IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

WENDY B. DOLIN, Individually and as Independent Executor of the Estate of STEWART DOLIN, Deceased,	)	Docket No. 12 CV 6403
Plaintiffs,	)	Chicago, Illinois
v.	)	March 15, 2017 1:31 p.m.
SMITHKLINE BEECHAM CORPORATION, d/b/a GLAXOSMITHKLINE, a Pennsylvania Corporation,	)	
Defendant.	)	

VOLUME 2-B
TRANSCRIPT OF PROCEEDINGS
BEFORE THE HONORABLE WILLIAM T. HART, and a Jury

APPEARANCES:

For the Plaintiff:
BAUM HEDLUND ARISTEI & GOLDMAN PC by
MR. R. BRENT WISNER
MR. MICHAEL L. BAUM
12100 Wilshire Boulevard, Suite 950
Los Angeles, California 90025
(310) 207-3233

RAPOPORT LAW OFFICES, P.C. by
MR. DAVID E. RAPOPORT
MS. MELANIE J. VAN OVERLOOP
MR. MATTHEW S. SIMS
20 North Clark Street, Suite 3500
Chicago, Illinois 60602
(312) 327-9880

Court Reporter:
GAYLE A. McGUIGAN, CSR, RMR, CRR
CHARLES ZANDI, CSR, RPR, FCRR
Federal Official Court Reporters
219 South Dearborn, Room 2318-A
Chicago, Illinois 60604
(312) 435-6047
Gayle_McGuigan@ilnd.uscourts.gov

APPEARANCES (continued:)

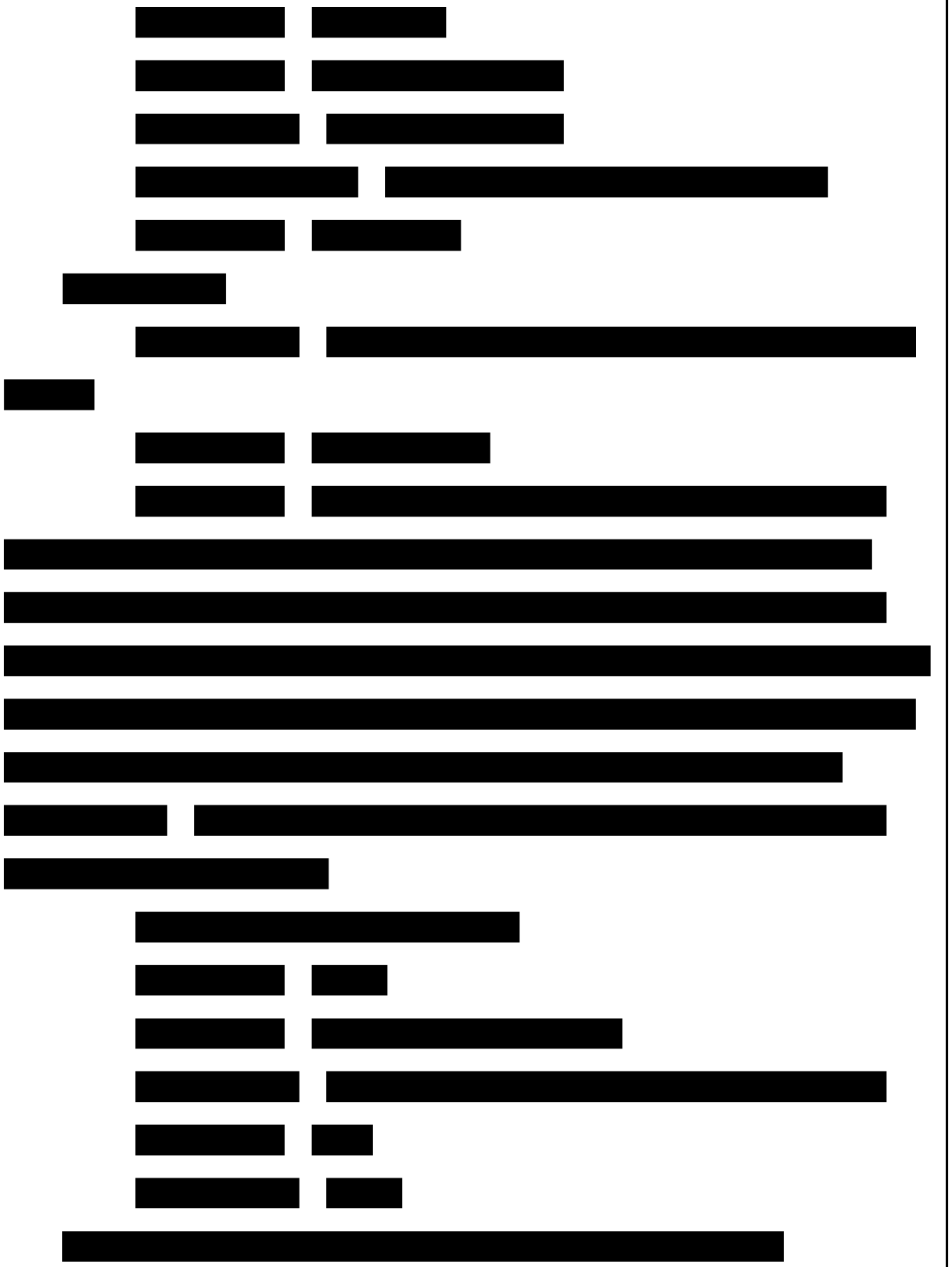
For Defendant GlaxoSmithKline:

KING & SPALDING by
MR. TODD P. DAVIS
MR. ANDREW T. BAYMAN
MS. HEATHER HOWARD
1180 Peachtree Street N.E.
Atlanta, Georgia 30309
(404) 572-4600

KING & SPALDING, LLP by
MS. URSULA M. HENNINGER
100 North Tryon Street, Suite 3900
Charlotte, North Carolina 28202
(704) 503-2631

SNR DENTON US, LLP by
MR. ALAN S. GILBERT
233 South Wacker Drive, Suite 7800
Chicago, Illinois 60606
(312) 876-8000

(In open court outside the presence of the jury:)



(Jury in at 1:32 p.m.)

THE COURT: All right. Thank you very much. Ladies and Gentlemen, please be seated, and we will resume.

You may proceed, sir.

MR. WISNER: Thank you, your Honor.

DIRECT EXAMINATION (Resumed)

BY MR. WISNER:

Q All right, Dr. Healy. Before lunch we were in the process of discussing akathisia, and specifically we were addressing the internal manifestations of it.

I think the last question I asked you was -- and if -- I apologize if we've already covered this, but when would you expect to see akathisia emerge relative to the initiation of an SSRI?

A It can be there from very early on after you take your first pill. Classically it builds up over the first week or two. It can happen with every change of dose. It can potentially happen if you are put on other pills that could play into it. It happens when you withdraw from the drug. That's one of the key times when it can also happen. For the most part, if I see a person having akathisia, I will want to stop the drug and change them to something completely different; but some people figure that it can habituate if you wait, but this always seemed to me to be a slightly tricky thing to do.

Q What does it mean to habituate, Doctor?
A Well, over time it wears off. It's a bit like -- lots of people when they take an SSRI may feel nauseated, particularly during the first few days or weeks, but over time that wears off. Whether it gets less severe or you just learn to live with it is a bit less clear. These things aren't teased out very well.
Q Now, if somebody -- would you expect a person to always experience this reaction to an SSRI?
A No. There are clearly people who can have an SSRI and have no problems. They don't have this reaction at all.

That's partly because, as I've indicated to you, we're all different as regards our serotonin systems.

There are people who can have their first SSRI and have a very bad reaction and will have the same kind of reaction to every SSRI they take every time they take it.

Then there are people who are in the middle who can maybe perhaps not have an awfully bad reaction, not a great reaction perhaps, but not a malignant reaction like this during the first SSRI that they take. But later on, if they halt that drug and go on to a different SSRI maybe months or years later, they can react badly to that.
Q Have you in your clinical experience ever had a patient who didn't have an akathisia reaction to an SSRI at one point but later on in treatment years later did?

A Yes, I have.
Q Can you explain why that is or do you know why that is?
A I can offer a few thoughts, but I'm not sure this is going to be absolutely conclusive.

One of the things obviously is if you've had an SSRI at one point and maybe had one five or ten years later, we're all a bit older five or ten years later, and as we age, the dose of most drugs should drop. And akathisia is a thing that's dose-dependent. You might take a low dose of an SSRI now and have no problems whatsoever; but if you're put on a higher dose, you do have the problem.

