previously read the study, yes, sir. 16:06:35
Q. Go to page 14. 16:06:37
A. Yes, sir. 16:06:52
Q. All right. In that very first 16:06:52
partial paragraph at the top left-hand side we 16:06:57
read: It can, however, be said with certainty 16:07:03
that the vast majority of boys were seen over a 16:07:06
particular period of time when the therapeutic 16:07:10
approach of recommending or supporting a gender 16:07:12
social transition prior to puberty was not 16:07:15
made. Indeed, in the current study, there was 16:07:18
only one patient who had socially transitioned 16:07:21
prior to puberty at the suggestion and support 16:07:25
of the professionals involved in this 16:07:27
individual's care and this particular patient 16:07:30
was one of the persisters with a 16:07:32
biphilic/androphilic sexual orientation. Did I 16:07:38

Page 235

read that correctly? 16:07:40
A. You did, sir. 16:07:40
Q. Do you agree that social 16:07:41
transition may affect rates of persistence and 16:07:51
desistance? 16:07:56
A. So, sir, the care of prepubertal 16:07:56
children with gender dysphoria is not an area 16:08:11
of my clinical practice and is somewhat outside 16:08:16
of the scope of my expertise. 16:08:21
Q. Okay, fair. It's the easiest way 16:08:24
to make me stop asking the question. Let's go 16:08:27
to the next sentence there. Second, it should 16:08:32
also be recognized -- 16:08:34
A. May I go back, sir? 16:08:36
Q. Yeah, yeah, yeah, go back to where 16:08:38
I was. I am just going to read the next 16:08:40
sentence. 16:08:42
A. No, you had just implied that you 16:08:42
were going to stop asking questions, and I had 16:08:44
closed the document. 16:08:48
Q. Not yet. Second, it should also 16:08:49
be recognized that for the boys seen in the 16:08:53
current study, none who were in late childhood 16:08:56
and had likely entered puberty, Tanner Stage 2, 16:09:00
had received puberty-blocking hormone 16:09:04

Page 236

treatment, GnRH analogs, to suppress somatic 16:09:06
masculinization until sometime during 16:09:13
adolescence. Did I read that correctly? 16:09:15
A. You did, sir. 16:09:17
Q. Okay. So if I am understanding 16:09:18
what I am reading, the children in this study 16:09:20
did not receive puberty suppression at Tanner 16:09:26
Stage 2, they received it later, correct? 16:09:30
A. So, sir, it's been awhile since I 16:09:32
have read this study. You are reading material 16:09:37
out of the discussion, and it seems as though 16:09:40
she is -- that the authors are making a 16:09:46
conjecture about what individuals' state of 16:09:48
pubertal development was based on their age 16:09:53
rather than having explicitly collected data 16:09:56
about individuals' Tanner staging. So I don't 16:10:00
know about the rigor or the evidence supporting 16:10:04
that claim without reviewing their methods and 16:10:09
results. 16:10:14
Q. Do you agree that the point -- the 16:10:15
point in pubertal development -- I'm sorry, 16:10:22
strike that. You agree in this study, as with 16:10:25
the Dutch studies we discussed earlier, they 16:10:44
did not measure the point at which a child 16:10:47
experienced desistance, the age or Tanner stage 16:10:51

Page 237

at which someone experienced desistance, 16:10:56
correct? 16:10:58
A. So my general recall is that 16:10:59
studies of so-called desistance measured 16:11:05
individuals' gender identity at two separate 16:11:10
points in time, as opposed to continuously. 16:11:13
But I would have to again review the methods of 16:11:16
this study to confirm that that is, in fact, 16:11:19
what these authors did in this specific study. 16:11:22
Q. And in a study like that of that 16:11:25
design, the child could have ceased experienced 16:11:30
gender dysphoria at any point between the 16:11:37
initial visit and the follow-up visit, correct? 16:11:40
A. Yes, sir. 16:11:43
Q. Okay. Let's go back to the Cass 16:11:48
report, Exhibit 15 for you, Dr. Antommaria. 16:11:52
A. I have it, sir. 16:12:00
Q. Great, the question is do I have 16:12:00
it. Go to page 38. 16:12:06
A. Yes, sir. 16:12:35
Q. Paragraph 3.31: The most 16:12:37
difficult question is whether puberty blockers 16:12:42
do, indeed, provide valuable time for children 16:12:44
and young people to consider their options or 16:12:46
whether they effectively lock in children and 16:12:49

Page 238

young people to a treatment pathway which 16:12:52
culminates in progression to 16:12:55
feminizing/masculinizing hormones by impeding 16:13:00
the usual process of sexual orientation and 16:13:01
gender identity development. Did I read that 16:13:05
correctly? 16:13:07
A. You did, sir. 16:13:07
Q. I will keep going, I'm sorry. 16:13:08
Data from both the Netherlands and the study 16:13:12
conducted by GIDS demonstrated that almost all 16:13:15
children and young people who are put on 16:13:18
puberty blockers go on to sex hormone 16:13:21
treatment, 96.5 percent and 98 percent 16:13:23
respectively. The reasons for this need to be 16:13:26
better understood. Did I read that correctly? 16:13:28
A. You did, sir. 16:13:30
Q. Do you agree, is it consistent 16:13:31
with your experience and understanding of the 16:13:35
literature that almost all children put on 16:13:37
puberty blockers continue on to cross-sex 16:13:40
hormones? 16:13:42
A. Yes, it's consistent with my 16:13:43
understanding. I am not sure that the 16:13:47
significant majority of individuals who begin 16:13:50
puberty blockers proceed to treatment with 16:13:53

