IN THE DISTRICT COURT OF THE UNITED STATES
DISTRICT OF SOUTH CAROLINA
CHARLESTON DIVISION

IN RE: LIPITOR 2:14-MN-2502

TRANSCRIPT OF STATUS CONFERENCE
THURSDAY, SEPTEMBER 24, 2015
BEFORE THE HONORABLE RICHARD M. GERGEL,
UNITED STATES DISTRICT JUDGE

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* * *

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THE COURT: Well, we have a bigger crowd of counsel than we normally do here.

MR. HAHN: Just a few, Judge.

THE COURT: It's good to have everybody here in Charleston.

And let me hear from counsel about the preferred way in terms of how you would like to open.

Mr. Hahn, do you want to --

MR. HAHN: Your Honor, we are happy, actually, for Pfizer to go first on arguments.

THE COURT: I know that. I'm going to plan to let you do that. I just wanted to know your motion -- you already talked to me a little bit about wanting to do some opening statement or something like that.

MR. HAHN: We have about ten minutes.

MR. CHEFFO: We do have about 10 or 15 minutes.

THE COURT: Mr. Cheffo, let me say this in terms of our format here -- we talked a little bit on the phone about this -- don't overdo the opening. I have -- you know, I usually say I've read everything in the file. I will not claim I have read everything that y'all have given me. But I have read, obviously, the briefs and the important cases and the important references to the record that y'all have made. I have gone back and read this. But I do think this is one of those situations where your particular insight on

what you think is important sometimes can get lost in these voluminous briefs and materials, so I do welcome that.

Once we do these sort of opening statements, we will begin with the defendant, since it is defendant's motion under *Daubert* and carries the burden. We will go forward witness by witness. That is, Mr. Cheffo can make the argument as to a particular witness. Mr. Hahn, I'll let you follow and respond to that. And when we finish that, we'll then move to the next witness. Otherwise, it just becomes such a jumble. And that's how I will eventually write the Order. We will go witness by witness through that. You've got to get kind of down in the weeds and address these individually.

And I will say, in y'all's briefs, we went back and forth. It's easier when y'all broke it down by witness to me in my own mind, because you've got all of these studies and all of these witnesses, some of them are talking about causation and efficacy, some of them are talking about one or the other. It's a little hard to keep it all straight. So I think that's a good way to do it.

So with that, Mr. Cheffo, you want to begin?

MR. HAHN: Your Honor, I would like to just introduce to the Court Andrea Bierstein. She is the PSC's lawyer. We need a real lawyer today. She's with the Simmons Hanly Conroy firm, and she will be --

THE COURT: What is your name?

MS. BIERSTEIN: Andrea Bierstein, Your Honor.

THE COURT: Where are you from?

MS. BIERSTEIN: From New York.

THE COURT: Good. Glad to have you here with us. I haven't seen you here before.

MS. BIERSTEIN: Actually, Your Honor, I was here when we argued the preemption motion on the Texas statute, but I did not get up and address -- I did not end up addressing the Court, but I was sitting here in case you had any questions for me.

THE COURT: You mean they need a real lawyer, you were here to answer? It's great to have you here. We just -- all these Charleston lawyers' wild arguments made by these New York lawyers. Glad to have you.

MR. CHEFFO: We are going to break them all -- lest I forget, Ms. Birnbaum is going to be arguing --

THE COURT: I know Ms. Birnbaum. Happy to have you here.

MR. CHEFFO: -- the efficacy argument, and Ted Mayer from Hughes Hubbard, also a New York lawyer, dealing with the Fleming argument.

May I, Your Honor?

THE COURT: You may.

MR. CHEFFO: First, let me thank the Court and your

staff, really I'm sure on behalf of both parties. We did file a lot of papers and the plaintiffs did file a lot of papers and we know Your Honor spent a lot of time. And we really do appreciate all that.

So I'm going to be addressing the plaintiffs' -- I'm sorry -- Pfizer's motion to exclude the plaintiffs' expert testimony on general causation.

Now, Your Honor, from the beginning of this case when it was first filed the plaintiffs told us that this case was about women who would not or should not have developed diabetes except for the fact that they took Lipitor. And they said there is a certain group, there is certain people, certain women who seek compensation and are deserving of it. That's what they told us. And they also told us throughout this litigation that they are certainly not seeking to have every woman who took one Lipitor tablet and develop diabetes, that's not a proper plaintiff in this case.

But, you know, what's happened, Your Honor, is that since the litigation was initially filed -- and I'll put this up on the screen, too, so counsel can see this -- there was a lot of advertising, Your Honor knows that, and a lot of cases were filed. And all those cases were filed essentially without any filter, without any guidelines. They were filed essentially, if you claim to have taken Lipitor and if you claim to have diabetes and you filed a lawsuit -- there is no

filter.

And essentially what plaintiffs are asking for is the extraordinary relief that Your Honor pass all of their witnesses on general causation as to any woman. Now these are just some of the guideposts.

So -- and let me just say this: I'm hoping -- and maybe I'll be surprised and Your Honor will ask questions of counsel or counsel will tell us, No, you've got it wrong, there actually are a bunch of parameters. We do suggest some limitations --

THE COURT: I've got to tell you, I haven't seen it and I've asked that question several times. Because I frankly thought that we would have this group narrow; that it would not be the universe of people. But up to this point I haven't seen that, either.

MR. CHEFFO: Thank you, Your Honor. Neither have I.

So, you know -- and, you know, we probably could have had 50 bullets on it but some of the things that jump out at us -- any dose. Is it 10, 20, 40, 80? Is it for any length of time? Can you take it for one day, five years, three years? Are there any parameters? So, I mean, does this cause an increase of 1 milligram per deciliter or 250 or 300 or can it be anybody? Does it matter if you take other medicines, other statins or other medicines that raise

glucose or cause diabetes? Haven't seen any parameters. Does it matter if you took another statin before or after? So the last six months before diagnosis? Haven't seen anything. Maybe we'll hear about that today. Does it matter if you have zero, one, two, three, four, 10 risk factors?

And I think Your Honor gets the point. Anyone who took Lipitor and developed diabetes, that's what the plaintiffs are saying this general causation hearing should be about and Your Honor should pass them. And we don't think that certainly satisfies *Daubert*.

Now, in addition, they've kind of -- these are very good lawyers, right? So we expect them to kind of move when they feel like they need to. But from the beginning they said this case is about causation. As I indicated -- and we said, Okay, we'll take you at your word. We will address that. The plaintiffs said it's about causation. And we said there is no causation here, certainly for this literally every single woman whoever took Lipitor and developed diabetes. And I think the plaintiffs realize that they were in an untenable position because they had this huge constellation of plaintiffs who just filed lawsuits.

So then they've told us, well, it's actually about acceleration. But we see that kind of a passing reference in their briefs, but it's not something that they even say they are waiting -- their experts are going to opine about.

And again, you know, I think we all, plaintiffs and defendants, should be guided by the reports and by the Complaint. And if you look at the Master Complaint, you see causation, causation, causation, causation. Fair enough. We got that. We don't see acceleration.

So we hear about acceleration. You know, I think Your Honor should focus on what the plaintiffs have alleged and what they told us that we should be focusing on.

Now, there are six experts -- there is some good news in this story, Your Honor -- when we initially filed our motion, it wasn't clear to us as to exactly who was going to be offering a causation opinion. And that's why we filed our brief kind of as a somewhat of an omnibus brief.

Since then in their papers -- there has been no controversy about this -- the plaintiffs have said, even though Dr. Jewell testified in his deposition that he was going to be offering a causation opinion, the plaintiffs have taken a different course. And they said at no point does Dr. Jewell assess whether the associations he quantifies are causal in nature. No causation opinion. Same for Dr. Abramson. He does not purport to analyze whether that association was causal.

So on this point, Your Honor, I just drop a footnote, I would ask that our motion be granted with respect to causation of Dr. Abramson and Professor Jewell, and that

they should not be allowed to offer a causation opinion consistent with our motion here or at trial.

Then we have the three next folks -- doctors, excuse me -- Dr. Michael Quon. What they say -- and I'm looking at their opposition brief, Your Honor, for how they characterize it -- they say Dr. Quon and not specifically provide a discrete causation opinion, although he does opine on that topic.

So I'm not really sure exactly what that means. And again, maybe counsel will clarify for us. I'm taking that to mean that he's not offering a causation opinion. He's a mechanism guy. And maybe what he's doing is offering some information that others rely on. We'll address it to the extent that he is offering a causation opinion, but from reading that, my kind of fairest reading is that he's not. Then we have Dr. Gale and Dr. Roberts.

Dr. Gale -- and the plaintiffs have chosen their words very carefully -- just to jump for a second to Dr. Singh. When the plaintiffs say in their brief, they say very clearly Dr. Singh is offering an opinion that Lipitor causes diabetes, right? We disagree, but can't fault them for their clarity. I got that.

With respect to Dr. Gale, though, again I think they are choosing their words very carefully. Lipitor increases the risk of diabetes in a sustained dose dependent manner.

They don't talk about causation. Increased risk is not causation. At best, it's association. But Dr. Gale should not be able to offer a causation opinion here or at trial, and our motion should be granted with respect to that. And we'll talk specifically about him.

And then Dr. Roberts said the only causation opinion is that Lipitor clearly increases the risk of diabetes. So the only opinion I have on causation is really, I don't have a causation opinion, I have an association opinion.

But then they tell us in their brief, Dr. Singh, Dr. Sonal Singh, is the primary general causation expert on whom plaintiffs rely. So we are going to focus, you know, with Your Honor's direction a fair amount on Dr. Singh.

THE COURT: He's the first one we are going to talk about.

MR. CHEFFO: Exactly. And some of the principles will cover others, so that's going to be a little longer. But I think Your Honor sees where we are going.

Your Honor we know very well has read the cases and the footnotes and certainly is familiar with *Daubert*. The reason why I highlight a few specific legal principles here is that this is very much, we see is, other than perhaps for Dr. Abramson, really a joinder analysis. It's a gap issue. You have the analytical gap on the one hand of plaintiffs looking at their analysis of Lipitor and diabetes, and the

gap probably across the room over there is the clinical data and also just kind of the medical and scientific realities of the diabetic process. That gap is too wide for any of them to formulate an opinion on causation that passes *Daubert*. We don't have to listen to the ipse dixit -- again this is the Supreme Court in the *Weisgram* case -- talking about Your Honor has an ability to look at the expert sources and whether they support the conclusions.

Again, I'm going to spend 30 seconds on this at most. I know Your Honor is certainly more than generally familiar with these principles, but they are important, right? Just to remind us all as guideposts that you first have to determine if there is an association. And in order to determine if there is, in fact, a real association or true association, you have to look at the data, and particularly the studies. Is it a result of chance? Is it bias? Is it confounding?

And really importantly in -- in this litigation -- and these issues where we have frankly so little data that the plaintiffs even rely on in the face of kind of the crushing amount of data that is available, is there replication? Is there consistency? Is there a there there? Do we actually see it in the mountain of evidence that the plaintiffs have available to them?

And then if you determine that there is a real

association -- and I think again as Your Honor knows this -- Bradford Hill says there has to be a clear cut association before you even get to the Bradford Hill factors. So we think it's kind of don't pass go, stop here. But if Your Honor disagrees and goes further, then you apply the Bradford Hill.

Replication, you know, briefly. Epidemiologists generally will not draw conclusions in the absence of replicated statistically significant epidemiological findings. I don't think that these are really going to be in dispute. You need to replicate these findings. Consistency is important. That's what Judge Rufe said in the *Zoloft* MDL just recently. This has been -- we've touched on this in our papers so I'm going to just briefly introduce the Court to I think these concepts that are at least very important as you think about this analytical gap.

Now, diabetes doesn't happen -- I think as we all know now, when you are kind of diagnosed, it's a process that is a 10-year process. People go from normal glucose levels to prediabetic to full-blown diabetes. So the fact of crossing the line really doesn't tell you almost anything about the story. It's when kind of the race began, if you will.

And here is just some of the parameters. They have changed over time, but the current parameters from the

American Diabetes Association, if you are below 100, you are normal, quote unquote, normal. If you are 100 to 125, you are prediabetic. If you go over the diabetic threshold of 126 -- and there is several tests -- you are kind of diagnosed with diabetes.

But here I at least thought -- found this to be a really helpful chart. You don't have to take our word for it, it's from the American Diabetes Association. But this kind of highlights -- this is a continuum. This is a process. And what is interesting when I first saw this is the process is starting when you have normal diabetes, right? That's what the ADA tells us. And it goes all the way through to now when you are prediabetic.

And here also this term hyperglycemic that you will be hearing a lot about, it's kind of a catchall that covers people who are both diabetic, who are prediabetic, it's anybody who basically doesn't have a normal glucose level. And again, continuum. And there really shouldn't be a dispute about this. This is the plaintiffs' expert. This is what Dr. Gale tells us. The progression from disease initiation to diagnosis is a long, slow process that takes at least a decade or so. So we agree with this and we agree with this.

He also tells us that it's a multi-factorial disease. The causal mechanisms remain unknown. I think his

words are there is -- maybe it's not his words -- but there are a quartet of risk factors: Age, weight, race, age and ethnicity. I suppose the plaintiffs would say that exposure to environmental toxins is something that he's referenced, but it's certainly not in the big four, if you will.

And, you know, I was going to say Your Honor may have been surprised to see this, but -- I suspect Your Honor is not surprised to see anything these days -- but Dr. Gale told us that Lipitor increases glucose about 2 to 3 milligrams per deciliter. Sworn testimony. He's a diabetologist. And then he says it's not going to matter and it wouldn't worry him as a clinician.

Dr. Quon says these small changes are not clinically relevant. Now, the plaintiffs are going to come back and say, Well, this is an average, and there could be more or less. But when we are talking about averages, when we are talking about general causation, when you look at the population based on the data that the plaintiffs agree with, it's an infinitesimally small, clinically insignificant elevation to the extent it even exists.

So what do the plaintiffs rely on? They primarily rely on SPARCL/Waters. I'm not going to talk about that now. I'll save that, with Your Honor's indulgence, until we talk about Dr. Singh.

They also rely on not just the whole NDA, but

certain tables from NDA studies, which we'll talk about, and observational studies, which everybody agrees can have some use but are the lowest form of evidence. These are the Bradford Hill factors, to the extent that we get to them, or Your Honor gets to them in your analysis.

And just briefly, when you look -- you know, I think to distill our kind of positions here, there is no association -- there is no clinical trial data that shows across the board causal connection between Lipitor. But to the extent they even look at the Bradford Hill criteria, they do not support a causal connection. So there is no consistency. The plaintiffs rely on one 80-milligram, 80-milligram dose, which is the highest dose. That's it.

There is temporality. So this coherence and temporality go hand in hand, I think in the analysis here, which is if you have kind of ingestion that starts after the disease process starts, well then you certainly can't have temporality or coherence under Bradford Hill. The strength of the association, I think in our papers you will see, is at best extremely weak. And biological gradient, that is kind of a -- I understand that as a fancy way of saying dose response.

And I think what is interesting is the plaintiffs say, Yeah, of course dose response is really interesting. You will see each of them say, We didn't look at dose

response. Again, plaintiffs have the burden here. And I think that we will highlight -- and Your Honor, it's very important here in light of the dose response to look at very critically, as I know Your Honor will, the data that they look at. And what they are going to point to is 80 milligrams information and then NDA and observational studies.

And I think we are getting near the end, Your Honor. I'm going to turn it over to my colleague. But, you know, you don't have to take my word for it. Dr. Gale made no attempt to stratify the data by dose and estimate the risk by dose. Dr. Quon made no effort to estimate the diabetes risk for Lipitor taking 10 milligrams. Their main expert didn't analyze the Lipitor data by dose. And Dr. Roberts, to the extent she offers even an association opinion, she refused to adopt the word causation and said nothing about dose.

So again, thank you very much for indulging me for a short opening. I'll turn it over --

THE COURT: Thank you. Very good.

Opening statement by the plaintiff?

MS. BIERSTEIN: Good morning, Your Honor.

THE COURT: Good morning.

MS. BIERSTEIN: I have to confess at being a little bit I think at a disadvantage here. I had prepared an opening that was going to be much more of an overview, and

Mr. Cheffo's gone into a great deal of detail on some of the points that I had planned to address later. And we are going to have to kind of play it a little bit by ear in terms of how much you want me to get into some of that detail in the opening. I've got a lot to say about the 80-milligram dose, but I'm not sure that it's appropriate to do now.

THE COURT: We are going to --

MS. BIERSTEIN: So --

THE COURT: -- I'm glad to -- in some ways I had -- I'm usually not a big fan of sort of these opening statements when it's me, particularly when y'all have briefed it so ably. But counsel asked me to allow you to do it to give sort of an over -- general summary. You need not get into the weeds because we are going to do that witness by witness. So don't feel compelled to answer everything he's raised.

And I'm glad to hear -- I'm more interested in sort of your sort of big picture assessment of sort of the plaintiffs' theory and why these motions should not be granted.

MS. BIERSTEIN: All right. Let me try to do that.

I think some of the points he raised I do want to address at least glancingly and try to give you an overview of what we think is most important.

And I think where we start in terms of what is the most important issue is kind of the why are we here? This is

not the place where we are going to prove to you that Lipitor causes diabetes, that it can cause diabetes at a 10-milligram dose, that it can cause it at a 20-milligram dose. That's going to be something that happens at trial or on summary judgment. The purpose of this hearing, as Your Honor is well aware, is much more limited.

And I really want to try to distill *Daubert* and Rule 702 I think down to the essence because there are two questions that Rule 702 identifies and that *Daubert* identifies, and I want to tie what I have to say about each of our experts to those two questions. The two questions that *Daubert* asks are: Is it science? And the second question is: Is it helpful to the jury? That was the Supreme Court's starting point in *Daubert*. And you will see that on page 592 of the *Daubert* opinion.

Looking at the text of Rule 702, because we were talking about scientific knowledge, at least where we are talking about scientific experts -- and there is a little wrinkle on that with *Kumho* and experts who are not doing science -- but if it's science, that reliability question, what the Supreme Court asked was, is this science? Because if it's not science, then it doesn't fall under it. So that's what these questions, is it science, is it helpful, were intended to replace the question of general acceptability and to liberalize admissibility. And the

Fourth Circuit has recognized that Rule 702 was intended to liberalize admissibility.

So when we get to the question, is it science, okay? If you look at our experts: Doctors Quon, Roberts, Jewell, Singh, Gale, Fleming, Wells and Dr. Abramson, every one of these experts is an eminently qualified scientist. They all employed standard scientific techniques. This isn't some kind of flakey novel, deception test machine the way we had in the *Frye* case, which is the beginning of all of this. These are doctors -- they didn't do this just as experts in this case, Your Honor. These are scientists who in their career as scientists, they perform randomized clinical trials in some cases. They analyzed clinical trials. They do observational studies. They analyze observational studies. These are working scientists.

And I think this is particularly the case, Your Honor, with Doctors Quon and Roberts and Singh. These are scientists who are in the lab, so to speak, running experiments, forming scientific opinions. This is not astrology. Dr. Jewell, Dr. Wells, using standardized statistical techniques. So this is science.

Now, can their work be criticized? Of course it can. Did they afford proper weight to each study they looked at? That's a question -- seems a fair question to ask. Did they choose the right statistical tool? That's a

question you can ask.

But I would suggest, Your Honor, under *Daubert*, for example, the choice of the tool is within the expert's judgment as long as the tool is one of the tools of science. So when you are deciding, how do you analyze statistical data? You've got lots of tools that are recognized, have been accepted in peer-reviewed science. The expert has to exercise judgment. Which one of those am I going to use?

Now, is there a limit to this? Absolutely. If the expert says, Well, I made up a new tool yesterday and here is what you do: You assign a color to each number and then you do a randomization and you throw the colors up on a sheet of paper and then you look at it like a Rorschach test, you say that's not science because that doesn't pass the tests under *Daubert* of, you know, has it been published? Is it peer reviewed? Is it testable? But once you've got a tool that is within the realm of science, it's the expert's judgment which tool to use; how to use the tool.

So, you know, again, are there questions here? Did they review enough documents? Did they look at all the right studies? Did they consider each and every one? These go to weight. This is all about how you cross-examine these experts. This is not the question that *Daubert* asked us to address, which was is it science?

And I just want to add, as I say, I mentioned the

Kumho caveat for a minute, because I think *Daubert*, with its focus on methodology, because we are talking about science, when you look at *Kumho*, you have to recognize that when you get an expert in an area that's not strictly science, you are less focused on methodology and which tools and you become more focused on experience and judgment. Does the expert have the experience and judgment to do that?

And so I think that's really the -- what sets the framework here. And I think there are a number of instances -- and we'll do this witness by witness -- where our experts, practicing scientists in the field say, I've done the experiments. I've read the clinical trials. I've read the observational studies. Here is what I take from them. And they explain point by point. And Pfizer wants to come in and say, but that's not really right. And we think you should read this study this way. And we think this study deserves more weight. And they are entitled to do that at trial, Your Honor, but that is not what this exercise is about. This exercise is about, is what they are doing science? And I submit that what all of these experts are doing in terms of the specific opinions they offer, and when you come to that, that is science.

Now, Mr. Cheffo asks, are there any limits on who the plaintiffs can be and what these cases are? And as I said, I've got a lot to say about the 80-milligram dose and

about risk factors. I'm not going to do that now because I don't want to get way into the weeds. But I do want to say in a more general way the answer to that is yes and no.

And it's yes in a couple of very important ways: It's yes in the sense that we are only talking about therapeutic doses here. We are not talking about, you know, the peanut allergy kid who if there is one grain of peanut somewhere in a room, it's going to have an anaphylactic shock reaction. Nobody is saying that Lipitor in infinitesimal doses, we are talking the therapeutic doses are relatively limited. So we are talking about therapeutic doses to begin with.

Second of all, are we talking about time limits? And I think this is where I get to the yes and no because some of these questions, Your Honor, are case specific questions. How long do you have to take it before the effect shows up? How many risk factors do you have to have? Well, maybe it depends on the particular plaintiff. What was -- what was the plaintiff's BMI when she started? How long was she actually taking it? What else was she taking? There are a number of issues.

And I think when we did the case-specific briefing you can see how those play out. So on the one hand I'm going to say, of course there is some limits here because, as I say, we are not talking about infinitesimal amounts.