So as we age, there's always the risk that where you might have had the drug before without problems, you can have it later on.

The other thing is a lot of SSRIs, and maybe all of them to some extent, cause you to get slightly hooked to them while you're on them, so when you come off them, there's a degree of --

MR. BAYMAN: Objection, your Honor. We're getting -- this has nothing to do with the issues in this case.

THE COURT: Overruled.

Proceed.

BY THE WITNESS:
A So -- so what I've seen can happen then is while some people can withdraw without any big problem, others can have

terrible problems. But as I indicated to you, at least I think, the serotonin system is not abnormal to begin with before you get a pill. After you get a pill, it's not the way it was before you got a pill. We do make it, to an extent, abnormal. We're doing this in order to try and produce a good outcome; but your serotonin system to some extent after your first course of treatment has been destabilized, so it's not quite the same serotonin system if you get put on an SSRI again a few months later or a few years later.

BY MR. WISNER:

Q And that's actually going to go to my next question, Doctor.

If -- what impact does an SSRI have on the -- the sort of -- the serotonin system itself? What happens to it after you've taken them for a year or so?

A Well, there's very few drugs in medicine that put anything right. Most of the treatments we give, whether they're for bone problems or gut problems or nervous problems, they're -- you know, it's maybe a slightly loaded word, but this is one of the core principles of medicine, that every drug is a poison; but the magic of medicine is that we want to bring good out of the useful poison. Essentially, whether it's medicine with a poison or surgery with mutilation -- like I broke my collar bone recently, and they put a plate in it, you know, but they had to mutilate me -- but they're doing it in order to produce

a good outcome. But you have to know that's what you're doing. Both the doctor and the patient need to know, you know, we're not necessarily putting things right. We're taking risks when we do this. And we can only take the right risks if we have the right information.

Q If a person has been taking an SSRI for an extended period of time, like a thousand pills or something, would you expect that their serotonin system could change?

A Yes, absolutely.

Q And could that then lead to later initiations of the drug causing reactions you didn't see before?

A Yes.

Q All right. So we've talked about akathisia for a bit.

Let's explore the other -- actually, let me ask you a few more questions about that since we're still on the topic.

The manifestations of akathisia that you've seen and you've documented in the literature, is it related to age?

A It can happen at any age. It certainly happens in the elderly. In my experience, some of the worst cases I've seen have been in people who are older. That means over the age of 60 and up. But it's not something that's confined just to young people. In fact, in many respects, if there is akathisia in younger people, it seems to be less severe.

Q Now, are you familiar with the term "psychomotor restlessness"?

A Yes.
Q And you've heard that be referred to as akathisia?
A Well, in clinical trials, one of the things when you look at the way this phenomenon gets coded -- and this is part of the reason why it gets missed, maybe -- is the word "akathisia," even for lots of doctors who ran these trials during the 1980s, 1990s, wasn't a word they were terribly familiar with. And the problems get -- got coded -- some people were coded as being anxious; some were being coded as being agitated; some were being coded as -- coded as having hyperkinesis; some were coded as being overactive; some were coded as akathisia. But when you have this kind of splitting of the coding, the problem can seem to be less because there's not a huge group of people who have any one of those codes.
Q Now, you've spoken at medical conferences before; is that right?
A Yes.
Q Have general family practitioners been at these conferences?
A Yes.
Q And based on your interactions with various medical practitioners, is this understanding, this comprehensive definition of akathisia as we've discussed today, generally understood?
A No --

MR. BAYMAN: Objection, your Honor. That goes to state of mind of other people.

THE COURT: Sustained.

MR. BAYMAN: Thank you.

BY MR. WISNER:

Q Looking at the information that we've gone over on akathisia, have you seen these definitions and discussions about akathisia published in journals directed at family practitioners?

A No, I haven't.

Q Where have you seen it published?

A I haven't. We've got -- one of the problems in this area is that even though the phenomenon is very well-recognized and is in specialist textbooks and people like me can lecture on it frequently, there's very few symposia that are held on just what is this phenomenon and how does it happen in the brain and what can we do to try and mitigate the problem.

It's one of the big things that everybody knows happens but nobody talks about. So that's fine at the upper end of the scale where everybody knows it happens; but lower down, when you've got people who may be using lots of other drugs other than just the antidepressants, this isn't the kind of thing they'll necessarily know about.

Q Now, Doctor, referring specifically to your experiences in treating akathisia, what are some of the things that you can do

to address it when it comes up?

A Among the key things is letting the person know that this is a risk, that, you know, if I put you on a pill, you might have a very bad reaction, you know. I'm not hoping you have a bad reaction, but one of the risks we're taking is that you might have a terribly bad reaction to this. I want to make sure that you don't think this is your illness, that you've gone more mad or you've got real problems now. It may just be the pill that I'm putting you on, and in which case, the trick we need to do is to get you off this pill as quickly as we can.

Now, we may get you off by simply just drastically reducing the dose or the good news is while you're reacting badly to this, it often means that there's a different group of pills that's really going to suit you a lot better, so one of our options is to make sure we switch you over to the other group of pills. I'm less inclined -- some people will try to introduce an antidote, something like Ativan or Valium, to see does that ease the problem a bit. Or, as one of the other people in this field who has actually described the problem, Tony Rothschild, has said you could introduce propranolol. After he wrote that article, lots of people like me tried that out, and it can work for the occasional person, but doesn't work reliably.

Q Why are you hesitant to prescribe a drug like Ativan to treat akathisia? What's your concern there?

A In general, my view would be it's not a great idea to pile pills on pills. And that's the thing I've felt for a long time and that generally I think medicine is beginning to come around to. We've now got a clearer view that if you're on more than five pills at any one time, this is not a good idea. We should be trying to get the number of pills down.

From the start, I've felt it's not a great idea to -- unless you've got a very strong reason to think that this is the drug you have to have for whatever reason -- that we shouldn't be introducing an antidote to get you over a tricky patch, because there's often pills that you would be better suited to. We've got about 40 antidepressants. Why just stick with this six SSRIs. You know, there are other options that we can look at.

Q What about non-pharmaceutical options?

A Yes. Well, I -- a key option here is -- let me make it clear. I use pills as part of the therapeutic approach that I take. I'm not here sitting here as an advocate for other forms of treatment. I'm here as an advocate for using pills, but using them safely.

Now, one of the safe uses of pills is for me to let you know that the condition you have is often one that will only last for a few weeks. And a lot of people -- I mean, they come to me thinking they've got a thing that's going to go on for ages. If they learn that the condition may only last for

six to eight weeks or just a bit longer and that I'm prepared to see them weekly during that time without using a pill, not doing any talk therapy, but just making sure that things aren't getting worse and that they do turn the corner, if they don't turn the corner, we always have the option of a pill, lots of people will say: Look, you know, I'm prepared to wait this out. Because often -- I mean, the evidence points to the fact that if you wait it out, without talk therapies and without pills, that you're often more resilient afterwards, you'll have less episodes.

So one of the -- there's an old phrase: It's great to have treatments that help, but there's an even greater art in knowing when not to give you a treatment.

So it's not a case of pills or talk treatment. It's -- you know, part of the use of pills may be waiting until we get to a point where you and I both think, look, you've put up with this long enough, let's see if a pill will bring it to an end.

Q Now, a physician -- strike that.

If akathisia was defined as psychomotor restlessness, does that adequately convey what you've described here to this jury?

A That would be much better than akathisia. I would be inclined myself to go towards emotional turmoil to try and -- to convey, but that would certainly be a lot better than

akathisia, which is a word that loses most people.

Q Okay. Well, let's move on to another one of these mechanisms that we have up here on this chart.

You mentioned emotional blunting. What is emotional blunting?

A Well, pretty well 100 percent of people who get an SSRI will have some degree of this. And what I'm aiming at, if I give anyone an SSRI, is to get the right degree of this. You know, A, we only want to introduce it when there's a need to; but if we do introduce it, we want to make sure that the person gets the right degree of emotional numbing, one that makes them more functional.