Page 239

gender-affirming hormone therapy. 16:13:56
Q. Do you agree that it is a 16:13:57
difficult question whether the effect of 16:14:03
beginning puberty blockers during adolescence 16:14:07
effectively locks children and young people to 16:14:09
a treatment pathway? 16:14:12
A. So I think it's difficult to 16:14:13
assess the statement in the Cass report that, 16:14:20
quote, the most difficult question is this one. 16:14:24
But I would agree that it is a important 16:14:30
question and methodologically difficult to 16:14:34
answer. 16:14:39
Q. Are you aware of any studies that 16:14:39
have attempted to determine whether the 16:14:45
administration of puberty blockers is changing 16:14:46
the path of gender identity development in 16:14:48
children and increasing persistence of gender 16:14:52
dysphoria or transgender identification? 16:14:55
A. Can you repeat the question, sir? 16:14:59
Q. Absolutely. Are you aware of any 16:15:04
study that has attempted to determine whether 16:15:06
puberty blockers are changing the path of 16:15:08
gender identity development in children and 16:15:11
increasing the persistence of gender dysphoria 16:15:13
or transgender identification? 16:15:18

Page 240

A. So the studies of initiating 16:15:19
individuals on puberty blockers continue to 16:15:27
follow their gender identity, so they are 16:15:30
investigating the persistence of gender 16:15:34
dysphoria. It's harder for me to understand 16:15:37
what you mean by the difference between that 16:15:41
and evaluating quote, unquote, changing the 16:15:44
path. 16:15:48
Q. Right. Any studies evaluating 16:15:48
whether the administration of puberty blockers 16:15:52
as opposed to some other intervention like 16:15:55
counseling or psychological support changes the 16:16:00
pathway? 16:16:04
MR. CHEEK: Objection, form. 16:16:04
THE WITNESS: So, in particular, I am 16:16:09
not aware of any randomized controlled trials of 16:16:10
puberty blockers and mental health care compared 16:16:16
to mental health care alone. 16:16:23
BY MR. FRAMPTON: 16:16:24
Q. Or any cohort studies? 16:16:25
A. So there are -- so I would have to 16:16:27
refresh my memory. There are cohort studies 16:16:33
that look at -- I don't recall off the top of 16:16:36
my head whether it is puberty blockers or 16:16:39
gender-affirming hormone therapy in adolescents 16:16:42

Page 241

and compare them to some types of control, 16:16:46
particularly the CoSta study. But I would have 16:16:52
to reacquaint myself with what the intervention 16:16:55
in that study is. 16:16:58
Q. The CoSta study is the only one 16:17:00
that's coming to mind? 16:17:06
A. Yes, sir. 16:17:07
Q. And you are not recalling what the 16:17:07
control was there? 16:17:09
A. Well, the control was individuals 16:17:13
who did not receive the gender-affirming 16:17:15
hormone treatment -- the gender-affirming 16:17:19
medical care. What I don't recall is whether 16:17:21
that gender-affirming medical care was puberty 16:17:25
blockers or gender-affirming hormone therapy 16:17:27
and/or both. 16:17:29
Q. Okay. And what was the conclusion 16:17:30
of that study as to whether the administration 16:17:40
of either puberty blockers or cross-sex 16:17:43
hormones is changing the path of gender 16:17:46
identity development, or was it not evaluating 16:17:49
that question? 16:17:52
A. I don't believe that there were 16:17:54
differences between the two groups in terms of 16:17:56
individuals' gender identity at the beginning 16:18:03

Page 242

of the study and at the end of the study, sir. 16:18:05
But, again, I would have to look at the 16:18:13
particular study and the outcomes that they 16:18:15
reported. 16:18:18
Q. Sure. 16:18:19
A. Are we done with the Cass review, 16:18:58
sir, for the time being? 16:19:00
Q. Yes. 16:19:01
(Thereupon, Exhibit 39, Medical 16:19:03
Decision-making in Children and Adolescents: 16:19:03
Developmental and Neuroscientific Aspects, was 16:19:03
marked for purposes of identification.) 16:19:04
BY MR. FRAMPTON: 16:19:04
Q. I hand you what I am marking as 16:19:17
Exhibit 39. This is a document titled Medical 16:19:18
Decision-making in Children and Adolescents: 16:19:25
Developmental and Neuroscientific Aspects, from 16:19:27
BMC Pediatrics. Do you have the article, 16:19:32
Dr. Antommaria? 16:19:35
A. I do. 16:19:35
Q. Are you familiar with this one? 16:19:35
A. I try to be familiar with much of 16:19:39
the literature, sir, but I am not familiar with 16:19:45
this article. 16:19:46
Q. Are you familiar with the journal, 16:19:47

Page 243

BMC Pediatrics? 16:19:51
A. I am familiar with the family of 16:19:54
BMC journals, but I do not frequently read BMC 16:19:59
Pediatrics, sir. 16:20:05
Q. Go to page 4, please. 16:20:05
A. I am on page 4, sir. 16:20:30
Q. Under adolescence and 16:20:31
decision-making competence, it says, the second 16:20:43
sentence: However, due to differences in 16:20:48
cross-talk between the various -- 16:20:51
A. Hang on one second, sir, let me 16:20:52
find it. 16:20:54
Q. Oh, I'm sorry. 16:20:54
A. Okay. Please go ahead. 16:20:56
Q. However, due to differences in 16:20:57
cross-talk between the various brain structures 16:21:03
over the course of brain development, 16:21:05
competence might fluctuate. A period in which 16:21:08
this is especially pronounced is adolescence. 16:21:11
In this period, great changes and developmental 16:21:15
leaps take place in the brain, which can have a 16:21:17
profound effect on decision-making competence. 16:21:20
Do you agree with those statements? 16:21:25
A. So, again, you have asked me, sir, 16:21:27
to read several sentences out of an article of 16:21:31