And I just want to say, there is a lot of evidence at the doses below 80 milligrams in the real world. And that's what I'm going to get to when we get there. Because I think that's -- that's a really important point. And I've got about six arguments on it.

But I think, you know, we are talking about therapeutic doses but we are also saying that some of this is case specific. Are there women who we -- who you can't say, yeah, Lipitor was the causal factor here? Yes, I'm sure there are. Can we get a specific causation opinion on every woman who took Lipitor once and got diabetes? I think the answer to that is no.

And the notion that these cases were selected with no criteria at all I think is wrong. I think that plaintiffs' lawyers are well aware that there are some people for whom you are not going to be able to get that kind of case-specific opinion. That someone is going to look at them and say, This person was too close, had too many risk factors, too many other issues. But I think a lot of that --

THE COURT: I've got to be honest with you, I had expected when I started this, with these experts, I had expected to see some of that delineation, that there were -- it wasn't the universal class. I didn't see a lot of that in y'all's briefing and in your expert reports.

MS. BIERSTEIN: I think the reason you didn't see

it, Your Honor, is because the science doesn't support it. And when I say that, I guess I mean -- and I confess I am going to get into a little of the weeds here -- the NDA trials were 10-milligram trials, the ASCOT trial was a 10-milligram trial. The safety updates that Pfizer had following the NDA trials, you can either call them the '99 and 2001 or you can call them the 2000 and 2002, depending on whether you are talking about --

THE COURT: Now you are really getting into the weeds. I haven't gotten that much into the weeds.

MS. BIERSTEIN: Those are dealing with 20-milligram and 40-milligram doses. We are also looking at a situation of other statins. We've got a class of some of the other statins are weaker than Lipitor. So you've got a strong statin at a lower dose versus a weak statin and you are still showing it as lower doses some of those other statins.

So there is a lot -- the reason our experts didn't draw a line and say it's only this dose and above, I mean, first of all, Lipitor didn't come in that many doses. We are not talking about a 10-milligram dose on the one hand and a 400-milligram dose on the other. The ranges are 10 to 80. So it's a relatively narrow band. And again, it is a strong statin compared to some of the other statins. So you are not seeing that here because the science doesn't support it. And that's also --

THE COURT: Does that mean you don't know the answer yet or that at any level it causes diabetes?

MS. BIERSTEIN: The evidence so far shows that at every level. We saw it in the 10-milligrams trials. We saw it at 20 and 40 milligrams. We see it in the observational studies. Mr. Cheffo is poopooing observational studies. And I understand we are not going to show causation primarily or solely out of observational studies, but observational studies give us real world confirmation about what happens when people take actual therapeutic doses in the real world. And we see in the observational studies, we see it across the doses. The science doesn't support the stratification. And that's what our witnesses are saying, that the science does not support that.

Now, the other thing Mr. Cheffo said -- and I think it's important to refute this -- he says none of our experts did a dose-response analysis. And that's simply wrong, Your Honor. I have the page citations where each of our experts talked about dose response. But they didn't find a basis -- and this is the testimony he's referring to -- they didn't find a basis to draw a line and say, No, we are only seeing it here. And as I say, partly because it's also we are seeing with the other statins, even when they are weaker statins. So even when they are weaker, they are still causing it.

So we can't get rid of these doses because the science hasn't found any reason to believe -- the science is showing it across all the doses. That's what our experts are saying. When they look at the 10-milligram studies, when they look at the 20 and 40, they are saying -- and you know, again, I was going to save this for when we got to Dr. Quon. I've got his specific testimony --

THE COURT: Let me ask you: Is there some difference between the phrase that Lipitor caused diabetes and Lipitor is causally related to diabetes? Does that mean something different?

MS. BIERSTEIN: I don't believe it does mean anything different.

And actually, Your Honor, that was a great segue into the next point I was about to get to. Because I think that takes us to, I think, one of the fundamental differences we have with Pfizer here, which is, what does it mean to talk about Lipitor causing diabetes?

And, you know, I think Mr. Cheffo is suggesting there is a lot of softness here. And I think cause and causally related are the same. I don't think any difference was intended. I think it's the way scientists talk when they say causally related. They mean the relationship is one of causation.

Now, having said that, where I think we have the

largest disagreement with Pfizer here is what does causation mean in this context? But what Pfizer's claiming -- they have a unique view of causation that's unsupported in the law --

THE COURT: What is the plaintiffs' view of causation?

MS. BIERSTEIN: The plaintiffs' view of causation -- and I think this is a legal point -- is first of all, you don't need to be the sole or original cause. It's sufficient to be a substantial contributing factor.

So if a disease process has started -- and this is a disease process in which maybe 25 percent of the people in whom it started may progress to diabetes, sometimes the estimate's a little higher. Many -- most of the people that begin that process will never progress to diabetes.

If Lipitor is a substantial contributing factor in getting them there, that, under the law, is causation. So is aggravation of an existing condition.

You know, we all remember from law school that eggshell skull plaintiff, the plaintiff with the, you know, thin skull. You clonk them on the head and it wouldn't have cracked somebody else's skull but it cracks his.

So if you have a plaintiff on a road that may go to diabetes or it may not go to diabetes and the Lipitor pushes you on to the diabetes road instead, even though you were

already on the path, even though your process started, under the law that is causation.

And again, this is an issue, there is a lot of overlap here. We briefed this in greater depth in our case-specific briefs where we got into Colorado law and Missouri law. But I think these concepts substantial contributing factor, aggravation of existing condition, these are not unique to Missouri law or Colorado law. These are standard, common law concepts about causation.

And so our view is that it doesn't matter if a plaintiff had begun the process or had prediabetes. If Lipitor made the difference and made it in a substantial way -- I mean, we are not talking about the straw that broke the camel's back; we are talking about a substantial -- not just a contributing factor -- but a substantial contributing factor. We are talking about an aggravation. And I think, Your Honor, we can be talking about an acceleration; that is, getting there sooner.

And that's another thing that Pfizer kind of dismisses. They say, Well, all you are saying is they got diabetes sooner than they would have. Well, I want to suggest, Your Honor, that every wrongful death case is about an acceleration. Somebody got there sooner than they otherwise would have. That doesn't mean there is no causation.

And in the case of diabetes, which is a progressive disease that attacks, affects the vascular system, the macrovascular system, you get the retinopathy, people go blind, they lose their limbs, whether you get that disease when you are 50 or whether you get it when you are 80 when it's much more common -- lots of people in their old age will develop diabetes -- makes an enormous difference. And if Lipitor -- it's an injury, and if Lipitor causes you to get it ten years, 20 years, five years, two years earlier than you would have, under the law that is causation. That is a cognizable injury that a person has suffered.

So I think, you know, that's sort of the last piece in our sense of causation.

THE COURT: And obviously if you would accelerate it from 50 to 80, somebody got it at 50 rather than 80, that would be a substantial contributing factor -- would be a substantial difference. How about if you get it 5.4 months earlier than you would have gotten it otherwise?

MS. BIERSTEIN: Well, I think, Your Honor, this is where you get kind of a jury question. You know, there is an issue, was the contributing factor -- was the contribution of Lipitor substantial or minor?

I think that's going to be something a jury is going to have to hear case by case and decide if this -- you know, in a person who maybe has so many risk factors and is so

close to it or, you know, they have some baseline glucose levels, a jury might say for a particular plaintiff, no, that wasn't substantial. But there is a reason that substantial contributing factor is the jury test; it's not the *Daubert* test.

THE COURT: Of course that's not our -- on an individual, you know, here is general causation. Obviously our next round will be case-specific causation, which is --

MS. BIERSTEIN: But I think on general causation what we can say is we are -- our experts are talking about the question for general causation, Your Honor. Before you bring in your case-specific expert which says diabetes caused -- for example, Ms. Daniels -- I mean Lipitor caused Ms. Daniels' diabetes, we need to know that Lipitor is capable of causing diabetes.

THE COURT: I agree with that.

MS. BIERSTEIN: So what I'm saying when we talk about is it capable of doing it, we mean is it capable of making the difference, of being a substantial contributing factor? Is it capable of aggravating it in a legally cognizable way? Is it capable of accelerating it in a legally cognizable way? And the answer to that question is yes. I think it's an unequivocal yes. And I think that's what our experts are saying.

So I think the problem here is that Pfizer seems to

want to have some very narrow approach to causation, which is not what the law requires. And if we look at the law and then we look at our experts' general causation opinions, we see that when they talk about increased risk and causally related, that they are squarely speaking to the legal meaning of general causation.

And that actually brings me to the last point I want to make on this overview -- and I know I've kind of gone a little long on this --

THE COURT: That's okay.

MS. BIERSTEIN: -- but I think when we go expert by expert, I think this will be clear.

But I think we've got to look at the specifics of the expert reports in a couple of ways: First of all, what opinions are these experts actually offering? And again, this is an area where I think there has been a lot of confusion. Rule 26 requires us to provide a report that includes not only the experts' opinions, but also the facts and the basis, the basis and support for those opinions, as well as the facts and data that were considered in forming them.

So we -- in most of these cases -- and I think all but one -- you've got a report that says, Here are my opinions, boom, boom, boom, boom, boom. And then you've got a long discussion of the basis for them.

Now, Pfizer thinks there is some confusion about what our experts are opining. They are opining what is listed in their reports. Now, Pfizer asked them at their depositions about other things that they might have had opinions about. As they said, Dr. Jewell did not offer a causation opinion. They asked him at his deposition, Well, do you have one?

THE COURT: Are you telling me that Dr. Jewell will not offer a causation opinion?

MS. BIERSTEIN: He will not.

But, you know, when Mr. Cheffo says, well, you should grant their motion, I'm thinking, well, you know, the defendant doesn't normally make motions to exclude opinions that the expert has never purported to offer.

THE COURT: Let me say this: It's a little hard when -- you know, one of the challenges -- I took a lot of expert depositions in my day, and you have an expert report and then you get in there and the expert will invariably offer -- what the offering -- the questioning lawyer will say is different from the report in which the offering lawyer says is merely an elaboration of it. So there is always this issue. And so it's entirely proper to get the full scope of his opinions.

To the claim by Mr. Cheffo that the only witness that will testify as to general causation, specifically offer

an opinion, is Dr. Singh; is that correct?

MS. BIERSTEIN: No, it's not, Your Honor.

THE COURT: Who else will say that?

MS. BIERSTEIN: I want to be clear on that.

THE COURT: That's important.

MS. BIERSTEIN: We have four experts that will talk about causation. What we said in our brief is Dr. Jewell is not one and Dr. Abramson is not one. We have four reports: That's Dr. Singh, Dr. Roberts, Dr. Gale and Dr. Quon. And I think this -- you know, this is something I will -- again, this is in the weeds, I don't want to do it in the overview. I have page citations, Your Honor, to each expert report where each of these causation experts considers the various Hill factors that would take us from association to causation. Even though they don't use the word -- they don't, you know, use the word Hill factors, but they -- actually, each of the four experts considers -- considers the Hill factors and reaches a causation conclusion. And it is our position that all four of those are general causation. And I think that's the way we briefed it.

I mean, Mr. Cheffo is parsing some of the words in the brief because some of the experts didn't isolate their opinions the way Dr. Singh did. But they -- the report is filled with causation language. You will see that in Dr. Roberts', and with the analysis to support it.

THE COURT: But the Hill factors involve not just a consideration of these itemized things, but a collective judgment based upon them as epidemiological matter and opinion, right?

MS. BIERSTEIN: But I think that's what you see in the report. I think when you see that each of Dr. Quon, Dr. Roberts, Dr. Gale -- I'm putting Dr. Singh to one side because he separated it as a separate part of his analysis -- but what you see in the other three is the progression as they -- there is very little in their opinion that is not part of the Hill factor. So it's not just a minor part of it. Each part of their opinion incorporates and is the basis of it, is in Hill factors.

But again, I would like to, if we can maybe postpone. But I do want to say something I think more particular about what I view as kind of the jigsaw puzzle nature of the experts, which I think is what maybe Pfizer doesn't get here, which is Dr. Jewell is not offering a causation opinion, but he is offering the statistical basis on which the other experts can then build their causation opinion.

As Mr. Cheffo put up the graphic, and we see we go from association to causation. We also know that the first thing you've got to do when you go from association to causation, you have to consider the strength of the

association.

Now, it's a fact that one of the things that epidemiologists do when they need to analyze their data and figure out the strength of the association is they will often hand it over to a statistician. Because it's the job of the statistician, who has special expertise to quantify that association and to tell -- to know which tool -- again getting back to the tools -- which tools, which data, how to isolate, you know, to cancel out factors, and the confounders. So the statistician is finding the strength of the association and then the causation experts are building on that --

THE COURT: Let me ask you this: When we get to Dr. Jewell, I have a -- I will tell you, I have some concern about some of the methodologies Dr. Jewell used. I'm going to tell you that. If I were to conclude that Dr. Jewell's, some of his opinions did not survive *Daubert*, what affect does that have on your other experts who are relying on that -- on general -- general causation opinions?

MS. BIERSTEIN: Well, I think, Your Honor, they are relying on it in fairly small ways for some of them. And so I think -- because Dr. Jewell, as I think I mentioned in our brief, they did not form their causation opinions based on his rebuttal report. They didn't have his rebuttal report.

THE COURT: The first report which -- frankly, the

rebuttal report seems to try to address weaknesses that were in that initial report. And to the extent the initial report doesn't survive, what does that do to your -- to the portions of it that don't survive -- what does that do to the physicians who -- or the experts who offered opinions based upon it?

MS. BIERSTEIN: As I said --

THE COURT: It's the foundation. Do they fail if Jewell fails?

MS. BIERSTEIN: Well, for one thing, Your Honor, I think they do not. Because as I say, Dr. Jewell's particular analysis of SPARCL, which is the only thing they relied on, is far from the sole basis of the opinion.

THE COURT: Is Hill's opinion broader than SPARCL?

MS. BIERSTEIN: In terms of what they relied on, yes, his opinion is, but I think in terms of what our experts built on I think it was not.

THE COURT: So it's -- your notion is -- I know when you get into the weeds there will be more specifics that might not be -- but generally speaking, the -- your view is that the experts rely on the portion of Dr. Jewell's work relating to the SPARCL stage?

MS. BIERSTEIN: Yes, primarily. When we get into the weeds -- but yes, that is primarily --

THE COURT: Let me tell you, I had less concern

about that analysis than any part of his report frankly.

MS. BIERSTEIN: I can hear that.

THE COURT: But I had real -- I've got to tell you, I have a -- and you will hear me on this because we will question it -- real concerns which look like to me like a lot of reverse engineering on his opinions. And, you know, as a court, we have a real concern with, you know -- I'm a light hand on *Daubert*. I don't -- I'm -- I don't think *Daubert* was intended that basically we had the trial before the Judge and basically decided the case based on the opinion of whether there is merit to the argument. I think there -- I share your view that there is a threshold you have to meet. And after that, it's a fight in front of the jury. I share that view. And I share the view that methodology is the centerpiece of that.

But I get really concerned when I see what looks like to me to be manipulation on data to produce a result. That seems -- particularly when it's -- you know, you've got all this peer-review material and you've -- and you -- and instead of offering your own peer-review studies, what you are doing is basically using different approaches that seem on their face pretty questionable to produce what seems to be a desired end. I have -- I saw less of that in the SPARCL analysis, which I think the studies go all over the place on those issues.

And SPARCL, I can understand why the plaintiff would focus on SPARCL. It makes a lot of sense. But I've got to tell you, of all your experts, Dr. Jewell left me with the greatest concerns. I've got concerns with a number of them, but Dr. Jewell left me with -- I had a low degree of confidence regarding his independent professional judgment. That he was -- that he looked like he was a member of your team. And that bothered me. And I will never master the statistics to the extent that I can make a meaningful judgment about the underlying stuff, but I can judge his input.

And, you know, they just got a computer program. They use a particular model that's in the computer. They just input it. We've got to look at what the input is. And when you start playing with the input, that makes me very concerned. And we'll get in -- when we get to Dr. Jewell, we'll get into the weeds of this, but there were a number of concerns that I had.

And I was -- you know, I wondered how dependent the plaintiff was of Dr. Jewell regarding these other issues. I mean, because I do see that a number of them -- I don't expect every one of these M.D.s to be statisticians. I mean, it's ridiculous. You don't need to do that. That's not their skill. But to the extent that's what they build it on, then you've got yourself a problem. You know, if

that goes, then does the whole house collapse?

MS. BIERSTEIN: Well, Your Honor, I think I would like to wait, and when we get to Dr. Jewell, try to persuade you whatever reservations you have are juror reservations; not *Daubert* reservations.

THE COURT: I don't want to confuse you that -- that -- I mean, I want to alert you where my concerns are. You know, I'm not a type of court that is going to leave everybody mystified about where the concerns are because part of this is to give you a chance to know what my concerns are and to answer them and to have the best opportunity to do that. And --

MS. BIERSTEIN: I appreciate that, Your Honor.

And the last point I wanted to make on Jewell and move on -- and then I think I'm done with the overview -- the last point I wanted to make about Dr. Jewell was to say Your Honor referred to, you know, whether one report versus another report passes muster. And I just want to note the issue here is not whether the reports pass muster, but whether Dr. Jewell can testify. The report is the pretrial disclosure of his opinions.

And if the rebuttal report gives Your Honor comfort that Dr. Jewell's opinions are -- have a better foundation than the initial report did, then I think what we are asking is can he offer certain opinions; not whether you like the

analysis in one -- I mean, I don't think what the issue here is --

THE COURT: I think in the end it's the final opinion he's going to offer is what's important.

It does present a sort of interesting dilemma when your experts relied on report 1 and you want to get him to testify on the basis of report 2. That gets a little complicated. But it may well be -- you know, I know he didn't do ASCOT initially. I know he did ASCOT in the second. And none of your experts relied on his ASCOT analysis, I mean, I understand that. And it may well be that on various witnesses he will say, you know, you can go this far, but you can't go -- you know, the methodology you use is not acceptable to go further.

I'm not trying to determine whether -- and we are now focusing, of course, on the issue of the -- of did -- does Lipitor cause diabetes? I'm not trying to settle that question. That's not for me to settle. But I want to make sure my jury is not misled. I don't want junk science and I don't want reverse engineering to produce a result that -- and that's why I focus not on the modeling. I assume these guys all have the computer programs down, standard computer, but I want to know how they did it. That they used valid -- valid scientific basis for what they put in and what they took out. That's what I'm concerned with. And you've got

to persuade me regarding Dr. Jewell that he did employ those methods.

MS. BIERSTEIN: I'm going to work on that, Your Honor.

But I did want to just add one last thing. In terms of the rebuttal report and people's reliance on it or testifying on it now even though they didn't rely on it, I think Your Honor remembers there is the whole story that we didn't have the ASCOT data and they didn't give it to us and where it was hidden. So the rebuttal report to some extent deals with data we didn't have at the time.

THE COURT: I'm okay. I know he got beat up about not using it and I allowed -- you know, listen, there was -- there is probably nothing the defendant disagreed more than my opinion to allow the ultimate rebuttal report. But my view was it was a close question. But y'all have in your hands not the claim of one individual, but thousands of individuals, and that the Court needs to make sure that everybody gets to put their best case forward.

So I -- you know, I did lean -- I've got to tell you, it was a very close question to allow it. But having done it, I feel like, you know, that report on its merits, whatever it is, I judge it on its merits.

MS. BIERSTEIN: Given that, Your Honor, I think our experts at trial would be permitted to rely on it to the same

extent that an expert can rely on later available information. The reports they gave were based on what they had at the time.

THE COURT: Well, you've got to disclose that. You can't -- you know, they said, I reach an opinion regarding number 1, oh, no, no, I didn't mean that, I meant it was report 2 now I relied on. I mean, at some point we've got to close the door on this. Because, you know, the complaint that Mr. Cheffo had is we've got a moving target. They won't stay fixed in one place. Y'all have got to stay fixed in one place. At some point you've got to put your feet down and say that's our opinion.

MS. BIERSTEIN: We are not offering new opinions.

What I'm suggesting, Your Honor, is that the expert who said, My opinion is supported by A, B and C can, as any expert can, say, Oh, and in the interim, D has come out and that provides further support. In the same way that I would expect Mr. Cheffo's experts, if a new study is published next week that supports his point of view, I don't think he expects that his expert can't reference the new study because they didn't have it when they did the opinion. The expert is going to say, I was right and we know I was right because this thing just came out last week that said it. I would like my --

THE COURT: I've got to deal with it as it comes up

specifically. But we can't be changing the argument every time the opposing side makes a valid point. Oh, okay, I've now got a new theory, I've got a new argument. Your experts came in and said, I relied on this statistical analysis. If it proves to be unreliable -- I mean, at some point they've got -- I mean, maybe this is we are ahead of ourselves. It may be irrelevant.

I told you if they are primarily relying on SPARCL, I was least concerned about his -- the input on the data in SPARCL. And, you know, I'm -- I frankly view the two issues primarily that we are going to be talking about, which is the -- the issue of causation regarding the connection between Lipitor and diabetes -- and the efficacy argument we'll get to a bit later -- as being frankly very different kinds of issues.

The -- I remember writing -- after I read all those -- absorbed all those different studies that have been done on causation, I remember saying there is something in it for everybody. There is studies. Some of them no association; some definite association; some increased but not statistically significant. It's for everybody. That is exactly what juries need to hear. You know, y'all sort it out. Y'all fight it out. I've got to say, the efficacy doesn't look like that.

I mean, you've got -- you know, you've basically got

people recalculating, re -- revisiting data, taking views different from authors. No peer-review studies. It's a really -- the contrast really is quite striking to me.

And I don't know -- y'all know strategy. I don't know how important the efficacy argument is to your ultimate position. It's a lot more difficult than your causation argument, in my own view. And the methods -- I mean, you have fewer witnesses -- but the methods of those witnesses cause me a lot of concern on efficacy, I tell you that.

MS. BIERSTEIN: I'm going to wait and address that when we get to those witnesses, Your Honor.

THE COURT: I'm sure you will. I just want to let you know what I'm thinking.

MS. BIERSTEIN: I appreciate that.

THE COURT: Excellent opening statement. I appreciate that.

THE COURT: Mr. Cheffo, let's go to Dr. Singh.

MR. CHEFFO: Okay, Your Honor.