The problem is if we don't get the right degree, if you get too high a dose, if these aren't the right pills for you, or if you are the kind of person for whom -- well, whatever the amount of emotional blunting we give you is just not a good thing for you, it just doesn't fit your personality, then the problem would be, or can be, that we end up with you in a very blunted state, so that things that you might like to be able to do, like cry at a weepy movie, you just don't. You just don't have the normal reactions. Things that should make most people anxious and scared about the consequences to them or the consequences to others, you may not feel those things at all. Lots of people, if we get the right degree of emotional blunting, can say to me, and they often have: You know, this

is helpful, but I do need to make a mental adjustment when I'm on these pills. I know I'm likely to do things that I might otherwise regret, and I need to sort of just stop and pause before I do a lot of things.

Q Now, you said this is related to dose.

Let's talk about Paxil specifically.

Is a 10 milligram dose of Paxil going to cause a potent effect on a person's serotonin system?

A Absolutely. It will cause a very potent effect, and it's enough to produce profound emotional blunting.

If I'm trying to explain this to people, I try and say, look, you know, it's a bit like having a car that will do 60 miles an hour around Chicago here and won't do any less than this. You've got a turbo-charged action on the serotonin system.

Q Now, specifically relating to emotional blunting, what -- how can that in any way lead to suicidal behavior?

A Well, when we get into problems with work or at home, if we get into crisis of one sort, we'll often march out of the room after a bad interview with the boss or march out of the room when we've had an argument with our partner and think, you know, hell, you know, why not do away with myself. Okay?

Now, most of us don't, you know, we think -- I mean, we take a bit of time to calm down, and once we've calmed down, we say, well, look, yeah, that's grim and I have a problem on

my plate but, you know, it's not the end of the world, I don't have to kill myself.

If you're numbed to the consequences for your children, for your parents, for your family, for others of actually acting impulsively, then you're more likely in that kind of situation to act impulsively.

If you combine the emotional blunting with akathisia, and it's giving you thoughts about harming yourself, even if you aren't involved in any kind of argument, you're more likely to act on those thoughts if you're emotionally blunted to a degree.

Q Can this combination of akathisia and emotional blunting lead to violence?

A Yes, it certainly can.

Q How is that -- how does that happen?

A Well, first of all, if you -- well, as I say, if I'm having an argument with the boss at work, one of my reactions might be to thump him, okay?

If I'm numb to the consequences of doing this, then I'm more likely to do it. That's even without akathisia.

But if I've got akathisia as well, and my mind is flooded with thoughts of harming others for no good reason, you know, total strangers, you know, you might get this insane, in quotes, urge to thump someone or harm someone or do something awful, and you're numbed to the consequences of doing this,

well, then you're much more likely to do it.

Q Well, that actually brings me to another point.

Can this combination of akathisia and emotional blunting react to an already existing stressor?

A Absolutely. Yes.

Q What happens?

A Well, you know, I mean, if you throw into the mix of having harmful -- thoughts about harming others or harming yourself, and being numbed to, you know, the consequences of all this, you might be just about living with it. If you add into that a further real live problem, then clearly you're producing a cocktail where, you know, we aren't sure what the outcomes will be. No one can be sure what's going to happen next.

As I say, a lot of people will say things like they have to learn to mentally take a pause in these kind of situations when they're on this kind of pill, but that's the kind of thing you need to be on the pill for weeks or months to learn to do. If -- if you've just recently been introduced to these pills, or if you've been off them for a while and forgotten this and then gone back on them, then that's a very vulnerable period where you might act out before you, you know, before you say, oh, yeah, I should actually remember, you know, I've been here before and I've learned not to do this.

Q Have you ever spoken with somebody who attempted to hurt themselves because of a drug reaction and asked them what they

went through?

A Yeah, I've talked to loads and loads of people who -- I -- well, both of my clinical practice, but also I do not just straightforward clinical office practice where a wide range of people come in to see me, I also do what's called -- called liaison work. The hospital that I work in, part of my job is to see people who have overdosed or harmed themselves and ended up in the general hospital, you know, because of that, so I get to interview lots of people who have tried to harm themselves.

Q How do these people describe to you this combined akathisia/emotional blunting reaction?

MR. BAYMAN: Objection, your Honor. Hearsay.

THE COURT: For the limited purposes of describing the phenomena, I'll let him testify, as distinguished from testifying as to any particular individual case.

Understood?

MR. WISNER: Yes, your Honor.

THE COURT: You may proceed.

BY THE WITNESS:

A People will often say to me, look, you know, I went on these pills recently, I was put on them by my doctor, and, you know, they haven't helped me and I've gotten worse. My reaction will often be, you know, well, look, listen, I can help you, you know, this isn't anything to do with your illness, it's the fact that the pills don't suit you, and what

we need to do is we need to get you off this pill and you'll be fine. It can take a while for these thoughts to wear off. It can take a week. And even if the person has only been on the drug for a week or two, it can be a week or two later before they -- before I meet them again and they're able to tell me, look, we -- I -- that I've actually come back to normal.

So even though I can identify for them that the problem is caused by the pill, these thoughts of harming others, which they've never had before, is caused by their pill, I'll often be tempted to say: You know, maybe you need to come over to the mental health unit for a few days, we're not going to put you on treatment, we're just going to make sure that, you know, this has passed before we let you go home.

BY MR. WISNER:

Q Now, the third one up here on this board is decompensation.

What is that, Doctor?

A Decompensation refers to the fact that on these pills, a person can go psychotic, become delirious. There may be a range of things that happen to them. Like from very early on in the course of treatment, they can hear the voice of God say, quite clearly, you know, I want you to kill that man Mr. Wisner there, or I want you to come to me, which people will read as, you know, jump off the closest bridge or whatever. So that can happen very early on. It's much less common than emotional blunting. It's much less common than akathisia. But it

happens frequently enough in clinical trials to have been picked up by all of the companies making all of these drugs.

The other thing is you can get very disorganized. As opposed to having a clear voice and seeming very calm and rational -- except for you're hearing this voice, for instance -- you may be delirious, which is, you know, raving. You're not with it, you're stumbling around the place, you're confused. Others may not notice that you're confused, but you're actually distinctly confused. And that's a little bit like the LSD effect, where the effects of an SSRI leak beyond where they usually leak to produce a reaction where you're almost on a trip.

Q How have patients described that being on a trip phenomena to you?

A Well, just --

MR. BAYMAN: Same objection, your Honor. Hearsay.

THE COURT: Overruled for the same reasons I've previously stated.

You may answer.

BY THE WITNESS:

A Yes. Just being confused that, you know, they're dazed almost, just -- just -- just out of it, not with it, not registering things in the environment the way they would usually do.

BY MR. WISNER:

Q Now, does any -- do you have to have all three of these possible mechanisms before a person might engage in suicidal behavior?

A Absolutely not, no. Any of them on their own can lead to people actually being suicidal or even violent. But obviously the combination of all three -- well, the combination of any two of them can cause problems, and the combination of all three can cause very serious problems.

Q Now, Doctor, are you -- you've mentioned violence a couple times here.

Is that something that you see in drug-induced suicidal behavior?

A Yes, it is. One of the things that struck people fairly early on with the effects of these pills was that the nature, the way people harmed themselves, often seemed to be disproportionately violent.

There's some people who are seriously mentally ill who are in great distress who can also harm themselves violently; but for the most part, very few of us ever thought the people who, you know, were working and, you know, and not actually in a hospital, seem to be generally functional, that if they tried to kill themselves, it wouldn't be anything particularly violent. But this was one of the striking things for a lot of people when this began to be reported first.

It was reported not -- I mean, it's a thing that

struck doctors, but also patients.

Some of the very first descriptions of this kind of thing happening on an SSRI were patients taking Prozac who went back to the doctors who reported it saying, look, Doc, I've been depressed before, I've been suicidal before, but this was something different. And what they were referring to was the fact that there was an intense violence about it or a bunch of thoughts they just had never had before.

Q How then do you go about distinguishing whether or not someone who has taken an SSRI is doing suicidal behavior because they're depressed versus something that's drug-induced?

A This can be tricky to do. One of the issues is this, which is a lot of the people who are given SSRIs because they're labeled by their doctor as being depressed or anxious are at almost zero risk of killing themselves. The primary care depression comes with a very, very low risk. There's a lot of talk around the place about if you're depressed, you're at huge risk of killing yourself, but that was melancholia, that was totally true of melancholia, the severe form of the illness that we had in the 1950s before we had any antidepressants.

The kinds of people who get antidepressants these days are at almost -- almost zero risk.

So if a person becomes suicidal, you need to be worried that it could be linked to the pills.