Page 244

which I am not familiar. There would be 16:21:36
reasons for me to have concern about some of 16:21:40
the claims that are being made in these 16:21:43
sentences, but I would need to read the article 16:21:45
in order to fully evaluate them. 16:21:49
Q. What concerns immediately come to 16:21:52
mind? 16:21:55
A. So in the US context, competence 16:21:56
would generally be seen as a legal category, 16:22:04
not a medical or ethical category. And the 16:22:08
relative -- relevant category would be medical 16:22:13
decision-making capacity and that the authors 16:22:18
refer to developmental leaps. And my general 16:22:25
understanding is that there are gradual changes 16:22:29
in neurodevelopment over adolescence and young 16:22:34
adulthood. But the categorization of something 16:22:39
as a developmental leap is language that I am 16:22:44
not familiar with, sir. 16:22:48
Q. Are you familiar in general with a 16:22:49
notion that adolescents -- that adolescent 16:22:57
decision making is affected particularly by 16:23:02
whether a context is, quote, hot or cold, the 16:23:08
emotional context? 16:23:15
A. I am familiar with that account of 16:23:16
increased risk taking in adolescents, yes, sir. 16:23:18

Page 245

Q. And the notion that adolescent 16:23:22
decision making is particularly affected by 16:23:26
emotionally difficult situations? 16:23:32
A. I don't know that my understanding 16:23:35
of hot contexts is specifically framed in terms 16:23:44
of -- your term again, emotionally -- 16:23:53
Q. Emotionally loaded. 16:23:55
A. Emotionally loaded circumstances. 16:23:57
My understanding is that, in part, hot 16:23:59
circumstances are related to things such as 16:24:03
peer influence and that as a clinician I try to 16:24:07
support adolescent decision making by creating 16:24:13
what in that frame -- that conceptualization 16:24:19
might be a cold environment. 16:24:23
Q. Other than peer influence, what 16:24:26
contributes to a hot context for adolescents, 16:24:29
in your understanding? 16:24:34
A. So I would say that the -- so I 16:24:50
would distinguish the relative risks and 16:24:59
benefits of the decision that is being made 16:25:02
from the emotionality of the situation and have 16:25:04
certainly interacted with adolescents in making 16:25:10
decisions that have significant risks and 16:25:12
benefits that they have nonetheless been able 16:25:15
to approach in a cool circumstance. So 16:25:18

Page 246

emotionality might be things like anger or 16:25:22
frustration, as opposed to other components of 16:25:30
emotionality. 16:25:32
Q. So are you saying that 16:25:33
emotionality can contribute to a hot 16:25:34
circumstance? 16:25:36
A. Some forms of emotionality can. 16:25:37
Q. Have you seen literature 16:25:44
suggesting that adolescents tend to overvalue 16:25:53
short-term rewards rather than long-term 16:25:58
rewards? 16:26:01
A. I am aware of literature that 16:26:01
reports that as an aggregate finding for 16:26:11
adolescent -- for children and adolescents, 16:26:13
yes, sir. 16:26:23
(Thereupon, Exhibit 40, Assessing 16:26:28
Medical Decision-Making Competence in Transgender 16:26:28
Youth, was marked for purposes of identification.) 16:26:29
BY MR. FRAMPTON: 16:26:29
Q. I am showing you what I am marking 16:27:00
as Exhibit 40, a document titled Assessing 16:27:01
Medical Decision-Making Competence in 16:27:17
Transgender Youth. Dr. Antommaria, are you 16:27:17
familiar with this document? 16:27:19
A. May I look at it for a moment, 16:27:20

Page 247

sir? 16:27:27
Q. Of course. 16:27:27
A. I am, sir. 16:27:29
Q. And this was a study of medical 16:27:30
decision-making capacity in adolescents who 16:27:40
were about to go on puberty suppression; is 16:27:45
that correct? I'm sorry, medical 16:27:50
decision-making competence. 16:27:51
A. So it is about individuals' 16:28:02
medical decision-making capacity to make 16:28:07
decisions about pubertal suppression, yes, sir. 16:28:10
Q. Okay. And the structure of this 16:28:25
study is the patients were all at a point where 16:28:29
the clinician was ready to prescribe puberty 16:28:35
suppression, and then they did both an informed 16:28:38
consent interview and then an interview where 16:28:42
they applied this MacCAT-T instrument, correct? 16:28:46
A. So I am just reviewing the method, 16:28:54
sir. 16:28:56
Q. Yep. 16:28:56
A. So yes, the population were 16:29:31
adolescents who were -- the language that the 16:29:36
report uses were about to start PS, or puberty 16:29:39
suppression. And the second part of your 16:29:43
question, sir? 16:29:48

Page 248

Q. So they did an informed consent 16:29:48
interview with them that was videotaped, 16:29:51
correct? 16:29:53
A. I'm sorry, I am looking at their 16:29:54
procedure, sir. 16:30:03
Q. And I am looking in procedures, 16:30:03
that this standard IC session was videotaped 16:30:14
and used to establish the reference standard. 16:30:17
A. Yes. And then it says in the 16:30:21
following sentence after the IC or informed 16:30:23
consent session, the MacCAT-T interview was 16:30:26
administered by one of the researchers. 16:30:31
Q. Okay. Is MacCAT-T an instrument 16:30:32
that you have ever used? 16:30:35
A. To the -- it is not, sir. 16:30:36
Q. All right. So with the informed 16:30:44
consent interviews, staying in procedures, they 16:30:54
then had two experts and the clinician review 16:30:58
those to determine if they thought the 16:31:07
adolescent exhibited medical decision-making 16:31:12
competence, correct? 16:31:14
A. Yes, medical decision-making 16:31:15
capacity, sir. 16:31:20
Q. Yeah. And then they had three 16:31:20
different people review the MacCAT-T video and 16:31:24