I'm going to talk about Dr. Singh. I think -- and this applies to Dr. Singh and the others, we certainly -- I'm not going to reiterate what I said earlier -- we understand what the parameters are. We are not attacking conclusions here. And I do think we understand, we do get it, of what the positions are. And I think that's why we brought these motions.

And frankly, you know, I've never heard someone get up and really say that it's -- this is a legal issue, causation of -- medical and scientific causation is a legal issue. That's why we don't ask lawyers whether Lipitor caused their diabetes.

I think the question here is about methodology and is this gap, and looking at the various factors. So what Dr. Singh tells us -- as I indicated, you know, we have obviously some criticisms, but I can't criticize Dr. Singh for telling us exactly what -- or counsel for saying what it is that he --

THE COURT: He actually goes through the Hill factors in a very specific way.

MR. CHEFFO: He does do that. He's the only one that does that. And he says -- and this is why I guess when you have this other association, it's fair. And we didn't hear a single word -- I mean, the only thing we heard about -- and I think we will talk about the dose issue -- is, again, the only limitation is whether the therapeutic dose -- so if someone prescribes something that is not legal, that's not approved by the FDA, if it's a .1 milligram, if it's 10, 20, 40 or 80, that's still in. So I still don't think we've heard a single limitation, and certainly Dr. Singh doesn't offer one. Within the therapeutic dose limitation is creative, but it's -- it's kind of a limitation on nothing.

So what does Dr. Singh say? He relies on SPARCL/Water's analysis. He relies on NDA data. He relies on observational studies. He conducts a Bradford Hill analysis. We think it's a flawed analysis. And he does not do a dose analysis. So I'm going to cover each one of these.

Now, as I said earlier, the good news/bad news is it's going to take me a few minutes to get through here.

THE COURT: I think it's useful for others, as well.

MR. CHEFFO: So let's talk about the Waters study and what it did. I mean --

THE COURT: SPARCL/Waters.

MR. CHEFFO: So Waters is -- so Waters and DeMicco and others -- David DeMicco is a Pfizer employee -- there is some Pfizer employees, Dr. Waters is not. He published a few studies. And I think this one looks at SPARCL, IDEAL and TNT.

THE COURT: These are the 2000 analyses of the SPARCL data?

MR. CHEFFO: That's correct, Your Honor. And Your Honor has obviously read all this stuff.

But really where this came about -- I think it does help you kind of frame your timeline -- there was the SITAR meta-analysis that you may have seen or referenced. And they covered a bunch of different studies. They didn't

address specifically the issue -- so this was kind of follow on. This isn't a causation analysis, it was an exploratory paper, albeit peer reviewed, had used -- it was important, but the idea here was not to determine whether, you know, these showed causation.

Because in fact -- a few things. One is it's a post hoc analysis. It has limitations. You can do it certainly, but it has limitations. And what they were looking at here was new diagnosis of diabetes, right? Not the issue of causation. And they looked at three 80-milligram trials. So you don't have anything in here with respect to 10, 20 or 40.

So no one is suggesting that you shouldn't look at it or it is a waste of time. I think you have to realize what it can do and what it can't do to find out if there is an analytical gap when you basically say, Well, I looked at this study and it -- so SPARCL was the only placebo-controlled trial. TNT was comparing Lipitor -- Lipitor or another -- another medicine. And post hoc they didn't look at obviously the new development of the disease.

So what did the authors find here? Their words. They found a slight association only in looking at SPARCL. So again, the Waters' paper looked at IDEAL, TNT and SPARCL and they found a slight association between 80 milligrams because that's all they looked at. And you will hear me

probably say it a few times: Dose does matter.

The plaintiffs kind of want to wave their hands over it, but it's 80 milligrams and new diagnosis, new diagnosis of diabetes.

And then when they looked across the three trials, what they found was that the association only stood up at 80 milligrams because all three were only 80 milligrams. And when you had people who had three or four risk factors for diabetes, so people who were sick, had other problems.

And Dr. Hennekens, he's kind of a world class epidemiologist -- not kind of, he is a world class epidemiologist -- and he says what I think is black letter epidemiology: "Simply because the results of an individualized randomized trial not designed to test the hypothesis, that doesn't necessarily apply the presence of valid association, certain level on causation. Causality is a judgment that is made on the totality of the evidence; not from the results of a single randomized trial."

This is really, really an important point for us, Your Honor. Because again, we are not here -- and we've made this point in our brief, right? I think we recognize that there was a hierarchy.

If you look at the first paragraph of our opening statement, we said to Your Honor, we think that there is not enough evidence to show causation at any level. However, we

did recognize that in the hierarchy of proof and evidence, there is some data on 80 milligrams. And if you are going to look at it, you have to judge that. But you can't use this as, we'll talk about for 10, 20 and 40 and other data.

So here is the problem. So this is at best an association, slight association, the authors say. It's only one study, 80-milligram dose. The interesting thing, too, is not only was this -- this kind of post hoc analysis not designed to determine whether Lipitor or Lipitor 80 caused diabetes, but the actual study itself.

So they are doing post hoc analyses from three studies that weren't even looking at the question of diabetes. Ironically, the only one that looked at it was ASCOT where they have an end point. And Dr. Singh didn't look at the ASCOT data, except as part of kind of a whole meta-analysis.

So if you want to ask the question, it's unreplicated, small association. This is what actually the SPARCL author said. 80 milligrams, three factors, those are the factors. You had to have -- well, you had to have three or four of baseline: Fasting glucose, you are prediabetic, you have fasting triglycerides of over 150, which again is a very significant risk factor for diabetes, you have to have BMI over 30, that's clinically obese, and you have a history of hypertension. So you have to have three of four of these

and be taking the highest dose and then you have a slight association. That's what SPARCL says.

Now I'm going to move to the NDA, Your Honor, if that's okay?

THE COURT: Yes.

MR. CHEFFO: This is one -- I'm going to put up my little chart here in a second because I, you know, I frankly need it and it will help me; hopefully it will help Your Honor.

This is table 42 that I'm going to put up in a minute. So it's real important with understanding what SPARCL says and doesn't say. We are not running away from SPARCL or Waters. We are certainly not running away from our -- our tables in our -- in our NDA from 20 years ago, but we have to be fair about it and understand what it is and what it isn't.

So this is essentially a cornerstone of all of their experts. And I will come back to Your Honor. This is the Jewell analysis. And I think it's just not true. And I have a slide later to say that the experts only relied on a small piece. They relied very substantially on Dr. Jewell's analysis and particularly with respect to the NDA. Dr. Singh didn't even do this analysis himself. This is all Dr. Jewell. And this is a cornerstone of their causation opinion.

First of all, they say, Well, this shows causation. But the NDA data only deals with glucose levels. And we know -- this is back from 1996, I think, a few things happened before we even got to this point. There is a medical monitor that was required from Park Davis -- that was the sponsor at the time, it became part of Pfizer -- and that medical monitor looked at it and said there is no issue here with respect to diabetes. And it wasn't just that. Then the FDA looked at the data and said there is little evidence of an effect of Lipitor on glucose metabolism looking at this data that they now say, a-ha, shows causation at all ranges. This is really important to understand what this data shows, what it is and what it is not.

So they would have the Court believe that there is a three times -- this is what Dr. Jewell says, Professor Jewell -- three times as many Lipitor subjects had glucose increases than placebo.

So by seeing this just for a second, Your Honor, here is the placebo. What this whole chart is about is there was NDA data that was checked. That's in table 40, right? When you look at the 40 data, if you find out all the people on Lipitor in the NDA data and what their average increase was, 2 milligrams, just like Dr. Gale said.

Then they pulled out 3 percent of the 100 percent. So this chart represents the 3 percent of people in all the

NDA data. And you see the numbers. These are smaller. So basically when you talk about glucose levels --

THE COURT: We are looking at 37 people.

MR. CHEFFO: 37 for Lipitor, three for placebo.

THE COURT: Right. A total of 40 and 25 plus two have preexisting 125, above 125?

MR. CHEFFO: You are going to make me skip through some of my slides, Your Honor.

THE COURT: I read the stuff.

MR. CHEFFO: I read it, too, but it took me a little longer to understand it. But apparently it didn't take you that long. You know, maybe you got a copy of my slides before, Your Honor.

THE COURT: I wish I had.

MR. CHEFFO: So, you know, again, the point here, right, is these are not kind of normal people with glucose levels. These are folks, you know, this -- I had the question about this: I said, Well, if all these people, 25 of them of 37 were over 125, wouldn't that mean that they are diabetic? And the answer is under today's standards they probably were but they weren't diagnosed. But they had high levels and only one of these people had normal glucose levels.

So they say that, Well, a-ha, because there is a three times as many more people in the Lipitor arm as there

were in the placebo of this kind of people who already had abnormalities; therefore, that's what they keep telling you, three times. But wouldn't you want to know what the starting point was?

And when you look at the starting point -- before you get to this chart -- when you look at the people who are actually in the Lipitor arm, before they ever took one tablet of Lipitor, those folks, 5.3 --

THE COURT: They were like just random, but they had higher complication of 5.3 versus 1.9.

MR. CHEFFO: Three times more.

THE COURT: Right.

MR. CHEFFO: Got it. So that is one point. This shouldn't be, you know, kind of a big gotcha surprise that when you pull the data from those folks it's three times more.

Now, Dr. Jewell also told us that there is a 30-milligram average glucose. Because they don't like, obviously, the clinically insignificant to from table 40 when you look at all the data or Dr. Gale's testimony. So they want to say, well, it's an average of 30. Could be more, could be less. But, you know, again if you are doing it -- if you are going to be fair about it --

THE COURT: This is the one where actually the placebo group has more glucose increase than the Lipitor

group?

MR. CHEFFO: Exactly. Not only does --

THE COURT: I mean, this really just to me highlights the importance of not just doing association. You've got to dig into the weeds to look at this stuff.

MR. CHEFFO: Exactly, Your Honor.

And, you know, what's even more kind of -- I'll use the word stunning kind of politely -- is if you are going to compare them -- which he didn't do -- but what he did, he basically said there is an average --

THE COURT: You and I both know why he didn't compare them.

MR. CHEFFO: Not only did he not compare them, but he joined them.

THE COURT: He joined them, which is completely unacceptable. And he didn't compare them because it would defeat his thesis.

THE COURT: These are among the reasons I have just grave concerns about Dr. Jewell.

MR. CHEFFO: And I won't, you know, spend too much time because obviously Your Honor has gone through all of these.

But the other thing here, too, is when you look across -- so this is from table 40 that I mentioned, the whole data. He's saying, well, it's 30 milligrams and look

at everything. When you look at everything, there is two things that I think are really striking here.

One is there is a 2.2 milligrams per deciliter increase. So it speaks to the absolutely clinically insignificant kind of extremely small amount. But it also speaks to dose response, to the extent that there was. Because at 10 you see 2. Then at 20, what do you see? 1.5. Then you go to the next page, at 40, if 10 was 2 --

THE COURT: This is the NDA data?

MR. CHEFFO: This is the NDA data. 40/0 and 80 is 1. That's turning dose response on its head. That is not going to -- you can't put this --

THE COURT: These numbers are so small, it's very hard to extrapolate a lot of information about dosage.

MR. CHEFFO: There is no question. And you raise the exact right point, Your Honor. It would be -- I would use the word ludicrous -- it would be ludicrous for me to stand up here and say, look at that data. People shouldn't take metformin, they should start taking Lipitor because it will lower their -- by 50 percent, right? That would be crazy. But it's also crazy --

THE COURT: Just like the Nate Silver thing about the Pittsburgh Steelers and something else, you know, the presidential elections have a -- they win on the same -- it's ridiculous. It has nothing to do with them. But in nature,

randomly speaking, things will happen that have nothing to do with each other.

MR. CHEFFO: Exactly, Your Honor.

And again, just not to, you know, kind of belabor this point, but this is really graphically displayed. If you are going to rely on them for one thing -- all the experts rely so heavily on this -- this is what a dose response would look like, but it's not the data that they say causation relies on.

THE COURT: This highlights -- and I don't want to fixate on Dr. Jewell -- but, you know, when you've got a lot of really credible peer review people go in and analyze data and someone later goes back in and has a completely different take than the author, we are told that ought to be something we ought to be somewhat skeptical about. And then we get in and realize, this is what the input thing is all about -- you know, they are combining things, they are -- I mean, it's -- it undermines the Court's confidence in the integrity of the person who is presenting the information.

MR. CHEFFO: Well, we agree, Your Honor. We were very troubled by it, as well.

And in the face of this, we haven't -- you know, two things happened: We haven't seen a correction. Yet the plaintiffs, you know -- again, good lawyers fought very hard to have this supplemental report. They do the supplemental

report, and miraculously no one relies on it. It wasn't that hard to say adopted --

THE COURT: The thing about that supplemental report, I couldn't tell that y'all were ever given sufficient information in the rebuttal report about what data he was using in that rebuttal report.

MR. CHEFFO: I think there is -- I mean, we can get to that --

THE COURT: We'll get it. Because I think Dr. Wei makes this comment about I couldn't really tell what he did. Well, we've had these other problems that when we did know what he did, it looked like he was manipulating data. So I think y'all are entitled to have that information. It shouldn't be a mystery.

MR. CHEFFO: I agree, Your Honor, and I think it would be helpful, I think frankly even without it for the points I think Your Honor just raised. Here is that person that -- ASCOT was peer reviewed, stopped because it was efficacious, the data is out there, and it says at 10 milligrams there is no causal connection. He kind of crunches the numbers in a way that only Dr. Jewell could understand and finds an absolutely different analysis.

And then what's really interesting, you know, what they haven't focused on, they said there is only one part of SPARCL. But remember -- and maybe Your Honor will get to

this with Ms. Birnbaum in connection with the efficacy -- they rely on Professor Jewell's analysis for the gender issues, right? You know, kind of comparing and saying, well, women are at a higher risk, which is -- again, Dr. Jewell seems to be the only person kind of in the universe that has come to that conclusion.

But interestingly, if that was really true, wouldn't you do it for IDEAL? Wouldn't you do it for TNT? And wouldn't you do it for ASCOT? He didn't do it because he knows what the answer would have been.

So then observational studies. I heard counsel say -- and we don't disagree, I think, really on this -- I think what we are both saying is no one is suggesting that you should just toss these things out and not pay attention to them. But I think you have to understand that they have very serious limitations and that's why this is, their experts tell us, they are the weakest type of evidence. They only form the basis of developing a hypothesis; they are not causation generating.

In terms of establishing a causal relationship, you rely on randomized -- this is their witnesses -- controlled trials because observational studies are hypothesis generating and don't address the question of causation.

Plaintiffs admit that the observational studies --

THE COURT: Another thing with these random studies,

you predetermine what tests you are going to use, so you don't get this bias in which you are hunting for a result, right?

MR. CHEFFO: That's the first point, right? Bias and confounding. That's why everyone recognizes -- there is a few things. That is the biggest, the biased and confounding.

The other thing is they tend to be short-termed. And if the issue was we had a disease process that occurred within, you know, a skin rash, within a month, then you might want to know, like, do these studies to find out within a short period of time.

But you will see, kind of in the next slide -- I'll skip to this for a second -- I want to come back to this -- but, you know -- sorry. So this is -- this is the point of the studies with these observational studies.

So Dr. Singh recognizes, like Dr. Gale did, that this is, you know, a 10-year process. But somehow, I mean, talk about ipsa dixit, he said, but it's different with Lipitor. There apparently seems to be some magical process that is going on that kind of speeds up the diabetic process like nothing else kind of that is known to man. How do you know that, Dr. Singh? Well, because I've looked at observational studies. And during the course of these observational studies, a bunch of people were diagnosed with

diabetes; so therefore, it must be that Lipitor is causing the diabetes. That makes no sense. And that's essentially the problem with observational studies.

Now, so, you know, let's talk about the Bradford Hill. In fairness, as Your Honor noted, and I think as we noted, Dr. Singh is really the only expert who kind of takes on the Bradford Hill criteria. The plaintiffs may have a citation somewhere that, Oh, you know, it's like this in their report. But frankly, if you are going to do a causation analysis and you are going to spend the time, you should at least do what Dr. Singh did and tell us, Here is the analysis.

THE COURT: I think it's also important, none of these are the fixed. You've got to have -- you know, absolutely you have to have two or three or one or a particular one. It is a judgment, an epidemiological judgment, based on a combination of all of them. So if you haven't done that, you haven't really followed the Hill factors. The Hill factors involve both a listing and then a collective judgment based upon that, correct?

MR. CHEFFO: Correct. Couldn't have said it better, Your Honor.

And I think -- again, our point is, as I said, you know, we have to do the alternative arguments in this. But our view is -- I can kind of turn the projector off right

now -- because when you are relying on SPARCL at 80 milligrams with three or four and then you have NDA data that certainly doesn't show what they say. That's not the kind of clearcut association that Sir Bradford Austin Hill tells you you should have before you look at these factors.

But for argument's sake, let's assume that there is an association. When you look at these factors, Dr. Singh conducts a meta-analysis, and this is his own information, which of course has various studies and observational, but kind of the best that he could do, the plaintiffs' expert, is a relative risk of 1.09, which Your Honor knows is really, really small. And, you know, when you compare it -- and this is not even a specific causation argument. I'm still kind of talking about the strength of association. You could make these arguments about how could you possibly rule out a 500 percent increase or a 2,000 percent increase in the face of a 9 percent increase? But putting that for another day, when you are weighing the strength of association, is kind of Lipitor at best 9 percent, is that stronger than weight gain at 500 or prediabetes at 2,000?

You know, and then the coherence factor. It can't seriously conflict with general facts. We talked about that. You know, the vast majority -- I won't say -- to be clear, I can't tell Your Honor that there is not a single plaintiff here who started taking Lipitor ten or more years

before. I think that's infinitesimally small. These are folks who took it all after the disease process, for the most part, came. So it's inconsistent.

Again, temporality is the same issue. It's really almost a commonsense perspective here that if the process started before you started taking the medicine, it certainly can't be the medicine that caused it.

This is the Eleventh Circuit looking specifically at diabetes: "Temporal proximity is generally not a reliable indicator of a causal relationship, particularly where the development of diabetes occurs gradually over many years." So speaking really directly to what Dr. Singh did in these kind of observational studies.

THE COURT: But a temporal relationship is just one of the many factors one looks at. To the extent it's there, perhaps it's not that important, but it's a factor. It's a factor.

MR. CHEFFO: Totally is a factor.

But I would say this: I would say temporality here not only is a factor that may not help plaintiffs, of course, but it absolutely weighs against them. Because the temporality that we think -- and I think the scientists think, not the lawyers -- think is important is not the temporality of when you get diagnosed, right? The temporality of when the disease process starts. And if you

take Dr. Gale at his word and says the -- and the ADA --

THE COURT: I mean, you know, it was mentioned earlier that some people may be on the path of diabetes but never get it, right? There are people who don't --

MR. CHEFFO: There are.

THE COURT: And to the extent that Lipitor pushed people who would not have been in the 75 percent we were just talking -- the 25 percent hypothetical was given was that 25 percent go on to have diabetes, 75 percent don't. Without arguing the point about whether that's valid or not. Using that, if Lipitor pushed some who would have been in the 75 percent into the 25 percent from having -- would not have developed to developing it, then those people potentially have a claim, right?

MR. CHEFFO: Here is what I would say: They might in another litigation, right? But remember what this litigation has been about and what their Master Complaint is, is that these are people -- Lipitor caused it.

If you look at each of -- and I know you have -- but if you look at what they say their experts are going to testify, they don't talk about acceleration or pushing over the edge. And if they did, Your Honor, then that would be even more important. So it's, you know, tell us -- I mean, because if you take these --

THE COURT: You don't have to prove the sole cause,

all they have to prove is a -- you know, is a substantial cause.

MR. CHEFFO: But what they haven't done in the cases is they have basically said, these are people -- that's what their Complaint said -- who would not have or should not have gotten it. They have not said, Oh, my gosh, this maybe arguably could be a claim. It would be a different litigation. If their claim is there is a bunch of women out there who were obese, who had risk factors, the five or 10 factors, these people were really, really vulnerable, eggshell plaintiffs. And I think the JUPITER study that you referenced talked about accelerating, I don't think it was 5.4 months, I think it was weeks, right?

THE COURT: You are correct.

By the way, Dr. Singh did look at JUPITER, didn't he?

MR. CHEFFO: He did or didn't?

THE COURT: He did.

MR. CHEFFO: I think he did consider.

THE COURT: He dealt with JUPITER with one of his studies.

MR. CHEFFO: I think he did.

But the point there, Your Honor, is that's very different than what their expert reports have been talking about. This isn't like -- because if the fact was -- and

there is a reference to the straw that broke the camel's back. But again, what this litigation, we have been told and what the Complaint said, is -- because otherwise it's everybody. So they either have to say it's causal or they have to tell us in their expert reports, what are the factors? Who are those people that are prone to this acceleration theory? Because otherwise, you know, every single case in a specific causation *Daubert* hearing is going to redo this, and this will essentially be an advisory opinion. So now is the time if their theory is -- which frankly it isn't -- is to say, Hey, where is the evidence?

And even if -- the one last point on this, Your Honor -- even if they were to credit this theory, where is the beef on that? Where is the -- I mean, other than like Dr. Singh saying it, where is the study? Where is the clinical trial data that says, Okay, if your -- you know, if you are kind of on this pathway, you may get it -- I mean, other than the JUPITER study, which is not related to Lipitor, that's 5.4 weeks. So it's kind of an interesting, lawyer-created argument at the eleventh hour.

THE COURT: The pool in SPARCL might be a group that arguably might factor into it, people that had a stroke, right?

MR. CHEFFO: I don't disagree with that. I disagree that it shows causation.

THE COURT: I understand.

I mean, in terms of association, it would suggest that's all it is, but it suggests that people with certain presentations may be more sensitive to the effects of Lipitor in terms of their glucose?

MR. CHEFFO: I would agree with that. And that's why we said to the extent that there is any -- you know, we want to be very straightforward, as we always are with the Court, to the extent that there is any science, you look at that and, you know, all we can do is look at what the science tells us. The only thing they should be able to do is what the science shows. We know we have an 80-milligram study. We disagree with it. It's only 80 with three or four risk factors and it's directly contrary to ASCOT, which is 10 milligrams. So it can't be ASCOT.