Another way is to just ask the person. I mean, you

know, it's -- we're in a world where you shouldn't be depending on an expert doctor these days. It's -- the patients who are on the pills often know far more about what's actually happening to them than any doctor knows, and so the tricky thing for the patient will often be the doctor will say, no, this can't be happening, it isn't in the textbook, when the person on the pill -- and it's not just the SSRIs, it's any pills -- may be absolutely certain it is happening.

So one of the things is to listen to people, to have a relationship where the doctor and patient are working closely together.

And, of course, the other aspect is for both the doctor and the patient when they go to check it up to find that well, yes, there is evidence that these pills can do it.

Q So then when we talk about how Paxil induces suicidal behavior, is "suicidal" the right word there?

A In some respects, not. And there's a tremendous number of people who feel very strongly about this.

Suicide, like murder, strictly speaking means you intend to do it. I intended to kill this person.

If, through some accident or whatever, or if it's not clear that I did intend to, but the person ends up dead, we usually say, well, this is homicide or manslaughter, it's not murder.

In the same kind of way, like a patient -- or a person

taking LSD who walks out of the 55th floor window thinking whatever they're thinking, they don't intend to end up dead. The fact that they end up dead is a different thing.

Now, lots of people have thought from way back in LSD days that it's not appropriate to call that suicide. And strictly speaking legally, unless there's intent, it's not suicide -- at least legally in the U.K., I'm unsure about here, but legally in the U.K. -- it's not suicide unless there's evidence that you intended it.

Q So then would you say that a person who makes the planned decision to end their life is the same sort of thing as someone who has a drug-induced reaction?

A No. I think it's a completely different thing. And this is where it's -- it's awfully tricky generally. And people have begun -- and, again, I'm not sure just what happens over here -- but people in the U.K. have -- when there's an inquest on a death in the U.K., a lot of coroners --

MR. BAYMAN: Objection, your Honor. We're getting into the way that things are done in the U.K. It's not in his report. This is really getting far afield.

MR. WISNER: They covered this extensively in his deposition, so they're on notice.

THE COURT: All right. Proceed.

BY THE WITNESS:

A The coroner will often return a verdict of -- well, what's

called an open verdict. You know, they're not -- they're clearly not saying that this person committed suicide.

BY MR. WISNER:

Q In your -- in your professional capacity, do you have to make a decision about whether a psychiatric patient you're treating is mentally competent?

A Yes, I do.

Q Would you consider somebody who engages in suicidal behavior because of a drug reaction to be acting voluntarily?

A No, I wouldn't. And this is -- I mean, this is -- this is where life gets very tricky for a person like me, because sometimes the right response to a person who presents in the evening when I'm on call or in the liaison service saying that they're going to kill themselves, the right clinical response is often to say, "Well, fine," you know, because the person is being manipulative.

It's not the right clinical response for a person who has got a problem induced by an SSRI.

And all too often, the worry is that if a person has, you know, got a problem triggered by the SSRI that they've been put on, and they come in and hit the mental illness services because they've tried to harm themselves or thinking about harming themselves, if the doctor or the nurse says, "Well, you know, you're responsible for your own actions," this can be a disaster.

Q All right. Well, let's turn to some of the evidence that you relied upon in coming to your opinion.

If you could turn to Exhibit 259 that's in front of you.

MR. WISNER: Your Honor, it's 259.

BY MR. WISNER:

Q Let me know when you have it, Doctor.

A Yes. I have, yes.

Q Okay. Are you familiar with this document?

A I am, yes.

Q And is this a document that you cited and relied upon in rendering your expert opinion in this case?

A Yes.

Q Is this document reliable?

A I believe it is.

Q Was this document published in a reputable journal that you relied upon?

A Yes.

MR. WISNER: At this time, your Honor, request permission to publish portions of this article and discuss it with Dr. Healy under Rule 803.18?

THE COURT: All right. You may proceed.

MR. WISNER: Okay, great.

BY MR. WISNER:

Q All right, Doctor. Let's start off with the top part here.

What is the title of this document?

A It's an article called "The Risk of Suicide with Selective Serotonin Reuptake Inhibitors in the Elderly."

Q And do you see the first author there?

A Yes, I do.

Q Who is that?

A David Juurlink works with the University of Toronto.

Q Are you familiar with his work?

A Yes, I am.

Q And do you work with him and relate with him in your capacity as a researcher?

A Not as such, no.

Q Okay.

A I mean, I have -- oddly enough, I have been in contact with him during the last week or two. I've known of him for 10 or 20 years, but only in the last week or two have I actually had contact with him. Nothing to do with this case.

Q Okay. So let's look at the Objective here.

Could you please read the Objective to the jury?

A "The authors explored the relationship between the initiation of therapy with selective serotonin reuptake inhibitors, SSRI, antidepressants and completed suicide in older patients."

Q So could you please describe to the jury in layman's terms what the Objective is here?

A Yes. They -- well, what they explain in the course of the article is that the group who has been thought of as being at the greatest risk of completing suicide has been middle-aged men. That's been traditionally, for hundreds of years, in the Western world at least, that's been the group who has been thought to -- most likely to go on and to commit suicide.

It's sort of -- it -- you hear that it's -- for every completed suicide, it's three times male com -- to compared with one female.

The biggest risk, though, isn't younger males, it's older males.

Now, with the advent of the SSRIs, there was interest in whether the SSRIs could be helpful for this group of people.

So what the authors are looking to do is to see what are the rates of completed suicides in an older population like this in particular compared with younger populations.

Q Now, if we look --

A Hang on. I've got that wrong.

Compared with other antidepressants. Sorry. SSRIs compared to other antidepressants.

Q Okay. Thank you, Doctor.

So if we look at the Method section here, do you see the mention here of 1.2 million Ontario residents?

A Yes, I do.

Q Can you explain to the jury what that means?

A Well, that means that they've got access to hospital records of people. It's not meeting 1.2 people -- 1.2 million people. It's having access to the hospital data, which lets them look at when the person came in to treatment, and after they come in to treatment, what happened afterwards, whether they were okay when the treatment ended, or whether they ended up dead for one reason or the other, including whether they ended up dead by suicide.

Q Now, 1.2 million residents. Is that a lot of data?

A That's a substantial amount of data, yes.

Q Okay. All right, Doctor. Well, actually let's just stay at the first page.

Let's take a look at the Results section here.

Why don't you just briefly -- do you see the last sentence there? "During"? Do you see that, Doctor?

A Yes.

Q Can you read that sentence? And then finish the sentence on the next column?

A Yes. What they were interested in in particular was the early phase of treatment. And what they're saying here is that during the first month of therapy with SSRI -- "During the first month of therapy, SSRI antidepressants were associated with a nearly five-fold higher risk of completed suicide than other antidepressants."

Q All right. I want to break that down a little bit.

Before that it mentions 1,329 suicide cases. Do you see that?

A I do.

Q Considering how rare suicides are, is that -- is that a lot of suicides?

A This is -- this is a very big sample, yes.

Q To give the jury some context, in the early clinical trials for Paxil, when it was submitted to the FDA, how many suicides were we dealing with?

A We were dealing with much fewer, one or two or three, often, from the clinical trials.

Q Okay. It goes on here to say "justified odds ratio" -- let me highlight that -- "of 4.8."

Do you see that?

A I do.

Q What is 4 -- what does that -- what's an odds ratio?

A Well, we're looking at -- what they're actually saying is that there was a five times greater likelihood of the person going to complete suicide while they're on an SSRI compared with other antidepressants that they could have been on.

Q Well, how do they know that this wasn't caused by depression or something like that?

A Well, they don't. What they're comparing is -- everybody is depressed. Some have been treated with SSRIs, and others have been treated with other antidepressants. So no one is not

being treated. One of the options clearly is that the other treatments are better than the SSRI, but they take that into account. And their view is, while there may be a little bit of that involved, that the issue seems to be that the SSRIs are not suiting some people.

Q So with an odds ratio of about five, if I have a group of depressed people, some of them get SSRIs and some of them get other antidepressants that are not SSRIs, what does that tell us about the people getting SSRIs?

A It says that there's a fairly substantial group of people here for whom these drugs aren't suited to them.

Just to give you a feel, when we're talking about odds ratios here, lung cancer is associated with tobacco smoking at an odds ratio of 15. That's thought to be very, very big. You know, there's a very tight connection. We don't doubt the link.