Page 249

make a decision based on that, whether they 16:31:28
believed the adolescent exhibited MDC, correct? 16:31:31
A. Yes, sir. 16:31:34
Q. And on the MacCAT-T, if you flip 16:31:44
back a page, you can see where they explain 16:31:48
what that is. There is no cutoff score, 16:31:51
correct? 16:32:00
MR. CHEEK: Objection to form. 16:32:12
THE WITNESS: So I am reading the 16:32:13
MacCAT-T is a quantitative semi-structured 16:32:17
interview used to assess the four medical 16:32:19
decision-making capacity criteria. I am 16:32:22
continuing to read, sir. 16:32:28
BY MR. FRAMPTON: 16:32:28
Q. You will get there. 16:32:29
A. So yes, it states that an overall 16:32:37
cutoff score for the MDC is not provided. 16:32:40
Q. So no particular score means that 16:32:43
the adolescent has medical decision-making 16:32:49
competence, correct? 16:32:52
A. So it states, sir, that the 16:32:53
overall cutoff score for the MDC is not 16:33:05
provided. The assessor weighs the sub scale 16:33:08
scores along with conceptual information and 16:33:11
judges the MDC in each individual case. I 16:33:14

Page 250

would assume that -- and we have talked about 16:33:18
the GRADE criteria earlier today. And, again, 16:33:21
often tools rely on individual judgment in 16:33:26
applying them. 16:33:31
Q. So the reviewers could -- one 16:33:31
reviewer could regard a score of 14 as 16:33:36
generally establishing competence, and one 16:33:39
reviewer could regard a score of 18 as 16:33:41
generally establishing competence, correct? 16:33:44
A. Well, that's assuming that they 16:33:46
were judging competence on the basis of a 16:33:51
score, as opposed to weighing the scores and 16:33:53
other contextual information. It would suggest 16:33:57
that using the cutoff score in the way you 16:34:00
suggest was not the way the tool was designed. 16:34:03
Q. Go to Table 2, please, if you 16:34:06
would. 16:34:09
A. On what page, sir? 16:34:12
Q. It's going to be page 6. 16:34:13
A. I am on page 6, sir. 16:34:16
Q. Okay. The study involved 16 natal 16:34:18
boys, correct? 16:34:25
A. Yes, 16 individuals who were 16:34:26
assigned male at birth. 16:34:30
Q. So far fewer natal males than 16:34:31

Page 251

natal females, right? 16:34:33
A. So there were 58 individuals 16:34:35
assigned female at birth in the study, sir. 16:34:38
Q. And if we go down to Table 3 and 16:34:41
count the number of natal males who were judged 16:34:49
incompetent on one or both standards, how many 16:34:54
do you get? 16:34:59
A. So if you combine the reference 16:35:00
standard and the MacCAT-T, it would appear 11, 16:35:20
sir. 16:35:26
Q. Now, how many of them were natal 16:35:26
males? 16:35:28
A. Four. It appears that the number 16:35:29
is four, sir. 16:35:40
Q. So 25 percent of natal males, 16:35:41
correct, adjudged incompetent on one or both 16:35:43
standards? 16:35:47
MR. CHEEK: Objection, form, 16:35:52
misstates evidence. 16:35:53
MR. FRAMPTON: No, it doesn't. But 16:35:55
go ahead. 16:35:56
THE WITNESS: Four out of 11, sir. 16:35:57
BY MR. FRAMPTON: 16:36:00
Q. I'm sorry, four out of 16 natal 16:36:01
males in the study, correct? 16:36:04

Page 252

A. Oh, can you repeat your question, 16:36:06
sir? 16:36:09
Q. Does it appear that four out of 16:36:09
the 16 natal males in the study were adjudged 16:36:14
incompetent on one or both standards? 16:36:18
A. Yes, four out of 16, sir. 16:36:23
Q. And that is 25 percent, is it not? 16:36:25
A. Yes, sir. 16:36:29
Q. Okay. Go to -- stay on that same 16:36:29
page. Go to the main column of text on the 16:36:32
right-hand side, first full paragraph. Do you 16:36:34
see -- 16:36:46
A. Yes, sir. 16:36:46
Q. -- where it says: In all of these 16:36:47
11 adolescents assessed incompetent except for 16:36:50
one, the involved clinician had no doubts about 16:36:53
medical decision-making competence. Do you see 16:36:59
that? 16:37:01
A. You read that sentence correctly, 16:37:01
sir. 16:37:04
Q. So in the 11 cases where the 16:37:04
adolescent was assessed incompetent on one or 16:37:08
both measures, the clinician got it wrong 10 16:37:12
out of 11 times; is that right? 16:37:19
A. Can I read the study, sir? 16:37:21

Page 253

Q. Uh-huh. 16:37:29
A. So I don't -- so the sentence that 16:38:18
you are quoting, sir, appears in the 16:39:06
discussion. I am just having difficulty seeing 16:39:10
where in the results, including the tables, 16:39:14
it's reporting the results that in all of these 16:39:18
11 adolescents assessed incompetent except for 16:39:22
one, the involved clinician had no doubts about 16:39:26
the MDC. 16:39:29
For example, in Table 3 where 16:39:32
those 11 individuals are described, it 16:39:35
describes the results for the reference 16:39:37
standard in the MacCAT-T, but I don't see a 16:39:40
separate column for the involved clinician. So 16:39:43
I am just having trouble putting the discussion 16:39:51
together with the results that the 16:39:54
investigators provide. 16:39:58
Q. They could be discussing results 16:39:58
that they did not separately report in a table, 16:40:00
correct? 16:40:02
MR. CHEEK: Objection, calls for 16:40:03
speculation. 16:40:05
THE WITNESS: In general, it would be 16:40:08
best practice to include all of the results in the 16:40:10
results section and not introduce new results in 16:40:15