This is sort of that same point of replication. They have one study -- and just to highlight here, I'm not going to cover this, we've talked about this, Your Honor -- it's not just ASCOT. So Your Honor knows ASCOT looked at 10 milligrams, peer reviewed, published study.

You know, putting aside Jewell's analysis, their experts, for purposes of today it's, at least as to these folks, it's irrelevant because they say they form their opinions without it. So all they have is what the authors say, right? They don't -- they haven't disputed that. And

then we have Navarese, which was a meta-analysis and it doesn't support causation at any dose; not just the 10 milligrams.

So to basically say kind of, I'm only going to rely on this SPARCL analysis and it's going to show me across every dose for every human being or every woman, you know, makes no sense from a *Daubert* perspective in light of Navarese and ASCOT. And maybe counsel will find some quote about how they did it.

But, you know, I think it's fair to take a quote from sworn testimony when Dr. Singh says that he didn't analyze the Lipitor data dose by dose. He may have had a reason for not doing it, right? He may tell you, Well, I didn't need to do that, kind of the dog ate my homework. That's fine. We'll hear that. But the fact is he didn't do it.

And finally, Your Honor, I think that, you know, ASCOT is critically important. You have to ask why someone who is their kind of core causation expert would not analyze the one study that is squarely at the 10-milligram dose shows no association, and how he can reconcile that with Navarese?

Instead what he does is performs his own meta-analysis, which is not published, much less peer reviewed, and you would expect him to say, Well, the reason why I didn't rely on Navarese, it was a terrible study. It

was not done properly. Under oath he says Navarese was quite reasonably well conducted. That's what he says about Navarese.

We've covered these I think briefly, Your Honor, but these just show why the factors not only don't support them, but weigh against a causational determination.

So unless Your Honor has questions, I'll stop there.

THE COURT: No. That's good.

Let me hear from the plaintiffs' counsel on Dr. Singh.

MS. BIERSTEIN: Your Honor, we are talking about Dr. Singh, but Mr. Cheffo spent about half his time talking about Dr. Jewell.

THE COURT: Bashing on Dr. Jewell every chance they get.

MS. BIERSTEIN: I'm not going to talk about Dr. Jewell right now.

THE COURT: You are going to get a chance.

MS. BIERSTEIN: I'm going to talk about Dr. Jewell, but not right now. I will have my chance and I'm going to take advantage of that.

But I think right now I want to talk about Dr. Singh because I think that's --

THE COURT: Isn't that kind of instructive that they want to talk about somebody else?

MS. BIERSTEIN: I did think it was instructive. And I thought it was particularly instructive because -- and I think Your Honor probably noticed this -- in the briefing on general causation where Pfizer did not go witness by witness when they did the briefing, they had almost nothing to say about Dr. Singh. A lot of the thrust of that briefing is to lump these four, or they viewed it as six causation experts together and attribute whatever they didn't like about one --

THE COURT: You know, it is a little peculiar that Dr. Singh didn't do the ASCOT review. And I mean, there may be explanations for that, but that's what cross-examination is all about. I mean -- but he didn't, you know, he did not. I mean, ASCOT is worthy, it has its strength and its weaknesses, but it is -- you know, it did have diabetes as an end point and, you know, he didn't address it.

MS. BIERSTEIN: Your Honor, there is some confusion in terminology here that I want to address, and then I want to talk about the Dr. Singh points.

There is a difference between a study and a particular paper reporting on the study. And lots of studies give rise to multiple papers. There is a paper, you know, published paper on the ASCOT study. And there are lots of problems with it, including the inability to tell what the definition of diabetes was and the question of

exactly when it was they made the end point.

In terms of the actual ASCOT data, that didn't become available until, you know, a certain point in the litigation. It's not like that was available for people to look at.

So I think there are reasons to not look at the ASCOT paper because of the issues with that paper. And when you get into the study data, you can try to figure out, like, well, you know, if he used one particular definition of diabetes, you will get this; whereas if, you know, you use another one, because Pfizer was never clear --

THE COURT: Are you telling me that the earlier literature before he got the underlying data didn't reveal that ASCOT was looking at diabetes as an outcome?

MS. BIERSTEIN: No, it definitely revealed that it was looking at diabetes as the outcome. What it didn't reveal was what was their definition of diabetes.

The ASCOT materials, depending on whether you are looking at the protocol or some of the papers afterwards, they are unclear as to what definition they are using. And it's kind of hard to assess something unless you can tell. And it's actually one of the things --

THE COURT: I just kind of thought that people -- if you were doing something like this and something seemed a little unclear and the authors are still alive, you just call

him up and ask him. I mean, if it's -- if that is really confusing, why would you just not make a professional inquiry and say, Listen, I'm looking at this data, this seems to be an important issue.

I mean, you know, I just don't understand -- you know, there is this remarkable scientific device called a telephone. You just pick up the phone and call or write him a letter and say, Listen, I'm working on this data, I need some clarification, and they could have gotten it. This is not -- this seems pretty basic to me.

MS. BIERSTEIN: Your Honor, we are wandering off of Dr. Singh.

But I want to say the question ultimately with ASCOT is not what they were using; it's if you used the ADA definition, what does the data show? Because that's the question we want to know is, what did the data show using the standard definitions that everyone else is using? And calling them up on the telephone to say, What did you do, is not as accurate a way to find out what does it actually show than to go into the patient-specific data, use the standard ADA criteria and see what the data themselves actually do show.

THE COURT: That seems like -- I mean, I'm sure that's a fine way to do it. But there is a really simple way to do it. Because if they use the ADA definition, then,

you know, it -- and you don't have to go through all this brain damage of analyzing all this stuff to prove something that a simple phone call, a simple e-mail, a simple letter could have satisfactorily answered for you.

MS. BIERSTEIN: As I say, I think looking at what the data show actually really matters.

But I do want to come back to Dr. Singh, and as I say, start with the idea that in Pfizer's briefs --

THE COURT: Let me just say this: It is a little curious that the major randomized study which reaches exactly the opposite -- opposite conclusion than the people who have hired him want him to reach is the one he doesn't have much curiosity about, it's a little striking.

MS. BIERSTEIN: Your Honor, I think -- I think that's a valid basis for cross-examination. But I think when you look at Dr. Singh's report and you -- you know, he describes how he selected the studies to look at. He describes an extraordinary number of studies --

THE COURT: Listen, I think he makes many of your other experts pale in comparison, frankly. He's a stronger methodological person, and that's mostly what I'm looking at. The absence of the ASCOT thing is frankly bothersome, but I weigh it against everything else. And I think there are many strengths to his approach.

And frankly, when I look at him -- and I did him

first -- and then I looked at many of your other experts, their methods seemed strikingly lacking when I saw -- you know, when I saw the application of very strong methodology by Dr. Singh.

MS. BIERSTEIN: Well, I mean, his methodology is the clearest. I don't think it's particularly different from Dr. Roberts or Dr. Quon who looked at all the same studies and did the similar type of analysis. Dr. Singh's is clearer.

My colleagues have handed me up some specific --

THE COURT: I always love these, pull my jacket, you know.

MS. BIERSTEIN: I know.

THE COURT: Very distracting.

MS. BIERSTEIN: You know, I'm going to look at this and talk to you about that later when we get to Dr. Jewell and some of the other studies because I think we've -- you know, I want to absorb that.

But I do want to say some things about Mr. Cheffo's points about Dr. Singh, you know, as I say, which are new points because we didn't hear about them in the briefs. But, you know, they claim -- they mention that when Dr. Singh does a meta-analysis, he comes up with the 9 percent. That 9 percent is not specific to Lipitor; it's statins overall. It's not specific to women. It's similar to what you see in

the -- in the Sever paper having the same issues: Multiple statins, multiple women -- I mean, both genders.

THE COURT: Let me say, both parties refer, understandably, to multiple studies, some which are just Lipitor, most of which frankly deal with statins generally. And you criticize, you know, the defense for relying on these studies, JUPITER, whatever, but if it's good for the goose, it's good for the gander.

I mean, do y'all -- I mean, just tell me your position. Do you think all the studies, other than the Lipitor specific, are invalid?

MS. BIERSTEIN: No. We not only don't think they are invalid, we don't think they are irrelevant, but we think they have to be understood. That is, we think it's important to understand that this glucose elevation and increased causation of diabetes is a class-wide effect of statins. It seems not to apply to pravastatin. It works differently. It's a class-wide effect. And I think it goes to their notion that you don't have a mechanism.

The fact that we see it across statins tells us something, that this is a consistent effect. It's something the statins are doing because they are all doing it. But what we know is the statins are not all doing it to the same degree.

And I mentioned this earlier, some statins are

stronger than others. And so they have the greater --

THE COURT: The JUPITER study had the different impact. I mean the Navarese -- I'm sorry -- it had the -- it showed they weren't statistically significant, but it did show Crestor at the top and 80 milligrams of Lipitor, and then 10 milligrams. So it did have -- appear to have some difference by type of statin and by -- potentially by dose. I don't want to overdo it because it's not -- it doesn't establish any statistics.

MS. BIERSTEIN: Exactly, Your Honor.

But the point is many of the papers don't break it out that way. So what we say is, yes, the studies that don't involve Lipitor are important and they are relevant, but you have to understand what they mean. And so when you look -- when you have a study that breaks it out by statin, that's very helpful. When you have a study that doesn't break it out by statin, it's nice to know that it's a class effect and you see it across all statins.

But when we get to the strength of the association, it's misleading to use an aggregate strength when we want to talk about just Lipitor because the aggregate strength -- yes, it may be that statins overall only raise the risk of 9 percent, but what if you are a woman and what if you are taking Lipitor? And that's what this case is about.

THE COURT: Do you think there is any dose

relationship? That is, is the plaintiffs' position that it doesn't matter how much you take? I mean, assuming a therapeutic dose, 10 to 80, it's irrelevant?

MS. BIERSTEIN: I don't think it's our position that it's irrelevant. I mean, if you asked me about a hypothetical plaintiff who started Lipitor today, went back to her doctor tomorrow and was diagnosed with diabetes, if you asked me do I think the Lipitor today caused the diabetes tomorrow? I would say I don't think so. And I don't think I'm going to be able to get a doctor who is going to say that. But if you ask me what's the cutoff? How long does it take and is it different if you are taking 10 than 80? Which I think since every one of our experts says they see a dose response relationship, you know, I think that it probably -- how long it takes may depend on how much you are taking.

THE COURT: Well, so are you telling me that -- we'll break it down. You are talking about the length of time.

Let's go back to dose for a second. Is there a point -- I mean, there are studies that suggest -- ASCOT -- that 10 milligrams there was not an association. There is a study like SPARCL that says 80 milligrams there is an association. Does that tell me anything?

MS. BIERSTEIN: Well, we think, Your Honor, that

ASCOT shows an association at 10 milligrams.

THE COURT: I understand that. I've got to say that I think the analysis has a lot of flaws, that was utilized by Dr. Jewell, I think it has a lot of flaws.

Let's go back. Assuming for purposes of this question that ASCOT's analysis done at the time, accepted by the FDA, is valid at 10 milligrams, there was not an association, but there was an association at 80 milligrams per SPARCL, does that tell us anything?

MS. BIERSTEIN: Well, it tells us that Pfizer only tested 80 milligrams.

I mean, here is the problem, Your Honor --

THE COURT: Don't you at some point have a burden to demonstrate -- I mean, if the answer is we don't have the data to prove it, then if you have a client who is on 40 milligrams, doesn't that present a specific causation problem for you?

MS. BIERSTEIN: Well, it may.

But I think there is a couple of points to make here, Your Honor.

First of all, this whole issue on the 80 milligrams. So Pfizer wants the experts to say, Well, you know, this only occurs at 80 milligrams. Well obviously I think Your Honor knows this, there is no basis and no precedent for Pfizer to edit the expert's opinions. So the issue is whether the

expert testimony of causation can be excluded entirely because they didn't answer the specific question of the 80 milligrams.

THE COURT: Well, I share that view. I mean, but I'm just trying to -- I mean, I've got -- this is over, I'm kind of thinking, where am I down the road? And I think my first two -- I just asked Adair this question, and she advised me Ms. Daniels had 80 milligrams and Ms. Hempstead had 40 milligrams. And, you know, I'm aware that not everybody has 80 milligrams.

I mean, frankly I had kind of anticipated -- and I raised this with Mr. Hahn and Mr. Cheffo about what -- were y'all going to get to a point where you -- you know, that you found that some people there was a causal relationship and at other times there wasn't? And reading over these experts, I didn't have them eliminating anybody. I mean, they were basically saying everybody is in the game. And I think that, you know, practically speaking, is a hard argument to make on the data y'all have given me.

So I am kind of -- I mean, I know the defense has made a big argument about dose matters. They think dose matters. And I'm more interested -- because if I face a case, 80 milligrams, it sounds like to me that if there is evidence of 80 milligrams, and my first plaintiff is 80 milligrams, that's kind of a nonissue, okay?

But the next case I get up, it may start mattering. It may be -- because y'all have got the burden to put up, you know, that you can establish general causation. And if your person falls outside of that by dose level -- and there may be other ways to differentiate it -- matters of people with two or more risk factors or three or more risk factors or whatever, I had frankly expected to see some of that in the expert reports.

And I kind of through -- they kind of dodged what I thought was the really tough issue here, which is to differentiate, not to create the situation that everybody who took -- who took Lipitor and later got diabetes is an injured person secondary to Lipitor. I just think that's a really difficult argument to make on the data I've seen.

And I don't know if y'all are looking for me to do that for you because y'all are not willing to do it, but I think it's a -- and to the extent Ms. Daniels gets through the other preliminary stuff, it doesn't look like it's going to be an argument for her case. I think it's a very relevant thing in this group of people you have out there you are representing.

MS. BIERSTEIN: It's an unusual MDL that does that type of general level. I mean, they did that in *Bextra Celebrex*, but most of the other drug MDLs we are seeing it across the doses and we are dealing with it case specific.

Now in the *Actos* case, for example, the defendants made the argument, Well, it doesn't apply to people less than a year. And the Judge says, Well, I can't say that on a general basis and denied that motion.

And so typically what you are going to see in, you know, in any of these cases is that it is unusual to be able to limit it.

Now, I will say the cases have already --

THE COURT: You say that may be case-by-base. I'm very cognizant of my role, however, of, you know, if this case is not resolved and I try these bellwether cases and then I send these cases back to my colleagues across the United States, if I have, you know -- if the plaintiff hasn't demonstrated that there is satisfactory evidence of causation at 40 milligrams or less or 60 and less, whatever, I mean, I don't do a favor by saying, I'm just not going to address that issue which has a tremendous practical significance and make every one of them go do something I could have done.

So I can understand the tendency to want to do it on a specific causation basis, it makes some sense. But in terms of my role as the MDL Court, it may -- it may be important.

I know the defense spends a lot of time talking about this 80-milligram thing. And it -- you know, I do think we are going to need to sort of at the appropriate

point -- and maybe it's going to be at some type of summary judgment or wherever -- we are going to need to address this issue about how far plaintiffs' experts can go to talk about causation.

MS. BIERSTEIN: Well, Your Honor, I must say, I understand, you know, defendants are saying a lot about this. It seems to be the major theme of Mr. Cheffo's presentation. It didn't show up in their brief until page 41 of a 45-page brief.

THE COURT: I'm not smart enough to figure all that out.

I'm saying I've got to focus on what's important to me. And what's important is, is I want to make sure that the -- that the opinions offered have a reasonable scientific basis, what you said right at the beginning. You know, is there a proper scientific method used? And there is something different to say, there is a causal relationship between Lipitor at any level and diabetes. And to say there is a causal relationship for a patient taking 80 milligrams, but we can't prove it beyond that. I'm just saying that's different.

And I will say for the first case it may well be that it won't be the issue we address in the first case, but it will be the issue we have to address in the second case.

Yes, sir?

MR. CHEFFO: I don't want to interrupt the argument. My understanding is that the *Daniels* case is a 40-milligram case.

THE COURT: I'm sorry?

MR. CHEFFO: My understanding is that *Daniels* is a 40-milligram case.

THE COURT: Okay. And how about *Hempstead*?

MR. CHEFFO: I think *Hempstead*, Your Honor -- and again, counsel may correct me, it's their client -- but Hempstead was a 20-milligram case that -- she only started 40 milligrams after diagnosis. That's my understanding of the record.

THE COURT: So we've got -- is that correct?

MS. BIERSTEIN: I would have to check, Your Honor, I don't have the --

MR. HAHN: Yes --

THE COURT: Okay. Thank you.

MR. HAHN: -- Your Honor.

THE COURT: I don't like counsel interrupting, but you just helped me here. So I'm going to have to address this issue.

And Mr. Hahn?

MR. HAHN: Yes, it's correct. We also have plenty of Pfizer evidence that addresses that issue that's not part of this particular argument that Ms. Bierstein is talking

about.

THE COURT: I'm not trying to make a decision right now, Mr. Hahn. I want to hear -- I'm just saying -- you know, I sit and read these studies and I notice -- I think SPARCL is a very strong argument for the plaintiff, and I notice it's 80 milligrams. And I look at ASCOT and I say, Well, you know, that's an argument for the defense and that's 10 milligrams. Now, that may mean nothing, okay? It may ultimately be meaningless, and it may just be the low number of women in the pool in ASCOT -- I mean, it just may not matter. But at least it's an important issue to figure out because I don't think with -- all the data is at 80 milligrams, I don't think somebody can simply say, I'm going to surmise the same effect at 40. I just don't know.

MS. BIERSTEIN: Your Honor, all the data is not at 80. But I need to say a couple of things on this.

First of all, Pfizer wants to surmise out of ASCOT that you would see the same results in women that you would see in men because they didn't have enough data to show that.

THE COURT: There is some weakness, obviously, in ASCOT.

MS. BIERSTEIN: But I wanted to say -- and one of my colleagues reminded me -- there is a huge difference between publication and study. And Pfizer doesn't publish the data it doesn't like. And this is some evidence that --

one of my colleagues can flesh out the source for this -- Dr. Waters has said that the 10-milligram looks the same as the 80-milligram, it just didn't find its way into a publication. Well, why would it? He works -- okay.

This is -- so this is in an e-mail that Dr. Waters sent to one of his collaborators and he says, the atorvastatin increases the risk of developing diabetes. The risks of 10 and 80 milligrams are similar. That's what Dr. Waters said with his collaborators. It's not what he published.

And so when we talk about what the studies show, you've got to be looking at the data because --

THE COURT: I mean, I think that's an interesting point. We don't really think about e-mails as peer reviewed, okay? And having the kind of rigor that we would expect from a review and so forth. And surely on something this important --

MS. BIERSTEIN: Your Honor, what he says in this is a very nicely done analysis. The results are certainly unambiguous. The results also dovetail nicely with the TNT results, I would draw these conclusions based on this data.

Now, he's paid by Pfizer. And amazingly enough, when he published, the 10-milligram piece doesn't make it into it.

THE COURT: Surely there is some other data. Y'all

have been going through all of this. Do you show the effect at 10 milligrams? Do you have the data that shows that?

MS. BIERSTEIN: We believe the underlying ASCOT data does. That's where Your Honor has a problem that we looked at the data instead of the publication, because the data doesn't lie; whereas, the publication can be selective.

THE COURT: When you start manipulating and adding people together and -- I mean, that --

MS. BIERSTEIN: That's not the ASCOT issue. I understand Your Honor has some questions on the NDA analysis, I'm going to get to that with Jewell later, but on the ASCOT issue, which is in the rebuttal report, that's not what we are doing. What we are doing is going at a patient-level data and applying a standard ADA criteria to see what the data actually shows. And it shows the association, just like Dr. Waters was saying, that you would see in TNT -- or not TNT -- but would show in some of the other studies.

And the other issues I have with this 80 -- I have a couple of issues.

One is once Pfizer has an indication that Lipitor can be prescribed at 10 milligrams, why are they ever going to do a study at anything less than 80? Because if you are going to see side effects, you want to do it only at the highest dose because no one can ever say that it could have happened at the lowest.

But the evidence we see -- and this again comes back to Your Honor's question about the significance of the studies involving other statins -- is because it's a class-wide effect and because we see it in the weaker statins as well as in the stronger statins, and because we see it in ASCOT and we saw it in the NDA.

And I know Your Honor has some issues with it because Dr. Waters himself, whose analysis Mr. Cheffo is suggesting should be the be all and end all, that should have been the end of the analysis for Dr. Singh, which it was not, fortunately. Even Dr. Waters thinks that.

So, I mean, there is this question Your Honor is raising about limits. But, you know, you can always come in with -- and say, Well, it's nice that Lipitor causes diabetes, but does it cause it for people who skipped it every other Tuesday? Does it cause it in people whose first name is Marilyn? I mean, those are obviously fanciful, rhetorical questions, but --

THE COURT: Dose related, that's a really core -- you know, dose relationship is like a really important issue.

MS. BIERSTEIN: We agree that dose relationship is important.

But as I said at the beginning, we are only talking about therapeutic doses. There is such a small band between the 10 and the 80. This is not a drug with 400-milligram and

10-milligram where there is a wide range. There is a narrow band. And all the evidence that we've -- nothing that these experts have seen suggests that you need to stratify it.

The fact that Pfizer chose only to study 80 in SPARCL is not a basis to say that that's the only place --

THE COURT: I agree. But then I say, give me the data -- do you have much more on Dr. Singh? My staff -- we have been going two hours. I don't want to kill my staff.

MS. BIERSTEIN: I do not have much more. I just have one other point on Dr. Singh, because I don't think, as I say, that there is, you know, very much of an attack, other than on this judgment. You know, they don't like, you know, which studies he considered or didn't or how he weighed them.

But I do want to say, you know, on this whole issue about peer review, just a reminder that it's the technique and not the application that has to be peer reviewed.

So, you know, yeah, a lot of these results that our experts did they didn't publish the results, but that's not the point. The point is they are using a reliable technique that --

THE COURT: Well obviously, y'all have gotten to the underlying data. And as long as your experts have a reliable, scientifically defensible way, method, analyzed the data and it demonstrates causation at 10 as well as 80, then you are fine.

The difficulty is if your expert did not use those. Because that's the only -- I mean, the data is available. I mean, you say that Dr. Waters made some kind of, you know, comment on an e-mail. I presume he based that on the data he had. I mean, he didn't just invent it. So that ought to be readily available.