Five is very high also. It's clearly not quite as high as lung cancer, and that's because SSRIs suit some people and they don't suit others.

Q What number does the odds ratio have to get to when you start being concerned as a physician?

A Well, I can be concerned if an odds ratio is less than one, which means that the SSRIs are not suited, that you can still have the drug causing the problem even if an odds ratio is less than one. Once it goes over one, we're into the ballpark where

the drug may be helping some people, overall in the entire group, it's less helpful to more people than it's helpful to. Once you get up to five, then there's a very distinct group in there who are having significant problems, and we really should be thinking about, you know, what do we do to minimize this risk.

Q Now, it goes on, it says "confidence interval 1.9 to 12.2."

What's a confidence interval?

A A confidence interval is just as the name -- just as the words suggest. It's can we have confidence in this figure of 4.8. And the tighter the confidence interval, that is, you know, if you had them saying the confidence interval was from 4 to 5.4, you know, very, very tight, you would say, well, this is absolutely for certain we know 4.8 is the right figure. If the confidence interval is a little wider, this isn't a hugely wide one, but if it's a little wider, as it is here, then what you're saying is we're less certain 4.8 is the right figure. If we had more people, even more suicides, we would expect that when we get the best figure, it might have shifted from 4.4 or might have gone up to 5.2. It's going to be around 4.8. We don't -- is it 4.8 -- 4.8, yeah -- but we're not as sure as if, say, the figures were, you know, from 4 to 5.4.

Q Now, it has 1.9 to 12.2 as the confidence interval.

Would it be fair to say that the risk is somewhere between twice and 12 times as high, but the best guess is about

5?

A That's a very good way to put it.

Q Okay. Let me call up the next sentence here.

The next sentence goes on, says: "The risk was independent of a recent diagnosis."

Do you see that?

A Yes.

Q What does that mean?

A Well, you're looking at the fact that the SSRIs, by the time this piece of work was done, they weren't just being given to people who were depressed. They were also being given to people who were anxious, people that had OCD, a whole range of problems. And what they're saying is, regardless pretty well of the problem that the person got put on the drug for, the outcome is the same: There's a bunch of people going on to commit suicide.

Q It even says -- it says: "Regardless of psychiatric care."

What does that mean?

A Well, it depends. Like, for instance, there's a bunch of people who get put on these drugs, and they're coming into mental health care, they're coming to people like me rather than going through their family doctor.

What they're saying here is whether they're going through the family doctor or whether they're going through a so-called expert like me, the results are the same in either

case: Neither the experts nor the -- neither the specialists nor the generalists are getting any better result.

Q And when you said the results are the same, you mean the risk of five times --

A Yes.

Q Okay. And then it goes on to say: "And suicides of a violent nature were distinctly more common during SSRI therapy."

What does that mean?

A Well, again, this is the point that I made earlier, that one of the things that struck a lot of people, both patients taking the pills and doctors and others looking at the problem, was there seemed to be a lot of particularly violent suicides among the people who were going on to commit suicide on SSRIs.

Now, this article seems to bear that out.

I mean, there's the impression that someone like me can have. This is an article that bears it out and was particularly interesting to me because Dr. Juurlink up until that point in time was not a person that I would have thought was going around the place saying: Look, SSRI drugs are dangerous. Quite the opposite almost. He didn't seem to be a person that was particularly linked with saying that they can be risky. So for his article to come out and say this was of interest in its own right.

Q Now, it says down here: "No disproportionate suicide risk

was seen during the second and subsequent months of treatment with SSRI antidepressants."

Do you see that?

A Yes, I do.

Q What does that mean?

A That -- well, the people who are going to have a problem have it in the first month. There's lots of people who will get SSRIs who aren't going to have a problem. The drugs suit lots of people. So they're not going to have a problem in the first month or the second month or the third month. The people who are going to have a problem are going to have it in the first month principally, but they're not going to be in the equation after that. So, you know, the second and third and fourth month are really people who for the most part are as suited to SSRIs as they are suited to other pills, so there's no higher rate of completed suicide later on on the SSRIs compared to the other pills.

Q How does that relate to what we discussed earlier about the habituation of the side effects?

A It relates quite well to the impression people had that it's a particular problem -- the akathisia and emotional blunting and all are a particular problem during the first week or two or three of treatment.

Q All right, Doctor. I want to look at a few more parts here. We'll be moving on in a second.

The -- I want to look at this diagram here.

Can you explain to the jury what this diagram is and what it depicts?

A This is just a visual way to show what you've heard me explain or what the words in the article that we've read also say, which is just trying to tease out the fact that the problem is there in the first month. After the first month, the blue bars and the red bars -- that's the SSRI bars and the non-SSRI bars -- are overlapping. There's really not much difference between the different kinds of antidepressants. But in the first month, there's a big difference between them. And this is a difference that's referred to as being statistically significant or it's a difference -- the confidence interval -- what you're seeing with the little coat hangers around the red dot and the blue dot is, that's the confidence interval. And you see that the confidence interval for the blue dot and the red dot don't overlap.

So what Juurlink and his group are saying here is, look, there's two distinctly different sets of results here. No matter -- even if our estimate of five times higher is wrong, there's almost no way that there's not an increase here.

Q All right. I want to look at one more diagram in this article -- well -- yeah.

This is Figure 3 in the article. And it has a red line going way higher.

Do you see that, Doctor?

A I do, yes.

Q Okay. This one right here.

What is that referring to? And what are these other lines?

A Yeah. What you're getting there, the -- you've got a red closed line and a red broken line. And you've got the same for the blue lines, a closed line and a broken line.

And what you're seeing here is with -- the SSRIs differ from the other antidepressants during the first 30 days in particular.

Look at -- if you look at the bottom line, you see 10, 20, 30. 30 there means 30 days. So it's the first month that we're looking at.

Now, I know later on, the SSRIs, the closed line still looks awful compared with the other two lines; but in actual fact, it's begun to flatten out. Okay? It's really during the first 30 days that you see the divergence, you know, that the problem is growing bigger and bigger and bigger from the first few days of treatment through to 30 days. And after that it's not escalating the way it had been before. And this is referring to people committing suicides violently.

Q Now, you mentioned these violent suicides.

Can you please describe for the jury some of the type of violent suicides you've examined or seen or come to an

opinion about as a psychiatrist?

A Yeah. These -- well, with the SSRIs in particular, you get a range of awfully scary things. People who have set fire to themselves. People who filet themselves, literally skin themselves. You get people who murder others, murder their wives and children and then themselves. You get people who -- I mean, a lot of people put a gun to their head. And this can be anyone from the clergy through to whoever. You're doing things that are not just violent, but at odds completely with the norms for them. You know, there's been some awful things like people killing themselves with a nail gun to the head.

Q Have you seen examples in the literature about people with drug-induced suicide committing themselves by jumping?

A Yes.

Q And what could -- what context have you seen that?

A Well, one of the early articles -- and a person who may be able to talk to it as well is Dr. Rothschild, who I understand may be here later, I'm not sure. He's given views in the case. He described -- well, he was one of two people who wrote an article back around 1991. The senior author I think was Carol Locke. And they described people who jumped off buildings given -- when they were given Prozac and ended up with multiple broken bones and in wheelchairs.

Now, they did something quite extraordinary, which was to re-expose the person to Prozac afterwards, and they were

able to say: Look, I'm having the same intense feelings that caused me to jump off the building and try and kill myself now that I've gone back on it.

They felt not comfortable, but at least they felt they could do it because they could keep an eye on the person. They were in a wheelchair, they couldn't move. They did a good thing as well. I mean, they reproduced the problem, you know, the violent impulses that led to the person jumping off the building. And they found that in one or two cases that when they gave a beta-blocker like propranolol, it made a difference.

This gave a lot of us a great deal of hope that, you know, this was an antidote that could make a difference.

But, as I say, I think for the most part, people think they may have been just lucky in the cases they had, that it did make a difference in their cases and maybe a few others, but not generally.

Q Okay. Actually, you were just mentioning the Rothschild article, Locke. Is that Number 14 right there?

A It is, yes.

Q Okay. So it's actually cited here in this -- this article. Is that right?

A Yes.

Q Okay. I also see two other citations to yourself.

Do you see those?