Page 254

the discussion. So I am just having difficulty 16:40:19
reconciling that with reacquainting myself with 16:40:22
this study this afternoon, sir. 16:40:26
BY MR. FRAMPTON: 16:40:27
Q. Okay. But you do see that in the 16:40:28
discussion, at least, they report that in 10 16:40:30
out of the 11 adolescents assessed incompetent, 16:40:35
the clinician believed the adolescent was 16:40:38
competent, correct? 16:40:40
A. Yes, I see that sentence, sir. 16:40:41
Q. All right. I am going to move on. 16:40:44
(Thereupon, Exhibit 41, The 16:40:46
Competency of Children and Adolescents to Make 16:40:46
Informed Treatment Decisions, was marked for 16:40:46
purposes of identification.) 16:40:46
BY MR. FRAMPTON: 16:40:46
Q. Show you what I am marking as 16:40:47
Exhibit 41. I am handing you an article titled 16:40:53
The Competency of Children and Adolescents to 16:41:16
Make Informed Decisions, from 1982. Do you 16:41:17
recognize this article, sir? 16:41:20
A. I do, sir. 16:41:20
Q. And this is a study that you 16:41:21
cited, correct? 16:41:34
A. I believe so, sir. 16:41:34

Page 255

Q. Look on page 1592, please. 16:41:36
A. Yes, sir. 16:41:46
Q. All right. The top left-hand 16:41:46
corner, the second sentence says: From 25 16:41:48
dilemmas that were pilot tested, four were 16:41:50
chosen because they represented a range of 16:41:52
complexity, content, and difficulty and were 16:41:55
not viewed as being too sensitive or disturbing 16:41:57
to present to the youngest subjects. Of these 16:41:59
four dilemmas, two described treatment 16:42:05
alternatives for medical problems, diabetes and 16:42:07
epilepsy, and two described alternatives for 16:42:10
psychological problems, depression and 16:42:12
enuresis. Did I read that correctly? 16:42:17
A. You did, sir. 16:42:17
Q. So the authors report that they 16:42:18
avoided scenarios that they deemed too 16:42:31
sensitive or disturbing, correct? 16:42:33
A. That's what you read, sir. 16:42:36
Q. And you don't have any way of 16:42:38
knowing if they would have judged gender 16:42:39
dysphoria too sensitive or disturbing, do you? 16:42:41
A. So based on what you have read, 16:42:45
sir, they don't identify the topics of the 16:42:50
scenarios that they excluded. 16:42:54

Page 256

Q. The scenarios they did include do 16:42:55
not involve potential loss of fertility, 16:43:00
correct? 16:43:10
A. That would not be a major risk of 16:43:10
diabetes, epilepsy, depression, or enuresis, 16:43:14
sir. 16:43:19
Q. Impairment of neurodevelopment? 16:43:19
A. I'm sorry, sir? 16:43:22
Q. Would impairment of 16:43:23
neurodevelopment be a major risk of any of 16:43:26
those diseases? 16:43:28
A. Potentially epilepsy, sir. 16:43:29
Q. If I understand the basic 16:43:32
structure of this study, they were presenting 16:43:46
the participants with these sort of medical 16:43:49
scenarios and then applying a couple of -- a 16:43:54
series of instruments to how they made 16:43:57
decisions based on the scenario, correct, in at 16:43:59
least general terms? 16:44:06
A. One moment, sir. So, yes, they 16:44:08
were presented with the dilemmas and then 16:44:37
interviewed about decision making relative to 16:44:39
those dilemmas, sir. 16:44:41
Q. Go to page 1596, please. 16:44:42
A. Yes, sir. 16:44:58

Page 257

Q. And before I ask you, these are -- 16:44:58
they are presenting these folks with 16:45:01
hypothetical scenarios, correct? 16:45:05
A. Yes, sir. 16:45:08
Q. So, by definition, the participant 16:45:11
has no sort of emotional stake in the scenario 16:45:14
that's being presented, correct? It's not a 16:45:20
medical problem they are actually experiencing, 16:45:22
right? 16:45:24
A. So I would have to look at their 16:45:25
inclusion and exclusion criteria to know if 16:45:29
they excluded individuals who might be 16:45:33
experiencing those conditions. Certainly, 16:45:36
enuresis is relatively common, and so I 16:45:43
don't -- again, looking at this again today, I 16:45:44
don't know whether they explicitly excluded 16:45:48
individuals with enuresis from this study. 16:45:51
Q. As a general matter, these were 16:45:53
hypothetical scenarios, correct? 16:45:56
A. That's my understanding of this 16:45:58
study. 16:46:02
Q. So unless a participant had a 16:46:02
particular one of these, they would not have a 16:46:04
particular emotional stake in the treatment 16:46:07
decision, correct? 16:46:10

Page 258

A. So, again, sir, I think that 16:46:10
that's an overgeneralization. Certainly, 16:46:19
diabetes and epilepsy and depression are very 16:46:21
common in the general population so that even 16:46:24
if the participant in the study did not have 16:46:26
one of those conditions, one of their family 16:46:29
members may have had those conditions and they 16:46:30
may have had a significant emotional investment 16:46:33
in the condition. Again, I don't know that 16:46:35
those individuals were excluded from the study. 16:46:36
Q. Page 1596, the first full 16:46:39
paragraph. It says, second sentence: Subjects 16:46:49
clearly were not influenced by a current 16:46:53
physical illness or physiological disorder or 16:46:58
by factors such as weakness, confusion, 16:46:58
depression, or anxiety, which sometimes 16:47:02
accompany such conditions. These factors may 16:47:02
decrease individuals' ability to use their 16:47:05
cognitive capacities in health care decision 16:47:08
making. Do you see that? 16:47:11
A. Which paragraph are you in, sir? 16:47:12
Q. Right-hand column, first full 16:47:14
paragraph. 16:47:17
A. So, again, sir, I take it that 16:47:33
that description is stating that the 16:47:36