And when I say to you, you know, do you have that data? To the extent your people have gone into the databases and used scientifically-legitimate methods rather than changing definitions and loading up people who shouldn't be in the pool and all this other nonsense that we see with Dr. Jewell, then you would be able to answer the question for me.

MS. BIERSTEIN: But then when we go into the data, Pfizer says we should have accepted the published publication.

THE COURT: You know, listen, I think that -- I mean, obviously there is a standard there that says that when you disagree with the authors, that is something the Court ought to look at. That's not the answer. The authors might have gotten it wrong. And the authors might not have been comprehensive, and the authors might not have been as creative and thoughtful about the data as someone else. It's not the end all, it's just a factor to consider. And you know --

MS. BIERSTEIN: I'm not even sure it's a *Daubert*

factor to say that because you disagreed with one of multiple studies. I don't see in *Daubert* that that's an issue. The methodology has to be peer reviewed.

But as to particular people who have applied the methodology and gotten it published, I don't see anything in *Daubert* that says that when your expert says, you know, I don't think that published study is really accurate, I think this one is better, I don't see anything in *Daubert* that says that the Court is supposed to second guess that. I think that is exactly the place for the expert judgment. If the expert has the correct expertise to be able to read a study and say -- read a paper and say, This paper did a better job than that paper, that's what -- that's what the experts are doing, and that's what they are supposed to do.

THE COURT: Well, the answer is is that -- you are correct -- that simply because you disagree is not the end of the analysis. I mean, because we would all be locked into just -- I mean, that's why the data is made available. And if there is a plausible, reasonable, scientifically-defensible explanation for the reanalysis, that's fine. It's just, you know -- I think I've said enough on this. I'm not -- I'm not nearly as troubled as the defendants are with Dr. Singh. So --

MS. BIERSTEIN: Just to finish, then, on Dr. Singh.

Dr. Singh offers an analysis of causation. He

doesn't offer an opinion specific to the dose. We'll get to Dr. Quon because he does offer that at his deposition. But I think his testimony that there is a causal relationship is completely admissible as to whether it's sufficient in a particular case with a particular dose. We can talk about that later. But I think it doesn't go to the admissibility under *Daubert* of Dr. Singh's opinion. Because I think if you look at his methodology, his conclusion about causation as he drew it in his report, I think is admissible.

And unless you have more questions about Dr. Singh --

THE COURT: Thank you very much.

MS. BIERSTEIN: Thank you.

THE COURT: We are going to take a 10-minute break, if we might. And unless you want to do a reply. Do you want to do a response now or are we okay?

MR. CHEFFO: In deference to Your Honor's staff, let's take a few minutes.

THE COURT: Let's take a few minutes. And then the next one we will do is Dr. Gale, okay? Good. Thank you.

(Thereupon, there was a brief recess.)

THE COURT: When this wing of the courthouse was being constructed, the Historical Preservation insisted that the building be built back further from the street. And as a result of that, some very smart person decided to compress

our courtrooms, and I can't see my staff below here, which Ms. Diaz, my court reporter, I can't see her. And if she's about to collapse, I can see her in other courtrooms. And Ms. Eunice here will stand up and speak to me because I can't see them. It's a defect, and I've asked that we redesign these courtrooms so that we can actually see. We also have trouble seeing the witnesses over here, which is another sort of, I would think, design defect. I don't know.

Okay. Let's go to the next witness, Dr. Gale.

Mr. Cheffo?

MR. CHEFFO: Yes, Your Honor. And I will do my best not to interrupt, except if anyone passes out, in which case I will let you know.

Your Honor, I'm going to get to Dr. Gale, but if I could just have a minute or two --

THE COURT: You do, absolutely.

MR. CHEFFO: -- to respond to some of these points. And I'm going to be real brief.

Temporality. We talked about the fact that the Bradford Hill factors are kind of -- they are not a checklist, but temporality is the one that is a must, if you will, for Bradford Hill.

Now, a few quick points. You know, we've heard a few times this idea that there is a narrow band. I'm not sure where that comes from. Apparently when we looked at

here the three-fold increase is a huge increase, but 10- to 80-fold increase is not, as Your Honor knows, 80 milligrams is not even indicated as a starting dose. It doesn't mean a doctor can't do it, but 10, 20, 40 is indicated. So the idea that it's a narrow band is simply not what I think the labeling or anyone kind of recognizes.

More importantly, you know, we haven't spent a lot of time on, you know, kind of what *Daubert* says, what *Joiner* says, what *Weisgram* have said, because it's in our brief and we know Your Honor is going to boil the ocean on all those issues. But I would be remiss, the kind of statements here about these are not *Daubert* issues, we just fundamentally disagree. And we disagree because it's not what the case law says. There is a difference. And we were very careful, or we tried to be, about not trying to challenge ultimate conclusions or pick every little issue that can be a cross-examination issue.

But the reason why we have *Daubert*, which is what I think is so important here, is that if somebody is in a lab coat or, you know, presents as a doctor, you can't cure on cross-examination methodological flaws. I mean, that's kind of what --

THE COURT: I'm concerned about my jury being misled. I'm worried about junk science. I'm worried about valid scientific methods. Because the issues are so

complicated that if you don't have proper input, you've got real problems and the potential for a jury to be confused and misled. And I'm concerned about those issues.

So I'm not a real -- as I mentioned, I'm not a heavy-handed *Daubert*. Most of my colleagues around here are not either. We sort of feel like that the system will take care of many problems. But with very technical information, I've got to be satisfied that valid methodologies have been utilized. And if that has been done, then I'll just sort of leave it to the combatants to go at it on cross-examination.

And, you know -- so I don't -- I don't see myself as a robotic person who simply says, They say, well, it was the doctor's judgment, and then say, Oh, okay, you get to testify. You know, I think -- I think the law expects me to do more than that than just trust the judgment of the doctor.

MR. CHEFFO: We couldn't agree more. We think we are asking for nothing more, nothing less. It kind of permeates this entire hearing, this idea that why would we talk about dose, or why would we figure out if there is other uses? Because it's not just Pfizer making this up. First of all, these are core principles of epidemiology with respect to causation.

As I said, it's not what the law says about causation or what either of the lawyers say, it's about, you are supposed to figure out what the right method is, what

they would use outside the courtroom. They do look at dose. On the one hand they are citing the studies, but now they want to run away from them.

Now is the time -- I'm pretty sure the parties are not going to agree on what the parameters of what the *Daubert* ruling should be -- so to the extent our view is and has been because of this kind of *Daubert* and joinder gap, really you can't use any of this evidence to have a causation opinion. But to the extent that you are going to rely on certain specific information, you know, all data, all studies are not the same, and you do have to look at it for risk factors and for dose at a minimum.

Can you put up slide 92? I just want to -- you know, I don't want to -- you know, we are very good lawyers, and Your Honor kind of understands that there is a fair amount of advocacy here, so I'm not going to address every single point that counsel made. But I would just highlight this because Your Honor, you know, wasn't in this timeline.

The plaintiffs basically in all of their reports, if you were to read them, they talk about Dr. Jewell. I mean, today they don't want to talk about Dr. Jewell, but before we actually wrote our briefs and before we moved, everybody relied on Dr. Jewell. He is -- and these are the quotes from them -- and we will give Your Honor a copy of these slides, to the extent you like them -- they relied on Jewell

and she talks about it.

Now they say, Well, you know, you pick the low hanging fruit in talking about Dr. Jewell, but you didn't talk about Dr. Singh because obviously he's a tougher target.

Well, the next slide they -- I may not have talked about it in my moving brief, but neither did their experts. So they didn't say Dr. Singh, let's point the finger at him, put the target at him and come get him. Basically Dr. Singh nobody else relied on.

So on the point here of kind of emphasis, things change, you know. They have kind of all throughout this hearing. It's been a moving target. And then they kind of blame us because we are not shooting straight. You know, so I think we have to take this all kind of with a grain of salt.

Now let's go back to Dr. Gale. These are the opinions. You know, I think we would challenge all of them.

But for purposes of right now, I think opinion 3 kind of addresses the core issue. I don't think there is much disagreement. So atorvastatin increases the risk -- again, there is no causation here -- and this is interesting -- of diabetes in a sustained dose-dependent matter.

So they say, Oh my gosh, why are we spending so much time talking about dose? Look at Pfizer, they don't want to

talk about dose. Well, this is from their own brief.

Next slide.

So, you know, in fairness, Your Honor, like there is a hierarchy of evidence, I think there is a hierarchy of our challenges with respect to experts. You've probably seen that in tone and approach.

And, you know, I think probably Dr. Gale was quoted in our papers probably more times than maybe our own experts were because much of what he said we don't disagree with, the long progression, the two or three points.

And I think if I had to sum up really what the point is, is Dr. Gale didn't go as far as the plaintiffs would have wanted him to, frankly. And that's why they are very careful about this increased risk and everyone knows it's not causation.

And, you know, then -- and the reason why -- and I don't even think he's named in there on their witness list for the first witness. I may be wrong, it may be an oversight, but I don't think he's even on their witness list. When you look at his testimony and his opinions, they absolutely undermine the causation analysis.

Again, what I would focus on from a methodological perspective, this would be the guy if you are saying that, to then show me that. Show me 10, 20, 40. He admits that there is no strong association.

He talks about observational studies. As we talked about -- I won't reiterate that -- he says the lowest form of proof.

Now, this is the kind of testimony that was elicited from Dr. Gale under the Bradford Hill factors. Estimates effect -- he estimates the effect of Lipitor is less than even night shift work and characterized it as the straw that broke the camel's back. Again, this two- to three-point average, it's not going to matter.

And this really is probably the most interesting point. Dr. Gale did not perform a dose analysis. And this temporality issue, as we talked about, he couldn't reconcile. He's a diabetologist. And the reason he didn't go as far as the good lawyers would have liked him to is he said, Well, you know --

THE COURT: What's his basis for saying -- he gives the opinion that it's dose dependent. What's his factual basis for that opinion?

MR. CHEFFO: It's not clear to me, Your Honor. I mean, I think he -- to me in order to -- in order to basically -- well, let me say this --

THE COURT: Has somebody else done a dose-dependent analysis? I mean, it is hard to know when y'all give me so much material, am I missing something, okay? And Adair and I were talking, where is the dose analysis? I mean, surely

with all this going back into the database and reanalyzing, did somebody do this? And I can't find it.

MR. CHEFFO: You can't find it because it doesn't exist.

But here is how the plaintiffs -- you know, they say, Well, look -- we talked about this -- this is kind of their -- one of their issues on, you know, cross the dosage range. Look at the NDA data. And then they say, Well, look at SPARCL, it's 80, but it should be applies to everybody else.

So we have produced, as you know, 10 million pages, things I can't even pronounce.

THE COURT: Have y'all thanked me for that?

MR. CHEFFO: We have. We very much appreciate that.

THE COURT: The plaintiffs only appreciated it until it started arriving, right?

MR. CHEFFO: Exactly.

THE COURT: By the way, I detected there is no unemployed lawyer in South Carolina because all were hired by one of y'all as contract lawyers to review that data.

MR. CHEFFO: I think that's probably true, Your Honor.

But the other thing is, you know, there is things -- it's not just documents, it's all the underlying -- you asked

the question, right? So you have been kind of asking for this and fighting about it. You have all this data and it's one thing, you don't want to kind of --

THE COURT: I don't want an argument later that, Your Honor, you didn't give it to us. We would have -- I wanted -- over your -- frankly over your strenuous objections at times -- I said, this is an MDL, 5,000 plaintiffs. We are going to turn it all loose and then we are not going to have an argument later, I didn't have access to information.

MR. CHEFFO: Exactly. And thanks for pointing that out because I didn't want my client to think that I actually agreed to all of that.

But the fact is, is that you ordered us to do it; we did it, over strenuous objection or not. And they have the information, right? So it's one thing to do kind of this analysis --

THE COURT: If they went and did the data -- which I agree with plaintiffs' counsel that just because the authors didn't do it shouldn't be the end of -- I mean, certainly some people will think about something, then think about the data in an original way, and that's -- I think that's fair. But you've got to do it with some integrity and you've got to do it in a way that makes, you know, scientific sense. I mean --

MR. CHEFFO: You do. And that's why we asked

these folks, and all of them said, I didn't do a dose analysis. It wasn't for lack of expertise, it wasn't for lack of having the information.

So, you know, this is not like, Let's kick it down the road to some specific causation issue. This is the time to answer those questions.

THE COURT: You are telling me Dr. Gale was asked in his deposition, What is your basis for the opinion regarding dose dependency? Was he asked that?

MR. CHEFFO: Um, I'm just going to -- I want to answer --

THE COURT: Very specific. I know it's a lot to ask. Because y'all had some --

MR. CHEFFO: I'm looking to Mr. Brown. He actually took Dr. Gale's deposition.

THE COURT: And I'm asking something off the top of his head.

MR. BROWN: It's okay. I've got it, Your Honor, I'll be very brief.

So, yes, he was asked about that. But all of them are basing their opinions on various literature that does report a dose-dependent relationship between exposure to various statins and new-onset diabetes as that's defined. There are a couple of meta-analyses that do it and they adopt those findings.

THE COURT: And do any of them -- of those meta-analyses, or other analyses, do they -- do they find an association at, or causation at lower than 80 milligrams?

MR. BROWN: They do not. In fact, the only meta-analysis that you will find that singles out Lipitor by dose is the Navarese meta-analysis, which Dr. Singh finds to be a reliable and well-done meta-analysis.

And if you look at 10 milligrams, there is no difference at all. It's not even a lack of statistical significance, there is no difference at all.

And so in all of the literature, the only analysis of dose on Lipitor alone is Navarese. And then of course you've got ASCOT, which you know about.

THE COURT: We have ASCOT and Navarese. Is there anything that shows with other statins at lower doses that there is a causation with diabetes?

MR. BROWN: So you have a JUPITER trial, which is a 20 milligrams Crestor, but it's not necessarily an apples to apples comparison, compare Crestor to Lipitor. Those medications have different potencies.

In fact, if you --

THE COURT: Is there an equivalent? If a doctor was taking -- if a patient wanted to move from Crestor to Lipitor and the patient was on 20 milligrams of Crestor, what would a doctor do in terms of a prescribing level?

MR. BROWN: I'm speculating a little bit. I'm sure it's possible that they could prescribe 20 versus 20, but that would be on the efficacy side. And many believe that Crestor is more potent than Lipitor. But you are still talking about cholesterol-lowering efficacy; not necessarily the effect on diabetes.

If you look at Dr. Quan's deposition, and Dr. Quan takes the position that all of these medications needs to be looked at separately because he believes that Pravastatin is actually safer than the others.

But I had a long Q and A with him about the need to look at these drugs separately. And they all agree in various forms -- and Mr. Cheffo has showed you that, Your Honor -- that in order to do a proper analysis by dose, you need to stratify out that dose and that drug, which none of them did, and which Navarese did.

THE COURT: Navarese did it and ASCOT did it. ASCOT had 10 milligrams.

MR. BROWN: For 10 milligrams ASCOT did it, yes.

THE COURT: Okay.

MR. CHEFFO: Thanks, Your Honor.

I think that is -- I was just going to --

THE COURT: You are telling me you kind of like Dr. Gale?

MR. CHEFFO: Well, I mean, you know, I like his --

THE COURT: You are going to have a smile on your face when they put him on the stand?

MR. CHEFFO: I like his view, which I think is candid about diabetes being a progressive disease.

I also like the fact that he -- not liked it -- I think it's valid that he would not form a causation opinion.

And I also think that what he said is, you know, where we may differ he may see an association, frankly. But I think what -- at best, his underlying analysis is frankly consistent with table 40, which is -- at best this is like night shift work and it's a clinically insignificant raise.

So essentially, my words not his, there is no there there, Your Honor.

THE COURT: Very good.

MS. BIERSTEIN: Sorry about that, Your Honor. My colleagues are --

THE COURT: Here is a question I have is: Obviously Dr. Gale gives an opinion that there is a dose -- a dose-related effect of Lipitor. What is his basis for that?

MS. BIERSTEIN: Well, Your Honor, I think before I answer your question I need to come back to what I think is an extraordinarily fundamental misconception that Mr. Cheffo has started with and maybe now pervades the entire discussion about what the Hill factor of the dose response relationship means, because it doesn't mean what Mr. Cheffo is saying.

It has nothing to do with identifying the point at which you see the effect. I won't say it has nothing to do with it, but it has very little to do with it.

THE COURT: Right. What it demonstrates is if you have more -- more response with a higher dose. It tends to validate the causal relationship.

MS. BIERSTEIN: That's correct, Your Honor.

But the idea is that if you see it on a dose-response curve, the ability to say, Here is the place where it starts, is not what Dr. Hill was getting at. And I've got --

THE COURT: I don't think it's a Hill factor.

My point is this: -- it's a little different. I know why -- I understand why it's a Hill factor, and I think it -- you know, if you get greater response with a greater dose, it certainly suggests -- it supports a thesis of association, okay? I get it. But it's another issue and that is I see studies -- I see a study at 10 milligrams that says no effect. I see another study at 80 milligrams that says effect, causal, I see that.

Now, I'm not sure what that means. Because it may be there are weaknesses in the 10 milligrams studies or in the pool; it may mean that the 80 milligrams if you checked it at lower doses you had exactly -- I don't know that.

But it seems to me I can't assume it. What I need

to do is, okay, we know if we are going to rely on SPARCL that's 80 milligrams. What is the evidence that at lower doses that we would still have the same effect? And I think that's kind of essential, if your lady, your plaintiff, is not at the dose you rely on in SPARCL. I mean, I think you've got to say -- and I agree with you, does somebody need to say 47.5? Absolutely not. Exact number? No. But if I have data that says at the lowest therapeutic dose it appears not to have a causative effect and at the highest dose it does, it begs the question if someone is in the middle.

MS. BIERSTEIN: There is no data that says at the lowest dose there is no effect. There is a paper that says it. There is a difference between a paper and data. There is a difference between a study and a paper. And I think we keep conflating the two with the idea that --

THE COURT: Is ASCOT -- I thought ASCOT was a double blind --

MS. BIERSTEIN: It is. But it's a paper about ASCOT that found --

THE COURT: But every report there is going to be a paper about it.

MS. BIERSTEIN: Yes, but the ASCOT data shows the effect. That's what Dr. Jewell's analysis tells us is that the paper is wrong. Because the paper -- we don't know what definition the paper is using -- but if you use the ADA

definition, you will see the effect in ASCOT. The paper may well have been using a different definition because the protocol certainly prescribes that it would. The paper says we didn't see an effect; the data shows that there is an effect.

So in fact, ASCOT supports the hypothesis of 10-milligram in the data, even though the particular paper, the Sever paper -- I think it's the Sever paper, but somebody will correct me --

THE COURT: Does Jewell get into dosage at all?

MS. BIERSTEIN: I think that he studied 10 milligrams and the data shows the effect.

THE COURT: This is the whole problem with adjudicated versus unadjudicated data. Which I've got to tell you of all the things he did -- and there are a lot of them that bother me -- that might be the worst.

MS. BIERSTEIN: But, Your Honor, the adjudicated data issue gets right to the issue of the definition. Because the committee decides, is this a case of diabetes or is it not?

The problem is if you don't know what definition they are using; or worse, if they are using WOSCOPS, which is different from ADA, has a much higher threshold, if you take the adjudicated data, then you are stuck with a nonstandard definition of diabetes.

THE COURT: You don't know because he didn't even ask. It seems to me when he launches off and uses unadjudicated data -- the panel, as I understand it, is operating -- you can correct me -- they did it blind. They did not know which group it was in.

Am I right about that?

MS. BIERSTEIN: That's my understanding.

THE COURT: They have a fixed definition. He didn't know what it was, but there was a fixed definition, right?

MS. BIERSTEIN: I assume there was.

THE COURT: Okay.

MS. BIERSTEIN: We don't know that. We don't know what they did.

THE COURT: We know now, though, they used the World Health Organization definition, right?

MS. BIERSTEIN: We don't know because there are different definitions in different places.

THE COURT: Okay. But he didn't inquire; he just came up within his own definition.

MS. BIERSTEIN: He used the ADA definition.

THE COURT: He used the ADA, but he then used unadjudicated data, right?

MR. SUGGS: Your Honor, can -- my name is David Suggs on behalf of plaintiffs.

The Sever article claims that they used --

THE COURT: I'm sorry, used?

MR. SUGGS: -- the World Health Organization criteria. The first element of that is two blood glucose readings greater than 125 milligrams per deciliter.

When you look at the actual data, the numbers that show how many folks had that level, which is replicated by their own expert, Dr. Wade, is higher than the number that is reported in the Sever article. The numbers don't add up.

It's demonstrated in the deposition testimony of Dr. Wade. Dr. Abramson is going to be talking -- I'm sorry -- Dr. Jewell is going to be talking about that. It proves that the Sever article is in error. What they said they did, the numbers don't add up, Your Honor.

MS. BIERSTEIN: So I think, Your Honor -- so the problem of asking Dr. Sever what he did is that the data shows that what he did is different from what he said he did, which is different from what they said they were going to do in the protocol.

THE COURT: What's the point of using unadjudicated data? Because obviously the adjudication process helps screen out -- they had access to the medical records, correct?

MS. BIERSTEIN: Yes, I would assume so.

THE COURT: I mean, and they are doing it blind.

And he's basically just taking the raw data unadjudicated?

MS. BIERSTEIN: I think, Your Honor --

THE COURT: Yes or no?

MS. BIERSTEIN: Yes.

THE COURT: Okay. What bothers me about that is it smells suspiciously like fishing for a different result. It just -- I can't imagine if you have adjudicated information and you have no information that the process didn't have integrity and you just decided to take raw, unadjudicated data, I just find that amazing.

MR. SUGGS: Your Honor, Pfizer produced to us the clinical trial data from ASCOT. In there is a column of data, but whether the data was fasting glucose or not -- what Dr. Jewell did was he counted up the number of instances from the data that was produced by Pfizer and he found a certain number of folks who had more than two blood glucose readings greater than 125 milligrams per deciliter.

THE COURT: That is only one of the factors.

MR. SUGGS: Well, the point is, Your Honor, if he counted more, just from that one factor, there is no way that the number is going to be less if you consider other factors because they are all additive.