A I do, yes.
Q Right here?
What are these articles? Just briefly. Don't get into super detail, but what do they relate to?
A Yes. Well, early on I produced some of the earliest case reports of people becoming suicidal on SSRIs and trying to kill themselves. And when the drug was removed, the problem cleared up; and when the drug was reintroduced, the problem reappeared. But these are completely different articles. These are articles looking at the clinical trial data that we had from Paxil and other SSRIs and adding up the number of suicides and the number of suicidal acts by the number of patients and working out what the risk -- risks were. And these were among the early articles that pointed to a risk from the clinical trial data.
Q There's another one here actually that I actually want to draw your attention to specifically.
This is the Fergusson article.
Do you see that?
A I do, yes.
Q And I believe you were actually an author on this as well?
A Yes, I am.
Q When was this published?
A This was 2005, and seems to have played a part in FDA's, as the Juurlink article did, played a part in FDA's deliberation.

Around 2005, FDA were looking at -- they had a lot of evidence that these drugs caused problems for children and had put a black box warning on the drug.

Around 2005/2006, they were looking at the issue of were there other problems for adults also. And this is one of the articles that they cited that they were influenced by, and it was one that I was involved in.

Q Where was it published?

A This was in the BMJ. That stands for the *British Medical Journal*.

Q Is that a peer-reviewed journal in the United Kingdom?

A It is -- well, it sees itself as a global journal, but maybe just a British delusions of influence perhaps.

(Laughter.)

BY MR. WISNER:

Q I forgot you're Irish.

A I'm Irish, yes.

Q Now, in -- at this time can you actually turn to Exhibit 165 in your pile?

MR. WISNER: Your Honor, 165.

BY THE WITNESS:

A Listen, I have caused a problem here. I have got them out of sequence. Let's just see if I can -- yes, I have it.

Q Do you have it, Doctor?

A I do.

Q Okay. What is Exhibit 165?
A This is the Fergusson article that you just mentioned.
Q Okay. And is this an article that you relied upon and influenced your opinions today regarding Paxil and suicide?
A Yes.
Q And is this article in your opinion a reliable article?
A Well, I think it's reasonably reliable, yes.
Q And when you prepared the article, did you use the principles of scientific investigation that people in your field typically use?
A Well, I would say that in all of the articles that I've done that I've done this, that I've -- that I've, you know -- there isn't a single article that I produced that I think is not valid from a method -- methodological point of view.

There's a range of different articles. The first articles I've mentioned were case report articles.

The articles you pointed to earlier were articles looking at compiling the clinical trial data.

This is a different kind of article, so it uses a different set of methods to either of the other two, but these are methods that are accepted within the field.

MR. WISNER: Your Honor, at this time permission to publish portions of Exhibit 165 to the jury under Rule 803.13.

THE COURT: All right. You may proceed.

BY MR. WISNER:

Q All right, Doctor. I have up here on the screen Plaintiff's Exhibit 165.

Is this the article we've been talking about?

A Yes.

Q All right. Let's try to break this down into different portions.

Let's start with the Objective.

It says here: "To establish whether an association exists between the use of selective serotonin reuptake inhibitors, SSRIs, and suicide attempts."

Stop right there.

Is there a difference between a completed suicide and a suicide attempt?

A There can be. It's tremendously difficult to look at completed suicides in clinical trials. They aren't the kind of setting where hopefully completed suicides would happen, partly because people who are at high risk of suicide get screened out of trials like this, but also because during clinical trials, as opposed to just normal clinical practice, people should be monitored more closely, so if things do begin to deteriorate badly, the person should be whipped out of the trial, so the hope is that there won't be completed suicides.

So what the trials do show is a lot of suicidal acts. And unlike suicidal ideation, suicidal acts are quite tightly tied to completed suicides.

Q And we'll get to that distinction in one second.

Before we do, in the last article we looked at, the Juurlink article, was that looking at suicide attempts or actually completed suicides?

A That's completed suicides.

Q Okay. And if, you know, the jury was told that there's no study that has ever shown that Paxil causes suicide, would the Juurlink article refute that?

A I don't know that it's specific to Paxil. Dr. Juurlink may well have data that does refute just that, but we'd have to get his data from him to look at it.

Q But it did show a causal relationship between SSRIs generally and completed suicides --

A And they had so many completed suicides during a time when Paxil was the best-selling SSRI, you have to bet that a significant number of them were linked; but we would have to have the data here before us to nail that one down.

Q Okay. Now, you said that suicide attempts are a better thing to look at than suicides ideation.

What is suicide ideation?

A Right. People can obviously complete suicide. They can make suicidal acts. Now, these can be very serious acts. A person who jumps off a building and breaks their legs and ends up in a wheelchair, that's a suicidal act. It's only when you're actually dead that you've got a completed suicide.

So that's why I say suicidal acts are closely related, and all the evidence points to the fact of them being closely related.

Suicidal ideation is the thoughts about harming yourself that lots of people have.

Suicides are rare.

Suicidal acts are fairly rare as well.

There's a number of suicidal acts that are done by people who never plan to kill themselves, they're just manipulative gestures, so it's not the same thing.

But suicidal ideation is extraordinarily common. Lots of people have it on a Monday morning, almost. But it's -- it's a very, very common thing.

So just noting suicidal ideation as such doesn't necessarily mean or doesn't necessarily link to suicidal behaviors, which include acts and completed suicides.

Q And when you prepared this peer-reviewed article, did you -- did you deliberately focus on attempts as opposed to ideation?

A Yes.

Q Why is that?

A Well, because -- well, the clinical trials in this case for this group of drugs were not done to explore the idea of could the drugs cause people to commit suicide. They were done to check and see do these drugs work. So the focus is on

something here, while lots of things over here could be happening. You know, awful things could be going wrong. And in the case of the SSRI drugs -- and transferring any drug, really -- a lot of the adverse events that are happening are missed in the course of the trial while people are looking at the main thing: Does this drug work.

Now, in the case of trying to check does an antidepressant work, the common -- there's two common rating scales. The one that's probably used the most is a thing called The Hamilton Rating Scale for Depression, the HAM-D. And of the 21 or 25 questions it asks -- there's two different versions of it -- only one links to the issue of are you suicidal or are you thinking about harming yourself, have you tried to harm yourself.

When people come into a clinical trial first, often the trick will be I'll go through all the -- well, the doctor who is trying to check you out will go through all the questions and ask you all the questions. After that, the way company clinical trials happen, and possibly non-company clinical trials happen as well, often you've made friends with a person. It's Mr. Wisner, you know, you're in our trial, and you come in to see me, you know, a few weeks after you're put on the pills first, and we've begun to chat, and I know you're a Cubs fan now, so you come in the door, and I ask you about the Cubs and things like that, and we work out -- I mean, I

have a look at you and I get a sense that, you know, you're doing better, et cetera, et cetera, and I don't bother necessarily asking you a few of the awkward questions, like are you thinking about killing yourself or how is your love life --

MR. BAYMAN: Your Honor, we're now getting into speculation here. This is really far afield.

THE COURT: Bring it to --

MR. WISNER: I can lay the foundation.

THE COURT: Bring it -- bring it to a point in the case.

MR. WISNER: I can lay the foundation.

BY MR. WISNER:

Q Have you conducted clinical trials?

A I have.

Q Have you conducted clinical trials for the defendant?

A I have.

Q And in the context of you conducting clinical trials, have you used rating scales?

A Yes, I have.

Q And in the context of being taught how to use those rating scales, were you ever instructed to not fill them out completely?

A No. That's different. And I'll explain exactly what's going on there.

First of all, when doctors are involved in company

clinical trials, it's often -- they make money out of them, so there's -- you know, it's not standard research as such. It's a complex form of research that comes with its own issues.

But as part of this, some of the doctors who are involved in these trials are -- well, it's a bit awkward. They're -- I have a look around the room and say these aren't always the best doctors --

MR. BAYMAN: Your Honor, we're getting beyond Paxil trials now and talking about all kinds of trials and doctors' motives. I mean --

THE COURT: Preliminary.

Go ahead.

BY THE WITNESS:

A So, as I say, they're often not doing the job terribly conscientiously. And if they were to ask all the questions, it would take time. And they don't always ask all the questions, particularly if they've got to know you over a few weeks and like you and you've talked about the Cubs; they might chat about the Cubs and might decide that, hey, he's better than he was the week before. So after you've left, they fill up all the questions, the answers, the scores to the questions that they haven't asked, and you'll have a better score than you had the previous week.

The score for your love life will improve as well, even though we haven't asked you about your love life, and even

though the SSRIs make 100 percent of people who go on them dysfunctional from the sexual point of view. But the clinical trials don't show this because the questions didn't get asked.