Page 259

participant in the study doesn't currently have 16:47:39
a physical illness or a psychological disorder. 16:47:41
I think the claim that I was making is that 16:47:44
certainly their parent or a family member might 16:47:47
have diabetes or epilepsy. I don't see that 16:47:50
that possibility is is excluded by that 16:47:53
sentence, sir. 16:47:55
Q. You don't have any reason to 16:47:56
disagree with the author's sentence, do you? 16:47:58
A. May I read the full paragraph, 16:48:01
sir? 16:48:08
Q. Actually, I'll leave it. Let me 16:48:14
go to the paragraph on -- left-hand column, 16:48:16
last paragraph. Although the performance of 16:48:19
the 14-year-olds was generally equivalent to 16:48:23
that of the adults, numerically small but 16:48:26
statistically significant differences between 16:48:29
these groups were found for the epilepsy 16:48:32
dilemma on two of the four competency scales. 16:48:35
These findings may relate to the concerns of 16:48:37
early adolescence about body image and physical 16:48:39
attractiveness, since the recommended 16:48:41
medication rejected by 12.5 percent of the 16:48:43
14-year-olds was described as sometimes leading 16:48:47
to periodontal problems and occasionally 16:48:50

Page 260

causing an excess growth of body hair, 16:48:52
hirsutism. Did I read that correctly? 16:48:56
A. You did, sir. 16:48:57
Q. And then it goes on to say: These 16:48:57
differences do suggest that competency, as 16:49:00
defined by certain legal tests, may depend to 16:49:02
some degree upon the dimensions of the specific 16:49:05
decision-making context. 16:49:07
A. You read that correctly, sir. 16:49:12
Q. Do you recall from looking at this 16:49:14
study that the 14-year-olds experienced 16:49:17
decreased decision-making competence with 16:49:21
respect to matters affecting body image? 16:49:23
A. Prior to your reading this, sir, I 16:49:27
did not recall that nuance of the study 16:49:32
results. 16:49:37
Q. Okay, that's fine. I'll move on. 16:49:37
(Thereupon, Exhibit 42, A Qualitative 16:49:46
Study of Adolescents' Understanding of Biobanks 16:49:46
and Their Attitudes Toward Participation, 16:49:46
Re-contact, and Data Sharing, was marked for 16:49:46
purposes of identification.) 16:49:47
BY MR. FRAMPTON: 16:49:47
Q. I hand you what I am marking as 16:50:02
Defendants' Exhibit 42. And this is an article 16:50:03

Page 261

titled A Qualitative Study of Adolescents' 16:50:19
Understanding of Biobank and Their Attitudes 16:50:23
Towards Participation, Re-contact, and Data 16:50:25
Sharing; is that right? 16:50:28
A. Yes, sir. 16:50:29
Q. You obviously recognize this one, 16:50:30
do you not? 16:50:33
A. I do, sir. 16:50:34
Q. You were one of the investigators 16:50:34
here, correct? 16:50:38
A. Correct, sir. 16:50:38
Q. What are biobanks? 16:50:39
A. Biobanks are large collections of 16:50:41
individuals' biological specimens and data that 16:50:49
are utilized to conduct research potentially at 16:50:54
a particular point in time and then in the 16:50:58
future. 16:51:03
Q. They are not used for treatment of 16:51:04
the individual patients who contribute, 16:51:07
correct? 16:51:10
A. So there is an ongoing debate 16:51:10
about the potential return of medically 16:51:17
actionable results to participants in biobanks. 16:51:20
But yes, the primary intention of a biobank is 16:51:24
to support research, not clinical care. 16:51:27

Page 262

Q. And in this study, you personally conducted all of the interviews, correct? 16:51:31 16:51:38

A. No, sir; I did not personally conduct the interviews. 16:51:40 16:51:44

Q. Oh, all right. Look at page 931. Oh, I see what happened here. You are not A.M.M. 16:51:45 16:51:52 16:51:58

A. I am not, sir. 16:51:58

Q. You are A.M.A. All right. So one of your colleagues conducted the interviews, correct? 16:51:59 16:52:04 16:52:06

A. Ms. Murad, the primary author, who was a graduate student in the genetic counseling program, I believe conducted the interviews. 16:52:06 16:52:14 16:52:17 16:52:20

Q. Okay. Go to page 932. 16:52:20

A. I am on 932, sir. 16:52:38

Q. All right. Under results, it says sort of second full paragraph, the second sentence: Following the presentation of the educational information about biobanks, participants were asked to restate in their own words what they thought a biobank was and were then asked to describe the benefits of participating in a biobank. Many participants 16:52:39 16:52:45 16:52:47 16:52:49 16:52:51 16:52:53 16:52:56 16:52:59

Page 263

did not have a good understanding of biobanks, and then it references Table 2. Did I read that correctly? 16:53:01 16:53:04 16:53:07

A. You did, sir. 16:53:07

Q. Was that, indeed, something you found in this study, that most of the participants did not ultimately exhibit a good understanding of biobanks? 16:53:08 16:53:11 16:53:13 16:53:19