And their own expert, Dr. Wade, looked at the same data that Pfizer produced to us and confirmed that Dr. Jewell's count was correct.

Now, there is no way that -- that the Sever article --

THE COURT: As to unadjudicated data.

MR. SUGGS: And the unadjudicated data, Your Honor, who is that panel? We don't know what their criteria were. We don't know what their qualifications were. And moreover, Your Honor, the evidence also shows that the ASCOT study was stopped before they added diabetes as an end point.

So to refer to this as a prespecified --

THE COURT: Did the panel screen out people with preexisting diabetes?

MR. SUGGS: We don't know what they did, Your Honor. It's a black box.

And the key point here is the science that Dr. Jewell did is subject to examination. Their own expert has looked at the exact same data and replicated it.

On the other hand, Pfizer is holding up this adjudicated data panel that was done Lord knows how many years ago by unknown people using unknown criteria, and the documents talk about different criteria that they are going to be using for diagnosing diabetes. But what the data shows is what Dr. Jewell found, and their own expert, Dr. Wade, replicated it.

THE COURT: Unadjudicated.

MR. SUGGS: Based on what the data shows that

Pfizer produced to us.

Now, if Pfizer is going to come back and say, We produced to you the wrong data, these weren't really fasting blood glucose --

THE COURT: But you are arguing to me he counted right on the unadjudicated data. I'm going to the point that he used unadjudicated data. You would think the panel -- it would be a reliable method, and to the extent you have no evidence to the contrary, just to assume it --

MR. SUGGS: Your Honor, there is nothing to adjudicate with fasting blood glucose. It's either 124 or 128 or 125.

THE COURT: I thought there were three criteria.

MR. SUGGS: There are three criteria, but they are all additive, Your Honor. If he finds more people under the first criteria alone, there is no way the number is going to go down by the other thing.

MS. BIERSTEIN: It's one or two or three. And so Mr. Suggs is right, when he finds more under criteria one, on the fasting blood glucose, that they claim to find over all --

THE COURT: Hold on just a second.

(Pause in proceedings.)

THE COURT: Okay. Go ahead.

MS. BIERSTEIN: This issue of adjudication is

interesting to me because, as Mr. Suggs said, it's a black box. We don't know who did it. We don't know what they did. We don't know what the criteria is. This is the opposite of a *Daubert* analysis where we are supposed to know, what was the methodology? Can it be replicated? Is it reliable? What Dr. Jewell did, though, is to take a data point as to which there is no judgment needed; that is a fasting blood glucose. So we don't need to adjudicate --

THE COURT: Wouldn't that data be mistaken? That is, was it fasting or they had preexisting diabetes or anything like that, in that the panel would be screening that out?

MS. BIERSTEIN: Well, if they did --

MR. SUGGS: Dr. Jewell screened out preexisting diabetes.

MS. BIERSTEIN: He was able to do that because that data was also produced. The data set is complete enough that Dr. Jewell can say, This one had preexisting diabetes. If the data was wrong, that's the only data Pfizer gave us.

So it's not like the panel would have said, Oh, well that piece of data is wrong so we've got to correct it in the records. This is the data they gave us. This is the only data set that exists. And apparently, because it's the only one they produced, and yet somehow the black box came up with a different count.

And so when I'm looking at it from a scientific or *Daubert* perspective on questions like methodology and reliability, when I say, Well, what do I trust, the black box? I don't know who, I don't know how, and I can't replicate it; or Dr. Jewell who takes the data, counts the numbers from the data they gave us. And when Dr. Wade does it -- so Dr. Jewell tells us what he does. He tells us which data points he's counting. Dr. Wade does it, replicates exactly what he came up with, and he tells us what definition he's using, which the black box doesn't tell us.

So, you know, if you are going to ask me what's more reliable, I understand the word adjudicated has some magic, maybe because we are lawyers and we like the word "judge," but in this context adjudication equals unknown black box, unknown methodology, inability to replicate. And Dr. Jewell's post hoc, as you would call it, analysis is raw data that anyone can count.

And when Dr. Wade counted it, he said, Yup, you are right, that's the count. So I think that we are going down -- we have been misled to go down the wrong road and being focused on this issue. Dr. Jewell's analysis is the one that *Daubert* would tell us to prefer because we can see it and we can see what he did.

Now, I don't want to beat a dead horse on this, and I was hoping to talk about Dr. Gale for a minute, we will get

back to --

THE COURT: Let you do it, right?

MS. BIERSTEIN: I've got more to say about Dr. Jewell and the NDA.

THE COURT: Let's talk about Dr. Gale.

MS. BIERSTEIN: I'm not going to do that now.

What I want to say about Dr. Gale, other than maybe what you might think is kind of a smart aleck remark, which is I don't know why they are moving to exclude him because they love him so much.

THE COURT: By the way, is he going to be testifying?

MS. BIERSTEIN: We did not designate him in *Daniels* or *Hempstead*. I want to note that Pfizer didn't designate any of their causation witnesses in their list of witnesses. So the experts they put up, they are not testifying, either.

So I'm not -- I'm not sure exactly what it tells us. But they weren't on their list, and Dr. Gale is not on ours for these trials, but --

MR. CHEFFO: They did have a list of 30 people or experts. If they are saying he's going to testify, that's fine.

MS. BIERSTEIN: No, he's not on the *Daniels* or *Hempstead*, not Dr. Gale.

But I will say I don't agree that he doesn't give a

causation opinion because I think increased risk is doctor speak for substantial factor causation in law.

So I think, you know, when we get to our burden at trial to prove causation, I think a doctor who tells us increased risk, he's telling us it happens more often with Lipitor.

THE COURT: Increased risk is not enough in itself.

MS. BIERSTEIN: Well, I'm not necessarily saying by itself. But I think his opinion is a --

THE COURT: Increased risk has to be a component of it. But that's at the beginning of the analysis.

MS. BIERSTEIN: Whether or not it's sufficient.

THE COURT: Significant and all that.

MS. BIERSTEIN: It would never be the only evidence at trial.

My only point is it is a causation opinion. Whether it's the ultimate -- whether it would be enough to go to the jury without any other evidence I don't think we have to worry about because it would never be the only evidence.

But the last point I want to make -- and Mr. Cheffo didn't get into this, but I know Your Honor was interested in it -- is the Hill factors.

And I do want to say that before I go through the Gale report, which I'm going to try to do very quickly, I would like to say in Dr. Hill's article where he set this

out, Dr. Hill said that we should consider these viewpoints. He didn't say, put them in a separate section, or use my name. He didn't say this is the ultimate synthesis. What he said was, I think you should look at each of these viewpoints when you are doing this.

And if you look at Dr. Gale's report, you will see that's exactly what he did. So you will see him considering the strength of the association in paragraphs 41 to 55. You will see him looking at, I'm going to say consistency. Now, I will tell you, Your Honor, there is some terminology issues here because the reference manual on scientific evidence uses different terminology for the Hill factors than Dr. Hill himself used.

THE COURT: I noted that.

MS. BIERSTEIN: Yeah. And Dr. Singh follows Dr. Hill.

And so, you know, there is a little bit of confusion sometimes. I tried to get to the bottom of why the reference manual terms are different and I was unable to find the answer to that. Maybe we need to ask the guys who wrote that section.

But in terms of consistency, which is also called replication, Dr. Gale, you know, again discusses the variety of the different studies across different populations and different study designs. Again, that was paragraphs 41 to

55. He -- in terms of specificity, everybody recognizes that diabetes is not specific to Lipitor; that is, it can have multiple causes. And Dr. Gale himself put it in that context in paragraphs 12 to 16.

Temporality. This opens a whole issue that, you know, I don't want to spend a lot of time on here. We believe that new onset diabetes does provide the required temporality. They obviously don't.

And again, I think we have a disagreement about cause and effect, because we think if you are on the road and Lipitor pushes you, that's the cause. So the push came before the effect. But he does consider it because he only looks at people who had new onset after they took it.

Dose response I think we've talked about. He gives a specific opinion about biological gradient. Paragraph 5 and paragraph 47. And you and I have already discussed what we think that means.

Plausibility. He discusses that at paragraph 55.

Coherence with other knowledge. This has to do with putting this issue in the context of the progression of diabetes and whether his opinion about Lipitor is consistent with that. You can see that in paragraphs 6 to 33 the --

THE COURT: You are telling me he actually does not issue a causation opinion; he issues an opinion that Lipitor increases the risk of developing diabetes. Am I right about

that?

MS. BIERSTEIN: I believe that's correct, Your Honor. I don't -- I don't believe his actual opinions used the word "cause," but -- well, he does use -- he does use the word "cause," but he's talking about it statins generally. He does -- but it's not in his list of six opinions. The six opinions don't use the word -- he does not use the word "cause". He uses increased risk. That's why I'm there, because in those opinions -- I don't know whether that means he gets excluded or he doesn't because maybe they haven't moved against him.

By the way, speaking of that, for all the emphasis on Dr. Jewell, there is no motion filed to exclude Dr. Jewell's testimony, there is only this omnibus motion that kind of lumps him --

THE COURT: I understood all these are up. I didn't interpret a need to make --

MS. BIERSTEIN: Putting that aside, I think Dr. Gale's opinion is, again, whether it would be legally sufficient to meet our causation burden. I don't suggest it would be. But he -- the opinion that they have moved to exclude, presumably, of increased risk I think holds up as valid in terms of the methodology.

THE COURT: My problem is is jury confusion. What does that mean? If it's -- if it's not, you know,

statistically significant and I'm allowing it, it may -- I mean, y'all are sitting there debating about what it means. I think it doesn't mean causation. And I don't think he means -- he thinks it means causation. And I don't want the jury to confuse it. That's exactly what -- that he's saying the opposite.

So I would -- I would be concerned for someone to say, Well, this increases the risk, because that doesn't meet the -- that's not a valid theological method to get to causation; it's just a piece of it.

MS. BIERSTEIN: I think it's two separate questions. One is, is it a scientifically valid opinion? And I think that it is. And the other is, does it help the jury? Now --

THE COURT: A sufficient opinion.

MS. BIERSTEIN: That's a different point. The sufficiency of it to prove causation is a question of whether if I came into trial and I just put up Dr. Gale and he said increased risk, and I put up no other expert, could you send my case to the jury or would you say I haven't met my burden? And I get that.

THE COURT: And then the next question is: If you put him up to say increased risk, is there a potential that the jury is going to misinterpret what that means? And that's one of my 403 concerns is I don't want my jury

confused and misled. So I just have to evaluate it on all that. And if he's not testifying in the first two cases, perhaps I won't specifically have to deal with that issue. But he's not going to testify about causation because it's not legally sufficient. If you want to offer something else, we'll probably deal with a motion in limine at that time. There are things obviously he offers that if you want it, it would be relevant and admissible.

MS. BIERSTEIN: I mean, Your Honor, I think we are back to the problem of you say, Well, he's not going to testify about causation. And what I say is we've offered him for the six opinions in his report. And the issue for the Court is can he testify to those six things? And I think that there isn't really much of a challenge here to the basis for the six opinions he actually offers.

THE COURT: So technically we may be looking at a motion in limine which would deal with the potential for jury confusion. And under 403 --

MS. BIERSTEIN: There could be a motion in limine. But I think from a *Daubert* point of view, he's very clear what his opinions are. He numbers them one, two, three, four, five, six, and we know what they are. And I don't think there is anything he said that undercuts admissibility. I understand sufficiency, but sufficiency is not the question. I understand your question about confusion.

But confusion may also depend on the context. What's the other evidence? What else are they hearing? What are the instructions? That -- to the extent that those opinions are in context, they might not be confusing at all. But I think from the *Daubert* admissibility point of view they pass muster for what they are, for what he purports to apply.

THE COURT: Mr. Hahn, do you want to make a --

MR. HAHN: Your Honor, I -- yes, there is confusion. I'm confused. With ---

THE COURT: The Court shares that.

MR. HAHN: -- with increased risk, Judge, for a general causation expert, all they can do is say that the drug increases the risk of a particular disease, diabetes in this instance. They cannot give a specific causation opinion until they have a plaintiff and they do the analysis of that plaintiff.

THE COURT: There is a general causation. You wouldn't go so far to say what he says is insignificant to the 3 milligrams' difference, perhaps it's the straw that breaks the camel's back. I mean --

MS. BIERSTEIN: Your Honor, those are not his opinions. I have to say that's a misrepresentation of his opinions. They said hypothetically if the increase is two to three, and he said, well, that would be clinically insignificant and he said that would be a straw that breaks

the camel's back. He did not give the opinion that that is the effect of Lipitor.

And I think that we have very strong evidence that that is not -- that the effect of Lipitor in people who are susceptible to it is way bigger. This is not clinically insignificant.

And this comes back to Dr. Jewell in the NDA. And we are going to get there, I'm not putting it off. I know Mr. Cheffo thinks I'm avoiding it. I'm raring to go on it. I just want to keep some order here. But Dr. Gale did not say that Lipitor has a trivial effect. He says, If you told me the effect was 2 to 3 milligrams, I would tell you that's trivial, but that's not the effect, and it's not his testimony.

THE COURT: Thank you. Any response?

MR. CHEFFO: Yes, Your Honor. I think counsel may have misspoken on an issue or two.

First, you know, this idea that we have this -- they keep this black box. What we are talking about is clinical trials, peer-reviewed clinical trials. It's the way they work. It's just a paper. Well, I mean, that's what the literature -- that is what epidemiologists rely on. It's data and information.

THE COURT: Help me with this. We noted this difference in discrepancy of numbers between adjudicated and

unadjudicated. What's the explanation?

MR. CHEFFO: The real explanation is it's not the way science works.

Can I have the slide? This is Jewell. This is from -- I kind of didn't address this before. Here we have -- he addressed the findings specifically of ASCOT, and they are opposite.

He was deposed in connection with the *Zoloft* litigation and others. He's testified in a lot. And what he said was: "I don't have any reason to second guess the published results in peer-reviewed literature of any of the authors until a mistake is brought to my attention."

So really, you know, here is the core issue, Your Honor, it's kind of what you said earlier is that if you keep torturing the data -- that's the famous quote -- you are going to find stuff. So the idea --

THE COURT: Randomly you will.

MR. CHEFFO: Exactly.

So we have a model. We have an adjudication process. This isn't about crunching the number. There is three criteria.

This idea it's a black box. If you look at the Sever paper, we know exactly who the panel are. These aren't people who are pulled off the street to just kind of randomly put it into a number generator.

There is a process, right? If we were to second guess every single clinical trial -- that's not the way science works. What I haven't heard is, Tell me the methodology by which you would go. That Dr. Jewell has ever, or any real scientist has ever gone, pulled apart, looked at unadjudicated information, put different parameters around it. It's not the way science works.

THE COURT: Is the adjudication process routine in clinical trials?

MR. CHEFFO: The adjudication process?

THE COURT: Yes.

MR. CHEFFO: Absolutely.

THE COURT: Is it generally recognized that the adjudicated process is more reliable than the unadjudicated data?

MR. CHEFFO: Of course.

THE COURT: And is there any evidence that's been offered in this case of any impropriety or lack of professionalism by the panel? There was a suggestion that it became unblinded and they were -- there was a lack of integrity in that process. Is there any evidence of that?

MR. CHEFFO: Not a shred. And right to your point I think Your Honor is making. This is like a heads I win, tails you lose.

Imagine if we had a bunch of people who if we say,

Here is the information, here is what it shows, this person is on Lipitor. The plaintiffs would jump up, too. There is an element of bias in there. The whole point of this adjudication process, you pick people -- it's not a black box, these are qualified people. Peer-reviewed journal published this. It's the way it's done all the time. They looked at the data. They didn't know. They were calling balls and strikes and they came out with a result. And this is frankly, you know, maybe good lawyer spin, but absolute total lawyer spin.

We keep hearing, as if it's like Ground Hog Day, We have no idea what the specifications are. We don't know what the qualifications are, what the criteria are.

Can I have the next slide? This guy is the -- he's the head of the end point committee, not affiliated with Pfizer. Because they keep saying we have no idea what the criteria are, we actually went out and he submitted a declaration explaining how the end point committee used their clinical judgment in reviewing the diabetes.

So this idea that there is this black box, that no one has any idea what's going on, it could be people off the street, is really just ludicrous. And we would not be able to have science or epidemiology if somebody kind of had a conspiracy theory behind every door and say, well, it's possible --

THE COURT: Basically what we would be doing is no study matters. It doesn't matter anymore. We are now going to use unadjudicated data. We are going to eliminate the adjudication process because we are going to assume they are a bunch of liars and cheaters. And at some point you've got to say, hold on a minute, it's a standard procedure to use adjudicated data.

And they didn't like the result. It was a bad result for their theory. So they are now going to go to unadjudicated, and bingo, you got a result you like.

I mean, that is the type of process that concerns me a lot. And if they could point out to me, Okay, we know they cheated, we know they manipulated, we know that this was Pfizer, you know, shaping the outcome, I would be the first guy to say, have at it, okay? Have at it.

But I keep asking where is the evidence that the adjudication process was improperly done here? And just to assume it is invalid and to simply assume the unadjudicated is thus reliable just seems to me deeply troubling.

MS. BIERSTEIN: I need to respond to that.

THE COURT: You are going to get a chance in just a minute.

MS. BIERSTEIN: I really do need to respond to that.

THE COURT: We can get in a ping pong match in just

a minute.

Mr. Cheffo, finish.

MR. CHEFFO: I really just have a point or two.

And I think we are -- we are talking broadly about ASCOT, but I think we are talking about Gale, too, right? Is that right?

THE COURT: Yes.

MR. CHEFFO: We are still on Gale, Your Honor.

THE COURT: He is just a stalking horse for all of y'all in every case about Jewell. But go ahead.

MR. CHEFFO: The end of the day is, you know -- and this goes to the same issue with his gender analysis, right? If someone comes in and says, I have a -- I have the same methodology, I do this all the time, right? Whether I'm doing it for my outside or in court. But when they come in and they say, Well, I have this really interesting gender analysis -- and we'll talk about it with Jewell, he did these, they are called heterogeneity tests. I hope you are not going to ask me a lot of questions about that.

THE COURT: I got that far.

MR. CHEFFO: The bottom line is you kind of run these tests in order to determine if there is a difference between men and women, right? He ran five of them and he didn't find any tests.

So normal science was if you don't find anything,

you then don't do a gender analysis, because that's the whole point of the heterogeneity. That's what he did with SPARCL, which is whacky and not scientific and not methodologically sound.

Even if you are going to stand on principle and say heterogenetic analysis, you would then expect to do it in ASCOT, too, which surprisingly he said that was not part of my opinions, I'm not relying on it.

Plaintiffs say we are not really relying on it, but who else are they relying on? And I don't want to steal Ms. Birnbaum's thunder on efficacy, if you still have any questions more about that. But again, it's a whole -- that's the whole point of he's the guy who is saying there is a gender differential.

So I would just leave the Court -- and finally, actually with Dr. Gale, this is from his testimony. And I can provide this. It's actually from, I think pages 135 -- I'm just going to read this for a minute because I think it is helpful.

"Answer. I would remind you of the old story of the camel and the straw. It can be the straw that breaks the camel's back.

Question. When you say, 'it can be the straw that breaks the camel's back,' are you talking about the very final step in a process that takes over many years?

Answer. Yes. It can be the final trigger that precipitates an event, a clinical diagnosis.

Question. And is it true that the diabetes disease process unfolds for many years before a patient reaches a blood glucose level that crosses the diagnostic threshold?"

There is an objection to form.

"Answer. I would.

Question. You agree?

Answer. Yes.

Question. When you say 'crosses' -- when you say it could be the straw that breaks the camel's back, are you saying that many other factors can contribute to a disease process for many years that brings the patient up to the brink of diagnostic threshold and that statins could be the last straw that pushes the patient off the threshold?"

There is an objection.

He says yes.

And then finally, he said:

"Question. Using the same analogy, would you consider obesity, age, family history and ethnicity to be straws or something bigger than that?

Answer. They are the major predisposing factors but modulated by other risks.

Question. So they would be bigger than straws in your analogy?

Answer. Yes."

Again, goes directly to --

THE COURT: Obviously -- let me say this: To the extent plaintiffs can prove -- and maybe they can demonstrate to me specific causation, they can -- that even if what Dr. Gale, and you interpret what Dr. Gale to say is true, that it has a relatively minor effect but it was literally the straw that broke the camel's back, that would be a proximate cause and it would be, Did I push him across? That would be potentially a plausible claim. It's more complicated than that.

MR. CHEFFO: Not to be too cute, Your Honor, but I mean, if I ate an ice cream sundae and it boosted my glucose levels from 124 to 126, should we sue Friendly's?

THE COURT: Well, you wouldn't do that.

But the -- you know, we are talking about something presumably in the definition that was sustained and that Lipitor actually didn't temporarily -- like the ice cream sundae analogy -- temporarily raise it, but actually did raise it so it kicks them into diabetes, I think that's a plausible case. We are not in specific causation.

So I don't know the *Daniels* or *Hempstead* details yet of exactly where the theory is on establishing specific causation, but I do think that I can imagine the methodological difficulties of proving the straw that broke

the camel's back. But if you could actually prove it, it potentially is a theory.

MR. CHEFFO: And again -- obviously I don't want to argue the specific causation issues, Your Honor -- here is what I would say: There are specific causation issues. But this comes back to the point, right, you -- I think you said it very well earlier, it's not just about what happens here, it's to the extent these cases survive, you have to pass them back or remand them to other courts. And, you know, this idea -- it's really in their briefs -- but that would be an acceleration or exacerbation. They are taking issue with all these words.

Well, increased risk, we are not sure what it means. It's from their brief. And nowhere in the opinions that they said in their opposition that they are going to be -- they don't say anything about acceleration or exacerbation.

And even if Your Honor would say, Well, they don't say it, I'm not going to hold them to that today, anywhere, they have not -- they can't even show anything other than the SPARCL 80 milligrams with the three or four risk factors. Where is the studies, the clinical trial data that says -- the peer-reviewed scientific evidence that says that if you are at 124, it could push you over to 126, so that is clinically sustained? Today is the day to figure that out, Your Honor.

THE COURT: Ms. Bierstein, you wanted to add something?

MS. BIERSTEIN: I do need to add a couple of things.

THE COURT: I want to reassure you, any time you need to make a statement, I'm going to give you a chance to do that.