So ideation, just add this one thing about ideation there, and it doesn't always get asked.

Just like the one about sex.

If you want to do suicidal thinking properly, you have a dedicated suicidal ideation scale, of which there were some at this time, but they weren't used.

If you want to look at sexual functioning, you have a dedicated sexual functioning scale that GSK actually did include in one of their trials that I was involved in, and told us, the investigators, not to fill it, which is what I think you were referring to there.

BY MR. WISNER:

Q Now, you said that you would use, to explore ideation, you would want to use an ideation scale.

Do you need such a thing for suicide attempt?

A No. And this is a big difference. If we haven't asked you the ideation questions, I mean, if I've just filled out the rating scale he's better and marked you down, maybe when you come in first you scored a two because you were thinking about harming yourself, but you look a lot happier now, and I might have scored you down to one or even down to zero. Four is the worst. It's either four, three, two, one, or zero. So when

you enter trials, people usually aren't much more than a two, so you will have come down to a one or a zero probably.

Okay. In -- that's where the ideation you're having -- I mean, you may walk out the door after I filled the rating scale and we've had a chat about the Cubs, and you may kill yourself. It's just I haven't asked the question. Maybe partly because the akathisia has on/offed, you know. You were feeling awful before, you're in a good period when you come to see me, and maybe I have asked the question and you just haven't answered it, you've said, no, I'm fine now, but a short while later you aren't. So ideation is a tricky thing.

But completed acts that lead -- you know, when you jump off a building or when you have to be hospitalized because you overdosed, that's something we can't miss.

The ideation can vanish, but the acts and the completed suicides can't be disappeared -- when I say can't be, I don't mean the company is trying to disappear. It's just -- it's just not something that goes away. After the trial is over, it's there to be seen.

Q All right. So now it says in this journal article here, it refers to data sources.

Do you see that?

A Yes.

Q Okay. What sort of -- what was the source of data that you used to help prepare this study?

A Well, this is -- it's more the -- an approach here. What you've got is what called a systematic approach where the group made sure that they tried to collect every clinical trial that was out there in the published literature, and then what they did was to go -- well, check and see, do -- did the publication show what the number of suicidal acts were, and if they didn't, there was efforts made to contact the authors of the papers to ensure either there were none or actually there were some that just didn't get reported in the paper.

Q Why did you focus on published or peer-reviewed data?

A Because -- well, this is -- we wouldn't be here in the court today, Mr. Wisner, if we had access to the data. Everybody here probably assumes -- someone has access to the data. FDA has access to the data. Or Dr. Healy experts -- experts on the opposite sides of the argument have access to the data, and they're just taking different views about the same thing. They're not. Nobody has access to the data. All we have access to is published articles --

MR. BAYMAN: Objection, your Honor. This goes to the motion *in limine*.

THE COURT: Overruled.

Finish your answer.

BY THE WITNESS:

A All -- all we have access to is the published articles, which may or may not report -- some of them report the results

very -- I mean, in the sense of they make sure they report the suicidal acts and the completed suicides. Some don't.

BY MR. WISNER:

Q All right. It says right here that 702 trials met our inclusion criteria.

Do you see that?

A I do, yes.

Q So through this process you just articulated, how many studies did you actually get to look at and combine into this analysis?

A Well, it was over 3,000 to begin with, but much less of them, I mean, as this indicates, were ones that we could work with, but it's a very large number of clinical trials.

When the FDA came to look at this and asked the companies for all their clinical trials, they didn't have any more than this.

Q Now, it goes on here to say -- why don't you read the next sentence, Doctor?

A "A significant increase in the odds ratio of suicide attempts," and it says "odds ratio of 2.28, confidence interval 1.14 to 4.55, number needed to treat to harm 684, was observed for patients receiving SSRIs compared with placebo. An increase in the odds ratio of suicide attempts was also observed in comparing SSRIs with therapeutic interventions other than tricyclic antidepressants."

Q All right. So I'm going to break that down just a little bit.

Now, a second ago we saw an odds ratio of 4.8, I believe.

A Yes.

Q Why is this -- why is this different?

A Well, it's not just an elderly population. It's all ages here. And the clinical trials -- I mean, there's -- for reasons that I don't understand, the clinical trials that have been done in the elderly often give quite different results to the Juurlink data that you just saw.

In clinical practice, Dr. Juurlink now, and lots of us before, figured when you give SSRIs to older people, that they can have just as bad reactions as anyone else and some of the most violent reactions, but the clinical trials don't show it. So in the clinical trials in the elderly in this paper, and so people over the age of 60, they don't seem to have had a high rate in this paper compared with the Juurlink paper, for instance.

So that's one of the reasons that drags things down a little bit from the 4.8 you saw before to 2.28 here.

Q This is also based on clinical trial data.

What was the Juurlink article based on?

A Well, that was -- that's based on clinical practice. And rather than taking a selected group of people, in clinical

trials we exclude the high-risk people, we exclude the people who are at high risk of suicide or the people who may be taking alcohol as well, and all sorts of other things.

The Juurlink article took people from the street, you know, who were maybe at high risk of suicide, maybe they've come from actually a family where people have committed suicide, maybe they're drinking as well, which can add to the risks, so it was real life.

This is -- this is less real life because these trials weren't, if you remember, weren't designed to look at what happens when people take SSRIs in terms of are they going to go on to commit suicide. They're designed to show the good side of SSRIs. And to some extent, that's what you see here, that the risky bit is from that point of view less in this article than it was in the Juurlink article.

Q I just want to clarify something.

You said in the Juurlink article it included people off the street who may have had high risks, but didn't that apply to both -- both groups?

A Well, in clinical trials, there's exclusion criteria. We exclude people who may be at high risk of going on to kill themselves. And one of the things would be, for instance, if they're known to be an alcoholic or if they're on a bunch of other drugs also.

Dr. Juurlink's article didn't exclude anyone.

Everything is in there. The kitchen sink is in there.
Q But my question is for the people that were compared in the Juurlink, were there an equal number of suicidal people in the people taking SSRIs as well as the non-SSRI group?
A No -- well, hang on. I've actually lost the point here slightly.
Q My question is in the Juurlink article, is that five point risk ratio being caused because of riskier patients? Or is it because -- or is that controlled for?
A No. It's controlled for that. They had just the same -- well, they didn't have just the same kind of controls as you have in what are called randomized control trials, which is what you have here, but they controlled for it. So, yes, the risk elements -- the alcohol, the age, the history of trying to harm yourself and all -- was the same in both the SSRI group in the Juurlink article and in the non-SSRI group. So the findings of SSRIs are riskier doesn't come from the fact that there were two different groups.
Q So if I'm an alcoholic, according to the Juurlink article, there's a five times greater risk of suicide with SSRIs.
A No. No, no. Whether you're an alcoholic or not --
Q That's my point.
A -- there's a higher risk.
Q Okay.
A Risk, yeah.

If you go on SSRIs, that comes with this high risk.

This is a different group of people, though. This is a group of people where we tried to exclude all the other risks completely.

And it's also a short duration thing. Most of these clinical trials just last six weeks, so people are being kept a close eye on during that period of time, whereas in the Juurlink article, it's a lot of people who nobody is monitoring at all.

Q Now, you said in your study you found an odds ratio of 2.28.

Do you see that, Doctor?

A I do, yes.

Q And it has a confidence interval of 1.14 to 4.5.

Do you see that?

A I do.

Q Can you please explain to the jury what that means?

A Again, you're looking at -- we're reasonably confident here that the true figure is going to be something like 2.28. And that's a relatively tight confidence interval, when you see what we did, which is we've got clinical trials here from the 1980s through to the early 2000s, over a 20-year period, clinical trials from Europe, clinical trials from North America, so a wide range of different settings over a 20-year period. And it's interesting that a signal comes through as

tight as this, you know. There's what's called a relatively tight confidence interval here. It doesn't range vastly beyond the 2.28.

Q Now, 2.28, Doctor, doesn't seem like a lot. Is it?

A Well, you need to bear in mind that the 2.28 means that, you know, that this is an excess over and above the number that have actually been helped by the treatment. So some people have been helped who would have otherwise gone on to harm themselves. What you've got here is an excess overall -- you know, if we take into account the people who are harmed and the people who are health -- helped, overall it's a doubling of the risk.

Q And specifically this is -- is this statistically significant?