A. So what a biobank, as you had asked me to describe a biobank, is not a concept that is very familiar or seemingly to adolescents. They were provided brief educational information. But as Table 2 suggests, that after that brief educational intervention, there were some misunderstandings that persisted, yes, sir. 16:53:21 16:53:30 16:53:32 16:53:38 16:53:39 16:53:43 16:53:47 16:53:51

Q. Go to page 935. 16:53:53

A. I am on 935, sir. 16:54:03

Q. All right. You list -- under discussion, you list four numbered findings, correct? 16:54:05 16:54:07 16:54:13

A. The first paragraph in the discussion includes four numbered findings, yes. 16:54:13 16:54:16 16:54:18

Q. The first of which is very few 16:54:18

Page 264

adolescents had previously heard of biobanks, and many of them had misconceptions about biobanks that persisted even after attempts at education, correct? 16:54:20 16:54:22 16:54:25 16:54:29

A. Correct, sir. 16:54:30

Q. Dropping down to the next paragraph, it says: Misunderstandings about the purpose of biobanks persisted throughout the interview. Some of these misunderstands were sufficient, for example, that the primary purpose of the biobank was clinical care rather than research, to suggest that some adolescents may have insufficient background knowledge to make an adequately informed decision about participation. Did I read that correctly? 16:54:31 16:54:35 16:54:41 16:54:42 16:54:45 16:54:46 16:54:49 16:54:52 16:54:54 16:54:57

A. You did, sir. 16:54:58

Q. So in this study, you found that at least some of your participants would not have been in a sufficient place to make an adequately informed decision about participating in a biobank, correct? 16:54:59 16:55:03 16:55:05 16:55:09 16:55:10

A. So it is to say that it is not uncommon for adolescents or adults to confuse research with clinical practice and, hence, the concept of therapeutic misconception. The 16:55:12 16:55:17 16:55:22 16:55:26

Page 265

objective of this study was not to consent individuals for participation in biobanks. And so yes, after a brief education about biobanks, there was still inadequate knowledge about what a biobank was. We did not conduct further interventions to see if that misunderstanding was persistent or whether that was surmountable with new -- with additional or improved educational interventions, sir. 16:55:30 16:55:34 16:55:41 16:55:44 16:55:47 16:55:51 16:55:54 16:55:58 16:56:01

Q. Go over to the next column. Tell me what the effect heuristic is. 16:56:03 16:56:10

A. Which paragraph are you in, sir? 16:56:16

Q. The second full paragraph on the second column of 935. 16:56:18 16:56:19

A. So the sentence in the paragraph reads, sir: The affect heuristic is when individuals who have favorable feelings about participating in an activity tend to judge the risks of participation as low and the benefits as high. 16:56:30 16:56:32 16:56:36 16:56:38 16:56:40 16:56:43

Q. And so the basic idea is if someone comes into -- if someone comes in with a preconception with favorable feelings about a particular activity or intervention, that may color their perception of the risks and 16:56:44 16:56:51 16:56:59 16:57:03 16:57:06

Page 266

benefits, correct? 16:57:10
A. So, sir, given the increasing 16:57:11
literature about behavioral economics, we 16:57:17
increasingly understand the heuristics that 16:57:22
both adolescents and adults use in decision 16:57:25
making. And in clinical practice, we attempt 16:57:28
to recognize those potential heuristics and 16:57:31
lead individuals in decision making in ways 16:57:37
that address ways that those heuristics might 16:57:40
mislead them. 16:57:45
Q. My question was is it the case 16:57:46
that if someone -- I understand what you are 16:57:50
saying you do in practice. My question is if 16:57:52
someone comes in with favorable feelings about 16:57:55
a particular activity, do we understand that 16:57:59
that may lead them to judge the risks as low 16:58:02
and the benefits as high? 16:58:08
MR. CHEEK: Objection, form. 16:58:10
THE WITNESS: So, sir, this is a 16:58:12
paragraph from the discussion. It is speculating 16:58:14
about a potential cause of a finding. The 16:58:18
sentence at the end of the paragraph reads: 16:58:23
Additional research would be needed to validate 16:58:26
this hypothesis. 16:58:28
BY MR. FRAMPTON: 16:58:30

Page 267

Q. And I am just saying as a general 16:58:31
matter, is that what the -- is the affect 16:58:33
heuristic something that you are aware of from 16:58:36
the literature? 16:58:38
A. We cite to the literature in this 16:58:39
discussion, sir. 16:58:43
Q. Right, right. And did I 16:58:43
accurately describe the affect heuristic as the 16:58:46
idea that if someone comes in with a favorable 16:58:51
view of a particular activity, then they tend 16:58:54
to judge the risks as low and the benefits as 16:58:56
high? 16:58:59
A. Yes, sir. And we discussed 16:58:59
earlier the risks of bias and masking. And 16:59:01
part of the reason for masking is to affect to 16:59:06
prevent those types of heuristics from 16:59:12
influencing the results of studies. 16:59:14
Q. Do you contend that Tanner Stage 2 16:59:16
adolescents can meaningfully understand the 16:59:21
importance of healthy sexual relationships to 16:59:25
mental health and happiness across the decades 16:59:26
of adult life? 16:59:29
A. Can you repeat your question, sir? 16:59:30
Q. Yeah. Do you contend that a 16:59:34
Tanner Stage 2 adolescent can meaningfully 16:59:35