MS. BIERSTEIN: I appreciate that.

You asked Mr. Cheffo three questions and I have answers to all of them.

THE COURT: You probably didn't like my questions.

MS. BIERSTEIN: I was okay with the questions; I was surprised at the answers.

THE COURT: I'm surprised I haven't had a lawyer that objects to my question.

MS. BIERSTEIN: You asked him if it was routinely done to adjudicate -- to adjudicate data.

THE COURT: Yes, ma'am.

MS. BIERSTEIN: And I would say for one thing it wasn't done in SPARCL. So I don't know how routine it is, but it isn't always done.

THE COURT: Let me say this: Whether you know that or Mr. Cheffo knows that, I think it's a relevant issue. It certainly was the process. If it has integrity, it makes sense to me. Because when you are doing a huge clinical

study, you are out there, people are everywhere, you need to have some centralized, standardized process of what things mean. And I certainly have seen it in other studies, having adjudicated -- now whether that is standard --

MS. BIERSTEIN: It is done, Your Honor, but it is not always done.

THE COURT: I certainly am aware it's done frequently. Now, whether it's everyone -- what bothers me is if you say, I'm now not going to honor that adjudicated, and I think there could be good reasons --

MS. BIERSTEIN: I'm going to skip ahead then. I'm going to skip point two.

You asked him if it's more reliable, and he said of course. And how does he know that? He's not a scientist; he's a lawyer.

I'm going to point three. Is there some reason for impropriety? And I'm going to come back to the slide that Mr. Cheffo put up with Dr. Jewell's question. No reason to second guess until a mistake is brought to our attention.

Okay. So in this case was there a mistake to make us think there was a problem? And the answer to that is yes because when we got the declaration that said, This is what we did given that there was a lot of confusion. Because one document said we are going to do X and another document said we are going to do Y. And when we get the declaration, it's

supposed to clear it up and says, Well, this is what we actually did, and then Dr. Jewell counts. And guess what? It's not what they did.

So when there is a discrepancy --

THE COURT: How big a discrepancy are we talking about?

MS. BIERSTEIN: I might need to get this for you after the next break.

MR. SUGGS: 50 or 30. I don't remember.

THE COURT: 30 to 50?

MR. SUGGS: Yeah.

MS. BIERSTEIN: But once there is a discrepancy, then you've got a mistake brought to your attention. And then maybe you say, adjudication may be often used, it may be often reliable, but something went wrong here because the adjudication doesn't --

THE COURT: There could be an explanation that is benign. It could be an explanation that is potentially nefarious. It does strike me as potentially just to abandon it without trying to get to sort out -- I mean, we are talking about, as I recall, several thousand people in the study. Are we talking -- it was 344 versus 288. I think that's the difference in the new onset diabetes in the experimental control group combined. So we have some discrepancy there. And so I think that estimate that was

given is maybe a little low.

MR. SUGGS: Your Honor, we can give you the deposition testimony of Dr. Wade where this exact point was discussed and where Dr. Wade said that he agreed with Dr. Jewell's count.

THE COURT: I don't doubt -- but the count is not what concerns me.

MS. BIERSTEIN: Your Honor, one of my colleagues has just pointed out is Pfizer itself, when they were dealing with the MRHA, the regulatory body in Europe, when they got to dealing with ASCOT, what did, they give the MRHA -- they didn't give them the adjudicated data, they gave them the unadjudicated data. They did what Dr. Jewell did. They apparently had some other reason of their own to believe that there was a problem with the adjudicated data. It is not what they used.

THE COURT: How do we know that, the thing about the European?

MR. SUGGS: We'll get the exhibit.

MS. BIERSTEIN: We have exhibits that demonstrate they used the unadjudicated themselves. There is nothing fishy about using the unadjudicated. Something went wrong in the adjudication process. 30 or 50 at a minimum cases of diabetes disappeared. And Pfizer itself went for the unadjudicated when the Europeans had questions.

So I think that's a -- I think this is, you know, this may be the case where there was good reason to use unadjudicated data. It's not what Dr. Jewell normally does. That's the testimony Mr. Cheffo put up. It's not what he normally does. He does it when there was a reason. There was a reason here. Pfizer did it. He did it because the numbers didn't add up.

And when we got the supposed clarification, the numbers didn't add up. So something happened here. I think what happened -- not a nefarious plot, I'm not a conspiracy theorist, I don't think that was the problem -- I think the problem was shifting definitions and a lack of clarity, definitions of diabetes. They had some unclarity about what their definition was going to be.

THE COURT: You are saying the panel had shifting definitions?

MS. BIERSTEIN: Because the protocol said one thing and something else said something else.

THE COURT: Is that your surmise?

MS. BIERSTEIN: That is a surmise, Your Honor, because there was a reference to paranoia and conspiracy theories, and I'm not a conspiracy theorist. I'm telling you this is not surmised; this is data.

Something went wrong because what Doctor -- and I have forgotten his name, I'm sorry, the witness who put in

the declaration what they did -- the numbers do not add up. So that's not a surmise; that's data, what they said they did and the numbers they came up with.

THE COURT: Mr. Cheffo, have we ever sorted out why the numbers don't match up?

MR. CHEFFO: Here is what I would suggest: This is absolutely -- this testimony apparently is absolutely inaccurate, Your Honor. And we can submit by tomorrow a, you know, that will weed this specific issue out. Because this idea that we only gave adjudicated, I'm not sure where that came from. We have actual documentary evidence. We have been hearing this same argument, the same spin, right? We don't know who was on there. We don't know what the -- whether it was adjudicated or not. We don't know the criteria. We then submit the Hemingway, and then again Ground Hog Day.

THE COURT: The one thing they have said here, which I think needs to be answered, is why was there a difference in the end point diabetes number between 344 and 288? What's the explanation for that discrepancy? If any.

MR. CHEFFO: I mean, there is frankly multiple pretty technical -- and I --

THE COURT: How do we know that? How do we know these explanations? Did Dr. Hemingway provide -- is that his name?

MR. CHEFFO: Dr. Hemingway provided certain of the information. I don't think he spoke to all of these issues.

THE COURT: Well, one of the things y'all have attacked Dr. Jewell for is, is that he utilized unadjudicated data.

MR. CHEFFO: Correct.

THE COURT: And you felt that was kind of changing the field, the play, to change. And they now come back and they have said he did it because the numbers didn't add up. And that might be a plausible reason to use the raw data if otherwise the numbers didn't add up. And I'm just asking, has anyone figured that out? Why is there a discrepancy?

MR. CHEFFO: I think we have -- can I -- would you mind if I allow Mr. --

THE COURT: Have him identify himself, if you can identify --

MR. BROWN: Loren Brown for Pfizer, Your Honor. Thank you.

Would it be easier if I move up? It's unorthodox to be back here.

So, Your Honor, I think there is just a couple of threshold issues that we haven't touched on yet that might be important.

First, Dr. Hemingway's declaration came after Dr. Jewell's analysis. There would be no way for Dr. Jewell to

say that Dr. Hemingway's work doesn't add up. It came later.

THE COURT: Well, he had a fact that some numbers weren't added up, though.

MR. BROWN: And so --

THE COURT: That's what I want to know.

MR. BROWN: And one -- to that point, the way this works -- Your Honor asked whether the end point committees in all these trials, and not every single time do you have one. But almost always when you have a prespecified end point of any kind, you have an end point committee.

But very importantly, that end point committee is made up of medical doctors in the specialty that's relevant to the classifications that they are making.

So you actually need medical doctors qualified to look at medical records and make those --

THE COURT: I understand that. I'm just saying --

MR. BROWN: So Dr. Jewell, as a threshold matter, is a statistician. Usually a statistician only comes in after those counts are made and decides whether that statistical --

THE COURT: You are not answering my question. There is 344 versus 288.

MR. BROWN: Yes.

THE COURT: There is a discrepancy. When Dr. Jewell

went in there, he found 344. Am I right about the end point diabetes? And the data from the study showed 288.

MR. BROWN: Possible explanations. One possible explanation is that the end point committee did not count certain cases.

For example, where they found that the measurements weren't taken in a fasting state. I believe he uses that example in his affidavit.

THE COURT: Okay.

MR. BROWN: Another possibility for the discrepancy is that the end point committee was using a different definition that had three components to it as opposed to one.

Now, that might suggest that you would be more overinclusive if you've got three rather than under inclusive. So I can't explain why they would have more.

One major additional reason for more cases is that Dr. Jewell may have been counting -- that the follow-on periods, that is the period of time that they are measuring, may have been different.

THE COURT: All speculation.

MR. BROWN: Now, it's not -- it's all speculation in terms of what, in fact, happened. And Dr. Hemingway doesn't remember why one case was counted and one wasn't.

THE COURT: It just gives a -- you know, if you have an adjudication -- it doesn't sound to me like they are

challenging the adjudication process; they are just sort of figuring these numbers don't add up, and let's just go back to before we went through this process, without any explanation, and let's just see what it shows. And then that may be subject to criticism. It's an unadjudicated result. But at least it makes it a little -- look a little less nefarious regarding Dr. Jewell than simply saying the guy just came up with a different set of rules because he didn't like the result of the first -- in the first game.

MR. BROWN: He did come up with a different set of rules, but nobody has access to those medical records today that the end point committee relied on. That's not part of --

THE COURT: I mean, you know, they haven't offered any evidence that there was any -- anything nefarious or improper or unprofessional or incompetent about the panel. They just say, Hey, there is a difference between 56 people, from 288 to 344, and, you know, something is not -- doesn't add up.

And you come up with three explanations and the plaintiffs' counsel may come up with others, but it at least doesn't make Dr. Jewell look so bad to have, you know, gone back to the unadjudicated data simply because, you know, the adjudicated process, somehow when you ran it through the grinder, it didn't come out -- the numbers matched up. I

can understand a basis for saying that.

Now, there are inherent flaws for using unadjudicated data, but perhaps there are flaws in using the adjudicated data. So we look at it all. You know, if you don't have anything more specific.

MR. BROWN: Not really, Your Honor. If -- I would just say that in order to even decide whether or not the numbers add up you need a qualified person who has access to all of the underlying information in order to try to replicate that.

THE COURT: I'm hardly the person that is going to be able to figure it out unless y'all give it to me, because I'm certainly not a medical doctor qualified to sit on the panel.

MR. BROWN: So the other portions, Your Honor -- I'm not going to take anymore time on this -- but we did include an appendix that contained a chart that attempted to highlight the differences between what the blinded qualified end point committee did compared to what Dr. Jewell did in our papers.

THE COURT: And what did it show?

MR. BROWN: So, I mean, it was just the -- the differences between what Dr. Jewell did and what the end point committee did from beginning to end. They used a blinded process, as Your Honor has already noted. They used

different definitions, as Your Honor has already noted. They were qualified medical doctors making these diagnoses; whereas Dr. Jewell was only a statistician. And no medical doctor on the plaintiffs' side --

THE COURT: It does trouble me -- we are getting a little far afield here, we will get to Dr. Jewell -- how he can come up with a different definition as a statistician to anything to me is odd.

One of the things I've got to determine is whether that he used proper scientific methods to apply to the data. What he did to input, was it valid? And there are parts of it that have the appearance, the suggestion, the inference, that he was fishing for a different result and manipulated methods to produce the result. I mean, it was somewhere, I can't remember where, he used five different methods before he landed on the sixth one. I mean, that's not what you consider sort of the scientific process where you just keep, you know, you keep running the -- running this thing until you get the results you want.

MR. BROWN: Yeah. I don't think you will find many, if any, cases in the entire medical literature where a process like this has been followed, after a clinical trial that's prespecified, that's approved by IRBs all over the world that approve the ethics of going forward with these trials, you create an end point committee with definitions,

you assign qualified people, not just one, but you put a few together so if there is a disagreement, you can resolve that case. Medical people doing this. According to those definitions.

The counts are critical because only after you have those counts does a statistician come in and decide whether those counts are meaningful, those differences are meaningful or not. We have no case like this in the medical or scientific literature where something like this has been approved of.

THE COURT: Ms. Bierstein, you wanted to say one more thing?

MS. BIERSTEIN: I did, Your Honor. I want to say there was some reference or some suggestion that Dr. Jewell had made up a definition. The definition he used is the ADA definition.

In terms of blinded or not on the unadjudicated, what Dr. Jewell did is count everybody who looked in the fasting glucose level column, counted everybody who was above the ADA definition, you know, and who wasn't at baseline.

This is not a question where, you know, you could be influenced by, you know, knowing something about it. This is simply a number. Fasting blood glucose, ADA standard definition.

So -- and I think in terms of this idea that he ran

multiple tests -- Your Honor thinks there is something suspicious about it -- Dr. Jewell ran some of the data through multiple tests to look for consistency to see -- because you don't want to be criticized, you say, Well, I ran it this way and I got this. Well, did you think of running it that way? So he ran it every which way. And I think that was very appropriate to run. Then if you get different results you don't get to cherry pick and say, Oh, I finally got the one I want. Now you've got to synthesize and deal with it. But I don't think it's suspicious to do it multiple ways.

But I think the main thing here, Your Honor, this is not an ad hoc definition. This is ADA. Standard American Diabetes definition. There was no judgment that he needed to be a doctor.

He just took their -- I don't know if it was an Excel spreadsheet, I don't know what the format was. He had a list of fasting blood glucose tests and he used what they had. And I think that this is -- and you know -- so in terms of, you know, what they say they did, you know, again, they said they did different things at different times.

One report they claim they used a random -- a single, random one; another time they said they did the who definition. When they tell you they did it three different ways, you are going to count to see, Well, what did they

really do? So I think there was good reason here. And -- but I was just concerned to hear the idea that he made up a definition. It is the ADA definition.

THE COURT: Okay. Thank you very much.

Okay, folks, we need to break for lunch here. And obviously the day is getting long. I want us to -- let's try to see if we can maybe get back in 45 minutes, but I understand that's very hard to do around the courthouse. I suggest a couple of places right across the street, but as soon as everyone is back, we'll begin again. I'll be ready to go in about 45 minutes, okay?

(Thereupon, there was a lunch recess.)

THE COURT: Let me start off, if I might, the break allowed me to realize that when I was talking earlier, I had confused a pretty fundamental fact. When I was told that the discrepancy between the two numbers, which I came up to be 344 and 288, I thought both of those were unadjudicated numbers and thus the numbers didn't add up.

I now realized that 344 is the unadjudicated data for new diabetes and 288 is the adjudicated data after processing for the panel. I then went into Dr. Hemingway's affidavit to explain -- so it's not like the numbers don't add up, the panel eliminated a certain number of people.

And I reread Dr. Hemingway's affidavit and he explained how that happened: That they had to confirm

fasting, glucose readings were conducted, that they -- that they wanted to make sure the blood glucose values met the World Health Organization standards, that the participant did not have a prior diagnosis of diabetes in his medical record and the participant did not have a prior history of impaired fasting glucoses. And he said they did it in a blind fashion. They didn't know.

And obviously if Pfizer was somehow manipulating the process, which has been the inference here, Pfizer would have wanted more placebo diabetics and fewer Lipitor diabetics if they were trying to show no association.

Well, I then went into the data -- we had to go to a couple of different sources to do this, but we were able to do it -- and the numbers come out fairly close to each other when looking at the adjudicated and unadjudicated numbers when you are looking at percentages. That is, they almost consistently -- they kept essentially the same percentage, within one percentage point between the placebo Lipitor group in terms of the people who had end points. So they proportionally decreased both the placebo and Lipitor group in a way that is highly reliable for independence and integrity.

I then realized that after that was done, if you ran even the unadjudicated numbers, you had no statistical significance even if you used that. And we know from Dr.

Wei, I believe, did this, there is no statistical significance. Dr. Jewell had to do a second manipulation, that is to adjust for risks, which was not done in the ASCOT study, to finally get an association.

And I spent the last hour figuring all of this out. And frankly, having come to realize this, I really -- it's the -- it's the assumption I had when this thing started that Dr. Jewell was manipulating the data. And he does not have the basis to -- you know, I asked the question: What's the evidence that the panel lacked integrity? And I was told the numbers didn't add up.

Friends, the numbers do add up. He took -- the panel reduced by 56, almost exactly proportional, and it didn't really -- it doesn't produce a statistically significant result. You do two adjustments before you do it. And if that was in isolation, perhaps we would say, I don't know, maybe it's not so suspicious, but it's in the middle of so many. And I wanted to correct for the record my confusion about what those numbers meant.

So, you know, if the plaintiff wishes to respond any further to correct my facts here, I would be delighted to get corrected.

Yes, sir? State your name for the record.

MR. SUGGS: David Suggs, Your Honor.

THE COURT: Thank you, Mr. Suggs.

MR. SUGGS: I wanted to point out that the analysis that Dr. Jewell did was the analysis that was called for in the protocol that was not done by the Sever group. He did what the protocol called for. That age -- all those adjustments that he made, those are specified in the protocol. But Sever didn't do them. That's why he did that analysis.

THE COURT: Well, when he did -- and he looked at un -- when he looked at unadjudicated -- but, you know, this goes back to the whole question of adjudicated versus unadjudicated. This has been my concern is why would you use unadjudicated? And he said because they had evidence of the numbers didn't add up. The numbers added up fine. This is all just -- y'all are just suspicious without any evidence that the panel lacked integrity.

I've read Dr. Hemingway, he said --

MR. SUGGS: Sir --

THE COURT: Let me finish.

Dr. Hemingway said he didn't work for Pfizer. I mean, and if you look at the numbers, it's just -- you know, it's not just -- it's just one piece of evidence of many I'm getting that Dr. Jewell is hunting for a result and he is going to find a way to do it. And if it was just one example and that was it, you would say, Well, you know, maybe, I don't know. But there is so many here that it

leaves this Court with a very strong impression that Dr. Jewell is basically going to produce a result of the people who hired him. That does not give me a lot of confidence. I have a low bar about *Daubert*, but it looks like we've got a problem here.

MR. SUGGS: Your Honor, I respectfully disagree with you.

THE COURT: You are entitled to do that.

MR. SUGGS: And, Your Honor, I would also suggest that if, in fact, you have some serious questions about this, perhaps what we need to do is have an evidentiary hearing with Dr. Jewell because he can explain exactly what he did and why he did it. And everything he did is scientific. Instead, this adjudication committee is the ultimate black box. It's unknown people making unknown judgments, and it's the ipsa dixit of that adjudication committee that we are supposed to rely on.

What Dr. Jewell does is he does this analysis. He uses the ADA criteria. He uses the data that Pfizer gave to us. He did standard statistical analyses. He did the analyses that were specified in the protocol that the Sever people did not do, and he showed all of his work. We haven't seen any of the work of the adjudication committee. All we get is this late date affidavit from Dr. Hemingway.

MS. BIERSTEIN: If I could just add to what

Mr. Suggs said? Because I was the one who talked about how the numbers didn't add up. And I think there has been a misunderstanding --

THE COURT: And I don't want to act like you misled me.

MS. BIERSTEIN: I understand that.

THE COURT: I have a factual --

MS. BIERSTEIN: I think there is a misunderstanding about what numbers don't add up, because they don't add up, but not the numbers Your Honor was looking at. I was not clear enough. And I think if Your Honor had a misunderstanding that it was my fault for not being clear.

What doesn't add up is Sever says -- so the protocol says here is what you do. The Sever paper reports the results. But if you do what the protocol says you are supposed to do, the numbers don't add up. It's Sever doesn't match --

THE COURT: How big a difference of these numbers when you say they don't add up?

MS. BIERSTEIN: That is the 30 to 50. Sever seems to be using the protocol. But when you do it, you get a different number. That's the 30 to 50 that is different.

THE COURT: What is bothering me here is if you take Doctor, you know, Dr. Jewell on his face, everybody is a fool but him. Nobody can count. Nobody can analyze. Nobody can

get it right. And, you know, he's going back in and he's redoing everybody's analysis.

And let me say, he uses -- you are talking about he uses the ADA definition for diabetes. In ASCOT he does. In IDEAL he uses another definition. He uses a third definition in TNT and a fourth definition in the NDA.

MS. BIERSTEIN: I don't think that's true. He used another definition for other purposes, but he never used any definition for diabetes itself other than the ADA. I mean, and this is something even --

THE COURT: I'm reading the reports. IDEAL he uses only if there was an adverse event report. The author --

MS. BIERSTEIN: The study protocols, Your Honor -- each study has a protocol, the whole idea that they talk about, you know, how a study is designed. So the study design says at the beginning this is what we are going to do. And what Dr. Jewell did is he did what the study prescribed you are supposed to do. So in IDEAL, the protocol specified to do certain steps and he did them.

The problem in ASCOT was that when he did what the protocol said, the numbers didn't add up. But in everything else, what Dr. Jewell did if his analysis in IDEAL is different from TNT or different from SPARCL, it's because the protocols were different.

THE COURT: He used only half the protocol

definition in IDEAL.

MR. MARCUM: Your Honor, can I address that? Because in IDEAL, there were only two -- what Dr. Jewell did when analyzing the ADA definition was look post-baseline for two fasting glucose levels that exceeded those ADA criteria. In IDEAL, in that study, there were only two glucose measures for any patient, baseline and one at the end of the study, as I understand it.

So he was unable to apply that definition in IDEAL as he applied to the remainder of his analyses. That's a function of the data as it was provided to us by Pfizer.

MS. BIERSTEIN: And, Your Honor, I just want to say, nobody here is suggesting -- and Dr. Jewell I think is among them -- that there is something nefarious going on; that Pfizer was manipulating the data. What we are suggesting in ASCOT is there was a mistake or some confusion.

But I do have to second --

THE COURT: What is the mistake?

MS. BIERSTEIN: The mistake is that there appears not to have been a consistent definition of diabetes applied --

THE COURT: Dr. Jewell would recognize that.

MS. BIERSTEIN: I mean within the -- in the Sever paper. The results that were adjudicated appear not to be the result of a consistent definition. And so if you are

adjudicating without application of a consistent definition, there seems to have been a problem with that study.

But I do want to second Mr. Suggs' point, if Your Honor has real concerns about Dr. Jewell, I do think that hearing from Dr. Jewell himself -- I think, you know, you are basing it on a report --

THE COURT: There is due process. And at some point, it's just got to -- you know, we've got to shut down the receipt of information and we've got to do analysis.