A It is, yes.

Q All right. All right, Doctor. Pulling up a chart here from your article, it's Figure 5.

Can you explain to me what this chart depicts?

A Yes, I can. This was a graph that the BMJ put on the front cover of their journal. It didn't just appear in the article, it became the front cover of the journal, and was a graph that really always appealed to me hugely.

What you see is we've got data from 1983.

What I said to you was that the first of the SSRIs was a drug called Zelmid. And early on, the confidence interval is

awfully wide as there's very few trials. As you see as you go down the graph, the more and more trials we get, the tighter and tighter the confidence interval gets, the more confident we are.

But what I want to draw your attention to is 1988 or even 1987, if you want. And that for me has always been very important, because the first paper about Prozac causing people to become suicidal appeared in 1990. And the response from a lot of people, including companies, was: Well, that's just anecdotes. They talked about six cases of people who went to Prozac, became suicidal, the problem cleared up when they halted the Prozac, and in some cases reappeared when they went back on the Prozac. But the article -- but the argument from people who didn't believe there was a problem here was always: Well, that's anecdotes, we have the science. The clinical trials show no problem.

Well, here you are two years before that ever happens, and the clinical trials are showing a problem. And every year for pretty well 20 years afterwards, the clinical trial literature has always shown a problem.

So from the point -- from the year Prozac comes on the market, and before Paxil and Zoloft come on the market, there is evidence from clinical trials -- which companies and others often say is the best kind of evidence, I don't agree with that fully, clinical trials have their place, but lots of people say

this is the best kind of evidence -- and what you see here is this so-called best kind of evidence saying there's a problem that people should be listening to. So it's not just anecdotes. It's not a few strange people like Dr. Healy reporting the odd case here and there. The bulk of people being given these drugs, the problem is showing up in them.

Q Now, are you familiar with something called a safety signal, Doctor?

A Yes.

Q What is that?

A A safety signal is where some evidence -- and it can be from a range of different sources. It could be just a doctor like me reporting having put you on some pill and you've turned blue and grown feathers, and I report on this, the problem cleared up, when we halted the pills, you turned back your normal color. That's a safety signal. If I've clearly -- if -- between us, and maybe I've consulted colleagues, and we've agreed the only way to explain this is this strange new drug you've been put on, reporting this in the academic literature or to the company is a safety signal.

The companies will often have seen this long before, in their own internal work with the drug, will have seen this often well before people like me, who are the kinds of people who have been using the drug for the first time when it gets put on the market. That's one kind of safety signal.

Clinical trials like you see here can throw up a different kind of safety signal.

Dr. Juurlink's article, which you saw, again throws up a different kind of safety signal. That's a cohort study. It's not clinical trials. It's not case reports.

So there's a lot of different kinds of studies, and any of them on their own can throw up a safety signal.

When they all say the same thing, you know, there's an overwhelming signal here.

Q Now, we have -- when was Paxil first submitted for approval by the FDA?

A Oh, it was around 1989 by FDA. It may have been slightly earlier in the U.K. It certainly comes in the market in the U.K. a little earlier. It comes in the market in early '92 here and was -- first went in in '89, I believe.

Q So starting in 1989, I see that this black dot that's on this, the sequence here, start -- moves to the right.

What does that tell us?

A Well, it's actually moved at the right the year before. The -- and, in fact, maybe two years before.

The black dot moving to the right means there's a risk from treatment.

If the black dot is over on the left, as you see in the first year or two, then the treatment overall is safer than not.

If it's on the right, then it's riskier than not.

In fact, in the early trials here, these were done in Europe, and I know that a number of suicidal acts simply didn't get reported back then, so I'm not sure that the black dots should have been over on the left. But working just from the publications, which is all we could do, this -- we reported the results as the publications found them. But once you begin to build up more trials, you see we become more confident that actually the black dot is over on the right. The drugs are riskier than not.

Q Is that illustrated by the black dot getting straighter and straighter as it gets farther down?

A Not so much straighter and straighter --

Q Less --

A -- but at the confidence interval, the coat hanger on either side of the black dot, that gets tighter and tighter.

Q Okay. Now, I know you mentioned that the black dot moves to the right before 1989.

When were most of Paxil's clinical trials, at least the registration trials, done?

A These were done in the early to mid to late '80s, from about '82 or '3 onwards through to '89.

Q Now, as a practicing physician, assume you weren't involved in all of this stuff and knew everything like this, the fact that there's a signal starting back in '87, is that something

you would have wanted to know?

A Absolutely. Yes.

Q Why is that?

A Well, I'm in the business of trying to treat people, which as I said involves giving a poison, but with the purpose of trying to bring good out of the useful poison.

If we're going to do this, I need to know the risks. And you who get put on the pills need to know the risks. And we also need to have a bit of confidence that if we decide that there's risks here that don't seem to be in the literature and report it back to the company, who may be looking at this, collecting all the data behind the scenes, they should be -- they've got a duty to collect everything that comes in from every source, so they should be collecting this kind of stuff and should know things about their pills that I don't know about and that maybe the wider world doesn't -- doesn't actually know about. So when things happen on the pills and we report it into the company, you would hope they would say: Well, yes, we've had other reports of this or, what do you know, there does seem to be a signal from -- from clinical trials.

Q Now, these 720 clinical trials that you pulled all this data from that was published, were those published generally in journals aimed at family doctors?

A No, they weren't. Very few, if any. I mean, I'm sure it's

a vanishingly small number of these appear in family medicine journals.

Q Have you published these kind of results in a family medicine journal?

A No.

Q Why not?

A Good question. I'm not sure why not. And maybe I should have. But -- but I haven't.

Q All right. Last thing I want to call out here in your article is this box you have here that has blue writing in it.

Do you see it?

A I do, yes.

Q It says: "What is already known on this topic."

Do you see that?

A Yes.

Q What were you referring to when you said that?

A Well, this is the kind of thing that a journal will ask. If -- I mean, they'll often want a simple take-home message like this for people who don't have time to read the whole article, so they're trying to introduce you to the fact that there's a controversy here, that -- one of the things that's known is that these drugs are used widely and there's a degree of controversy. That's what they mean by divergent studies exist. That's a tame English way for saying people are on different sides of this debate.

Q So the first thing says: "Selective Serotonin Reuptake Inhibitors, SSRIs, are a widely prescribed medication."
A Yes. Well, that's -- that's known. I mean, the entire readership knew that, but ...
Q Okay. "SSRIs are used to treat an expanding list of indications."

Can you just tell the jury what an indication is?
A Yes. Companies, when they bring a drug on the market, are restricted by FDA to just making claims that FDA approve. So if any of the companies bring an SSRI on the market, with trials done on people who are depressed, they're licensed to say this drug is indicated for or may be helpful to treat people who are depressed.

If they stray off that and say, look, you can treat people who are anxious, FDA should jump on them.

In order to be able to say that, they need to do trials as well in people who are anxious or people who have eating disorders or people who have got obsessive-compulsive disorder, and these are called other indications.

And during the late -- well, during the 1990s and just before this article came out, the companies, and in particular -- in particular GlaxoSmithKline were busy doing trials in all sorts of other indications so that they could claim our drug is useful for social anxiety disorder, for panic disorder, for obsessive-compulsive disorder, and other

disorders.

Q These other disorders, like obsessive-compulsive disorder, I mean, how does an antidepressant treat that?

A Well, you see, I would say it's a bit of a misnomer to call these drugs antidepressants. The main effect is not, you know, to make you happy or to give a boost to your mood. The main effect is a degree of emotional numbing, which can be tremendously helpful for some people who are anxious about other people or some people who are -- who have got OCD or even some people who are depressed, because if you think, a lot of what we call depression these days used to be called nervousness or anxiety. You know, so it's not classic melancholia. These drugs are relatively ineffective, maybe even completely ineffective, for melancholia --

MR. BAYMAN: Objection, your Honor. This is subject to the motion *in limine* --

THE COURT: Sustained.

MR. BAYMAN: You granted that --

THE COURT: Sustained. Your objection is sustained.

MR. BAYMAN: Ask the jury to disregard it.

THE COURT: Disregard the last comment.

Stay with the topic, please, sir.

THE WITNESS: Okay.

THE COURT: Right on the topic.

THE WITNESS: Okay.

THE COURT: This may be a good time for a break.

(Jury out at 3:00 p.m.)

[redacted]

(Recess taken.)