Page 268

understand the importance of healthy sexual 16:59:38
relationships to mental health and happiness 16:59:40
across the decades of adult life? 16:59:42
MR. CHEEK: Objection, form. 16:59:45
THE WITNESS: So I think the 16:59:47
fundamental thing to say is that medical decision 16:59:52
making for adolescents generally requires parental 16:59:57
consent and that adolescents are not being -- 17:00:01
Tanner Stage 2 adolescents are not being asked to 17:00:06
give informed consent to the use of GnRH analogs. 17:00:10
I would say that there is variability in the 17:00:17
medical decision-making capacity of adolescents 17:00:21
and that there are adolescents who are capable of 17:00:27
understanding the implications of a variety of 17:00:32
medical treatments for their adult life, including 17:00:36
having biologically related children. 17:00:42
BY MR. FRAMPTON: 17:00:44
Q. You believe that they can 17:00:46
understand the importance of being able to 17:00:47
become a biological parent? 17:00:50
A. Can you repeat the question, sir? 17:00:52
Q. Sure. You believe that a Tanner 17:00:55
Stage 2 adolescent can meaningfully understand 17:00:58
the importance of becoming -- being able to 17:01:00
become a biological parent? 17:01:03

Page 269

A. Yes, I believe that there are 17:01:04
adolescents who are at Tanner Stage 2 who are 17:01:08
capable in a meaningful way of understanding 17:01:11
that. 17:01:17
Q. And also meaningfully 17:01:17
understanding the importance of healthy sexual 17:01:18
relationships? 17:01:21
A. Can you be more specific about 17:01:21
what you mean by healthy sexual relationships, 17:01:31
sir? 17:01:34
Q. Sure, the ability to orgasm. 17:01:34
MR. CHEEK: Objection, form. 17:01:37
THE WITNESS: I would say that many 17:01:45
Tanner Stage 2 adolescents do not have personal 17:01:50
experience with the experience that you have 17:01:54
described, but certainly they may well understand 17:01:57
the importance of sexuality broadly understood in 17:02:01
their parental relationships and may be able to 17:02:06
understand in some ways the way that that would 17:02:08
affect the relationships which they wish to have 17:02:11
as an adult. 17:02:14
BY MR. FRAMPTON: 17:02:14
Q. And I simply asked the question 17:02:17
because would you agree that anorgasmia is one 17:02:19
of the risks associated with starting pubertal 17:02:23

suppression at Tanner Stage 2 and continuing immediately to cross-sex hormones, particularly for natal males? 17:02:27 17:02:29 17:02:32

A. So I understand that there is some discussion of that in the literature. I haven't seen substantial data about the frequency with which that occurs. 17:02:33 17:02:40 17:02:43 17:02:48

MR. FRAMPTON: Let's take a quick break. I think I have got about five minutes left. 17:02:51 17:02:52 17:02:54

(Recess taken.) 17:02:56

MR. FRAMPTON: Let's go back on the record. 17:04:25 17:04:26

BY MR. FRAMPTON: 17:04:26

Q. Dr. Antommaria, are you aware of any published literature documenting a Tanner Stage 2 natal male beginning puberty suppression at that point and continuing on cross-sex hormones immediately and then in adult life being able to achieve orgasm? 17:04:26 17:04:28 17:04:36 17:04:41 17:04:43 17:04:47

MR. CHEEK: Objection, form. 17:04:50

THE WITNESS: So that's not a subject that I have searched the literature in order to find an answer for, sir. 17:04:51 17:04:57 17:04:59

BY MR. FRAMPTON: 17:05:00

Q. So you are not aware of one sitting here today; is that correct? 17:05:01 17:05:02

A. I am not, but there would not be a particular reason that I would know whether that type of literature exists or not. 17:05:03 17:05:10 17:05:14

Q. It's not something you have ever looked for? 17:05:16 17:05:17

A. No, it's not something I have specifically looked for, sir. 17:05:18 17:05:21

MR. FRAMPTON: I think we are done. In fact, I know we are done. 17:05:24 17:05:26

(Thereupon, the deposition was concluded at 5:05 p.m.) 17:05:41 17:05:42

STATE OF OHIO)
COUNTY OF MONTGOMERY) SS: CERTIFICATE

I, Monica K. Schrader, a Notary Public within and for the State of Ohio, duly commissioned and qualified,

DO HEREBY CERTIFY that the above-named ARMAND H. ANTOMMARIA, M.D., Ph.D., FAAP, HEC-C, was by me first duly sworn to testify the truth, the whole truth and nothing but the truth.

Said testimony was reduced to writing by me stenographically in the presence of the witness and thereafter reduced to typewriting.

I FURTHER CERTIFY that I am not a relative or Attorney of either party, in any manner interested in the event of this action, nor am I, or the court reporting firm with which I am affiliated, under a contract as defined in Civil Rule 28(D).

IN WITNESS WHEREOF, I have hereunto set my hand and seal of office at Dayton, Ohio, on this 4th day of May, 2023.

MONICA K. SCHRADER
NOTARY PUBLIC, STATE OF OHIO
My commission expires 4-18-2025

To: Jason R. Cheek, Esq.
Re: Signature of Deponent Armand H. Antommaria, M.D., Ph.D.
Date Errata due back at our offices: 30 days

Greetings:
This deposition has been requested for read and sign by the deponent. It is the deponent's responsibility to review the transcript, noting any changes or corrections on the attached PDF Errata. The deponent may fill out the Errata electronically or print and fill out manually.

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I, the undersigned, do hereby certify that I have read the transcript of my testimony, and that

___ There are no changes noted.
___ The following changes are noted:

Pursuant to Civil Procedure, Rule 30. ALA. CODE § 5-30(e) (2017). Rule 30(e) states any changes in form or substance which you desire to make to your testimony shall be entered upon the deposition with a statement of the reasons given for making them. To assist you in making any such corrections, please use the form below. If additional pages are necessary, please furnish same and attach.

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DEPONENT'S SIGNATURE

Sworn to and subscribed before me this ___ day of
_____, _____.

_____
NOTARY PUBLIC / My Commission Expires:_____