And listen, over the screaming objections of Pfizer, I let Dr. Jewell do a rebuttal report. That was a very close question in my mind. And I'm not going to have him come in here and now give me a further explanation.

At some point, this case is too complicated, we've got to take the record as we've got it and we've got to analyze it. And I'm just saying it's just -- you know, it bears a suspicion that he keeps doing manipulations that seem designed to second guess all the author's studies, all the analysis that was done, using different definitions and it all comes out with one result.

I just -- you know, it's leaving me with a bad taste in my mouth about his independence and his integrity. And I know y'all don't agree with me about that. But, you know, at some point I've got to take the information I have in front of me and I've got to analyze it and -- you know, it's

not my desire to knock any witness out.

I'm -- as I've said, I'm not a heavy hand on *Daubert*, but, you know, there is a threshold y'all have got to meet. And, you know, we have been talking around Dr. Jewell probably long enough. We probably ought to go ahead and just square up deal with it because this is obviously just one of many issues that concern me. And maybe that's the best way to do it here. I was going to save him for the last in this group, but we are -- you know, I think everybody is shadow boxing on every other witness basically on this issue.

So perhaps Ms. Bierstein, let's let Mr. Cheffo start on what he's got to say about Dr. Jewell and then give you a full opportunity to respond.

MS. BIERSTEIN: I will do that, Your Honor.

And I want to say one last point, which is not really about Dr. Jewell, which is why I want to get it in before Mr. Cheffo speaks about Dr. Jewell.

I want to be clear on something that came up in the morning which relates to Dr. Jewell, which is in the discussion of the 10-milligram trials, the NDA trials, I just want to be clear that the 3:1 ratio -- we are going to get into that 10-milligram issue later in greater detail -- the 3:1 ratio that was reported, it was not Dr. Jewell's calculation, it was Pfizer's. Dr. Jewell did a different

calculation with the NDA, and we'll talk about that one, too.

But this whole issue, to the extent you are concerned about Dr. Jewell, I want to make clear that this 3:1 issue -- we'll talk about what the 3:1 was -- it was not Dr. Jewell, it was Pfizer. I wanted to be clear because when you asked me what does it affect? How much were people relying on Dr. Jewell? They did not need to rely on Dr. Jewell for the 3:1 because it's not his computation, it's Pfizer's.

THE COURT: Thank you, ma'am.

Before you start, Mr. Cheffo, let me just say this: I think it's fairly obvious we are not going to finish today, okay? I'll go as long as y'all want to. Just a practical matter -- and I have a roster meeting, both civil and criminal roster meetings, tomorrow morning and I have to be somewhere at 4:00. So my roster meeting at 11 probably will be over by 11:30. And I don't know what counsels' schedule is on both sides, but we -- I think we probably need to anticipate we are going to need some more time tomorrow. We haven't gotten to, you know, efficacy, Abramson, Fleming, we haven't done any of that. And I really want to give everybody an opportunity to fully state their position.

I do find it helpful, having counsel having a full opportunity -- and I've said to Ms. Bierstein earlier, I'm going to give her -- I'm going to give everybody a chance to

say what they need to say. And everybody -- so I say that to -- I'm saying it to you, Mr. Cheffo, but is there a problem tomorrow with your schedule?

MR. CHEFFO: No. In fact, I would say we would welcome that. Because, I mean, of course, as you know, we have a number of things that are cascading off of this, so -- and obviously Your Honor has been very -- given us a lot of time. So quick answer yes, we will come back at 11:30.

THE COURT: Ms. Bierstein, are you okay with that tomorrow?

MS. BIERSTEIN: I'm fine with that. I have a 5 PM flight tomorrow night.

THE COURT: I have a 4:00 appointment I need to keep. So we are good and we'll get you out.

And, you know, I do think -- we've spent most of -- frankly, if you look back at it, most of the shadow boxing about Dr. Jewell, right? We talked about Dr. Dale, Dr. Singh, but everybody keeps -- you pop up a picture with arrows pointed, you know, you could point it the other way as a target, Mr. Cheffo. And so I do think it's appropriate for us to focus with some precision on what the problem is.

Because I realized when I came -- it just -- I walked out of here and I said something isn't right about those two numbers. And it's just easy to get misapprehension about the numbers and what they mean.

Because in every one of these -- and there was a discussion about different definitions and different studies that highlights the point there is a lot of detail, the devil is in the details here.

So let's go through your problems -- your specific problems with Dr. Jewell. And on each of these, let's be very precise about what we are talking about.

MR. CHEFFO: Sure.

THE COURT: Because I know that your client's view is that he's manipulating data. Is that sort of --

MR. CHEFFO: I think that's fair.

THE COURT: Okay.

MR. CHEFFO: So before Your Honor did kind of the heavy lifting, as you often do, I actually had the -- I had spent my lunch going through the Hemingway affidavit. And we were going to make some of those points, but I think you made them.

The only two additional points on that is we heard over and over -- and this is Jewell specific, and we'll talk about it, you know -- he did the protocol that they should have done. But -- that makes no sense to me in the sense that these are three doctors. You read -- they are three -- he's a statistician. If you ask him anything, his kind of standard answer is, I don't know anything about anything in science. He backs off of that.

So if you have three doctors who two of them are looking at it, and then if there is a disagreement or question, and they meet with anyone, and they look at the medical records, and then they make determinations, and it's all blinded, to get up here and stand up here and say he did exactly the same thing as those folks, I'm somewhat perplexed as to how that can be.

THE COURT: Well, they were saying -- I didn't understand they were talking about that. What I understood was, I said, even when they did the unadjudicated data, he didn't get statistical significance, according to Dr. Wade. And then Mr. Suggs and Ms. Bierstein made the point that he was simply following a protocol that the -- that the study had anyway that hadn't been followed.

MR. CHEFFO: But again, I don't know how -- he would kind of know that because of the protocol from the affidavit. You look at the data, you look at the medical records, you meet and talk about it.

THE COURT: I was understanding that that was -- that there was some adjustment for risk factors. When he went in and the -- and that he did it because that allegedly was what ASCOT was supposed to do and didn't do it, I don't know anything about that. It's new to me.

MR. CHEFFO: Maybe you understood it better than I did, Your Honor. Basically, I think we come back to a few

principles just for the record.

I think we've now heard it a few more times, black box. If you want a black box and hide things, you probably wouldn't publish it in *Lancet*. These are the names of the three people that were published on the document.

THE COURT: I haven't heard the slightest evidence to suggest that the panel did not handle this matter with integrity, professionalism and thoroughness. There is no evidence of that.

I do think the plaintiffs don't know -- I mean, it's just -- when you have a panel and they are not publishing their adjudications, which is kind of routine, these are individual people -- you know, there are medical records and so forth, you might -- if you are suspicious of the integrity of it, you would say, you know, I just doubt they have integrity. But that's not evidence. Just sort of a suspicion that somehow something nefarious or improper happened is not evidence.

MR. CHEFFO: It's also -- I mean, isn't it odd that that suspicion only occurs if it's a study that goes against them? They don't seem that suspicious about --

THE COURT: I haven't seen anybody doing unadjudicated data about anything else. Why do you do it? You do it because you don't like the result and you are trying to get a different result. And you play with all

these different adjustments and you finally get one that works for you. You know, as they say, a clock -- even a broken clock is accurate twice a day, right?

MR. CHEFFO: Exactly.

And that's why I think really kind of the core, the core issues we have -- and I do want to be specific. So, you know, before we get into -- and I think again Your Honor knows this record probably better than I do at this point -- there was kind of a discussion here about how we got to -- and I think this is important, right? So I think I put up a slide, you know, from *Zoloft* where he said, you know, if there is a problem -- I don't look at it unless there is a problem. And the question here was, well, he noticed a problem. Let's go back in time --

THE COURT: I don't see any problem he had. He had a lower number from the panel than the unadjudicated, which would be anticipated if they were doing their job.

MR. CHEFFO: Exactly. And even the point of looking at it. And there was, I think, an implication or a suggestion that he didn't have the data. That's just simply not true. At his deposition he said, I chose not to do it, right? I chose not to do it. Then he realized he was vulnerable on it.

THE COURT: You are talking about the original not looking at the ASCOT?

MR. CHEFFO: Yes.

So the point being is there was not this big a-ha moment that I saw something was wrong and I went and looked at it. He chose not to look at it. It was only --

THE COURT: We are not going to relitigate that. I gave them a chance to do it and he did it.

MR. CHEFFO: Fair enough.

The point is they did have all the data. He made a decision not to do it. You've highlighted that there is really not a discrepancy.

I guess my main points on that was they didn't have the medical records. This is a blinded group. And again, not to belabor this point, Your Honor, this is really kind of a much broader attack on kind of science generally.

If we could kind of go back and redo every time we have a suspicion, it creates problematic issues for not just this case and this Court, but going forward. Here is what -- apologies for the small font here, but -- Your Honor has read these reports -- the original report and then you have the rebuttal report. Obviously the original report doesn't deal with ASCOT and the rebuttal report does.

You know, I think what they have basically told us is that he's not offering a causation opinion. We know that he's only done this limited analysis. We've talked about the limited post hoc analysis. And certainly for all the --

I'm not going to reiterate all these, I think we've covered them.

Here is the one thing I do want to talk about: You know, I think the plaintiffs are essentially trying to a little bit, you know, heads I win, tails I lose. So on the one hand they say, Let's talk -- we heard this morning. I think you asked specifically, If I was to disallow either Dr. Jewell -- maybe you said the ASCOT -- would it have any impact? And the answer this morning was not really. That's really important. And as the day has gone on, it's much more important because if it's his ASCOT analysis, they have no way of challenging what's the peer-reviewed study. That's the first thing.

But what's perhaps even gotten lost in this discussion -- my fault -- is that the plaintiffs have said, Let's talk about his kind of subsequent studies, his second paper or opinions. They've said no one has relied on it.

So for purposes of all these other folks, they say it three or four times in their brief, it doesn't matter because he wrote it afterwards and none of the plaintiffs formed their opinions. So if that's true, then they should be judged on their opinions.

And I think what is equally as important is that, you know, Your Honor is not asked, I think, nor has any court, to check your commonsense kind of at the door here.

If this really was this a-ha moment, this great issue that they went through great lengths to get a supplemental report, it's not that hard to file a one-page adoption of it. But none of their experts have done that. But they are asking you --

THE COURT: I've got a feeling tomorrow morning in your e-mail box will be those.

MR. CHEFFO: A little bit too late for that, Your Honor, because they wrote their briefs and they've said it.

So the irony is they are asking you to rely on it and the jury to rely on it, but their own experts won't rely on it and haven't relied on it.

So what is it ultimately that Dr. Jewell is trying to do? He is relying on SPARCL data and then he does kind of a gender analysis.

And here is what I think is -- excuse me for one second --

THE COURT: Does he do the gender analysis on SPARCL data or another data?

MR. CHEFFO: He does the gender -- and that's kind of the problem. He does a gender analysis on SPARCL, but he doesn't do it with respect to ASCOT and it doesn't support his findings with respect to TNT.

THE COURT: ASCOT has its own problems with the lack of women, so that might be an explanation for not doing that.

MR. CHEFFO: It might be, but it's not one that he articulated. In fact, he backed off of that.

THE COURT: Right.

MR. CHEFFO: So let's just talk about his gender analysis for a minute. You know, this was absolutely litigation driven.

In fact, Dr. Jewell's really main purpose in this litigation, Your Honor, as you probably figured out by now, is to come in and talk about gender. That's what his main point was, to do a gender analysis. And it's not something that he would have done in the --

THE COURT: Gender analysis is that Lipitor affects women more adversely than men?

MR. CHEFFO: Yeah. I think there is a safety -- there is a gender analysis with respect to safety and then with respect to efficacy. I'm talking about the safety issues.

THE COURT: That's what I want, to make sure we are on the same page.

MR. CHEFFO: Yes, Your Honor.

And obviously, Ms. Bierstein will talk about the other half to the extent you have questions about that.

Kind of one of their theories that seems to have fallen by the wayside, but one of their initial theories was women are more at risk, or that Lipitor has a more impactful

negative influence on women than it does on men, right? So that's why he did this initial -- that was kind of the crux of his initial report. So he ran five tests in SPARCL called heterogeneity tests.

This is what the plaintiffs say of them -- I agree with this -- heterogeneity refers to the possibility of different results amongst the five -- I'm sorry. Heterogeneity refers to the possibility of different results among the study population depending on the gender of the subjects. So he ran all five of those tests.

THE COURT: That was it, right?

MR. CHEFFO: That was it.

But in the face of that -- science is not about just like, Hey, let me just run some -- you know, if you are going to do and avoid chance and confounding and bias, you have to have a reason, go from here to there and follow a methodology, particularly if you are a statistician and you are not a doctor. But in the face of all that, you know, he now opines that the risk of diabetes is higher in men than women.

And here is a few other points that I think are -- he hasn't properly addressed. There is no difference between men and women in the risk of diabetes in any of the other studies that Jewell analyzed, including TNT and IDEAL. And Professor Jewell didn't analyze the risk by gender in ASCOT

because it was unhelpful. There may have been other reasons, but I think you know it didn't stop him from --

THE COURT: You are telling me he looked at IDEAL and TNT and found none?

MR. CHEFFO: That's my understanding, yes, Your Honor.

THE COURT: Okay.

MR. CHEFFO: And you know -- and he -- his kind of primary answer, when kind of confronted with this, why he didn't do this in ASCOT, was that, he said, Well, the gender analysis was not a central feature of the report. Even though that's really -- if you take out the gender analysis, what is it that Dr. Jewell is adding here in his first report? It's this gender safety analysis. And then he essentially reiterates the ASCOT -- I'm sorry -- the SPARCL data. But he does it in a way that ignores the points that we've talked about, the three risk factors. That's basically it.

And then we've kind of talked about --

THE COURT: What do you mean -- explain to me what you just meant by the three risk factors. What are you saying?

MR. CHEFFO: One of the things that he doesn't account for -- let me take a step back. You will recall in the Waters paper, in SPARCL, they looked at SPARCL and they

found a slight association. When they did their analysis, they said they looked at SPARCL, IDEAL and TNT and they said the meta-analysis there is a slight increase, 80 only, but for people who have three or more -- three of the four risk factors that they identified. Three or four of the risk factors. So that's not something that Dr. Jewell has taken into account.

So, you know, it's essentially -- bottom line, it's a cherry picking argument, kind of take some of the data, ignores the other. But at best, he's really relying on the SPARCL study. And then his gender efficacy arguments or positions are kind of inconsistent with the methodology that he would follow kind of anywhere else. And this is just really --

THE COURT: What does he conclude? What is his opinion in SPARCL? Get me down to the weeds on this, because I'm not quite sure I understand it. What does he actually say is the -- and what -- how does he get there on gender?

MR. CHEFFO: He draws a conclusion. And there is probably folks, the Verizon network here, who will help me.

THE COURT: They seem very willing, by the way.

MR. CHEFFO: I shouldn't have come back after lunch. I think we would have been better off.

THE COURT: I think both of y'all are doing great. And everybody else wants to rush up. I haven't noticed

either one of y'all needing much help.

MR. CHEFFO: I'm going to raise my hand when it gets beyond my -- in all honestly, Your Honor, I want to make sure -- these are really hard issues and Your Honor has very specific questions.

THE COURT: I appreciate that.

MR. CHEFFO: I'm going to ask someone who actually -- make sure I tell you exactly what you need to know.

The bottom line is he draws a conclusion that there is a higher -- there is a higher risk for women as a result of looking at the SPARCL data, even though that in our view, we think the proper -- and I think scientific view -- the proper methodology would be -- would not run and come to that conclusion when you've looked at the heterogeneity analysis. There was no difference. And then when he does the same kind of look in IDEAL and TNT, you don't see that difference between men and women. And then the third kind of point is he hasn't done that analysis with respect to ASCOT.

If you have very specific questions, in all seriousness, Your Honor, we can talk about those.

THE COURT: So he -- he finds it on the data in SPARCL. Does he offer an opinion generally based just on that data?

MR. CHEFFO: That's my understanding.

This is Michael Hogue.

THE COURT: If you will come forward. It's hard enough for my court reporter to hear everybody.

Yes, sir, Mr. Hogue?

MR. HOGUE: Michael Hogue.

He -- Dr. Jewell did analyses of SPARCL. He did a bunch of different analyses of SPARCL.

THE COURT: The five analyses.

MR. HOGUE: A Breslow-Day test that he did. And under the conventional standard of P.05 none of them met that criteria.

THE COURT: Then what did he do to get there? The five studies?

MR. HOGUE: He did different ways to analyze it. He used adverse events. Then he used adverse events deleting certain patients with baseline glucose values. He did an analysis that he called new onset diabetes where he actually looked at glucose values instead of the adverse events. And then he put the glucose values and the adverse events together.

And as you might -- one might guess, when you do these different definitions of diabetes --

THE COURT: You get slightly different results.

MR. HOGUE: -- you get different results. And he gave opinions about SPARCL and finding a statistically

significant increased risk at the 80 milligrams on the adverse event or the glucose. But he also then says, Well, there is a risk that's higher in women, even though statistically there is no difference in the risk between men and women.

THE COURT: Well, SPARCL is a distinct group of people, right? It's prior stroke victims. Am I remembering this right?

MR. HOGUE: Yes, Your Honor.

THE COURT: And obviously, they -- they are loaded up with risk factors, if that's their prior history. And they get 80 milligrams. And it's -- I think it's fair game to make some analysis. It does show an association, which I think is something I understand the plaintiffs do. Then how do you conflate that to everybody, even those who don't have the risk factors, who don't have 80 milligrams? How do you get there?

MR. HOGUE: I don't think you can, Your Honor. I mean --

THE COURT: Are there other studies that -- that he relies upon, other things showing -- you tell me IDEAL and TNT don't show it. Does he look anywhere else, any other studies show the increased risk of women?

MR. HOGUE: The only studies that he looked at, Your Honor, were SPARCL, TNT and IDEAL, and then later ASCOT.

He also looked at the NDA data. For NDA data, he did not look at diabetes because diabetes was not the data set that you looked at.

THE COURT: Blood glucose values. I think it was one. He had to do one because that was all that was available or something like that?

MR. HOGUE: The glucose analysis, based upon the 40 groups, which was 3 percent versus 1 percent that had a lot of patients with glucose values greater than 125 at baseline or 1.25 upper limit of normal, as it was described, and only one of those patients had a normal glucose value of baseline.

So in the NDA data, it's really for the looking at diabetes.

THE COURT: Right.

MR. HOGUE: Can't possibly be looking at diabetes.

So what they are looking at is difference. When you ask me "other studies," he did look at certain glucose values, but not diabetes.

THE COURT: Doesn't, like, the JUPITER study show some association? I know that is Crestor. That does show some association with women.

MR. HOGUE: The JUPITER study did show some small risk.

THE COURT: Generally not by women?

MR. HOGUE: It didn't -- when they reported it in

2008, which was the article they -- it had men and women in it. It didn't --

THE COURT: Just generally.

MR. HOGUE: Yes, Your Honor.

With respect to Dr. Jewell, he did no analysis of any of these other studies. So when you are looking at -- talking about Dr. Jewell, he did not look at the JUPITER study. He did not look at the Navarese meta-analysis.

THE COURT: The Culver study. Did he do the Culver study?

MR. HOGUE: He did not look at the Culver study.

THE COURT: Chen?

MR. HOGUE: He actually says in his report that these observational studies have, which are Chen and Culver, are subject to a lot of biases and confounding. So he didn't evaluate any of the observation studies.

THE COURT: So you are telling me he has basically data from three studies, which are IDEAL, TNT and SPARCL. And that he runs five studies, heterogeneity studies. SPARCL does not get a result showing an increase with women, but then does other manipulations that eventually gets that result.

Is that what you are telling me?

MR. HOGUE: On heterogeneity, he found no difference between men and women. He reports in the

studies, the analysis he did, he says there is an increased risk in this population.

But then he goes further to say it's a higher risk in women, which is where the heterogeneity does not show that there was a higher risk in women.

THE COURT: Okay. Thank you, sir.

MR. CHEFFO: Thank you. I think I owe Mr. Brown and Mr. Hogue something after this hearing, Your Honor.

So this is my last slide on Professor Jewell. And this is really just -- not really -- it's a methodology issue. It's one of these -- it's a little bit, you know, perhaps death by a thousand paper cuts.

But this is one of the patients -- this goes back to this 37 to 3. He says, Well, I'm going to try and figure out what a fair way -- what a methodology is to figure out what the increase is.

So he looks at patient 77, who was in the Lipitor, and she -- the patient had, you know, 132 but had a 176 right before taking Lipitor. And after taking Lipitor, it's kind of a very small increase.

THE COURT: She's a diabetic, right?

MR. CHEFFO: Yeah. She's a diabetic most likely, right.

I can't play armchair doctor, but let's assume that that's true. But here is the thing, this is -- if you wanted

to figure out what the impact of Lipitor is, it's four. He reports it as 48. Because he looks back at the first test; not the second test.

THE COURT: That's just an individual patient?

MR. CHEFFO: That's individual.

THE COURT: You are really down in the weeds now.

MR. CHEFFO: It is, but it kind of highlights the point.

I think unless Your Honor has additional questions --

THE COURT: I do. In the initial report of the -- let's talk about the NDA data for just a second. We talked about this a little earlier. He had -- he identified 40 people.

MR. CHEFFO: Yes.

THE COURT: He combined placebo and Lipitor groups into one.

MR. CHEFFO: Yes.

THE COURT: He did not account for the fact that 25 of the placebo group -- of the Lipitor group and two of the three of the placebo group already were diabetics or were over 125, correct?

MR. CHEFFO: Correct.

THE COURT: And then he sort of reanalyzes the NDA data in this combined -- combining these pools; is that

right?

MR. CHEFFO: Yes.

THE COURT: And he counts subject to the NDA data with one elevated glucose when all his other studies required two.

MR. CHEFFO: I missed that one.

THE COURT: He had -- he counted people who had elevated glucoses with just one glucose.

MR. CHEFFO: I think that's right. Or he basically used the table 42 data.

THE COURT: Yeah. It may only have been one actually available.

And he does not compare the glucose increase in the placebo group and in the -- and in the Lipitor group in the NDA data; is that right also?

MR. CHEFFO: Correct. Because if he did, it would have shown a 50 percent increase.

THE COURT: A higher increase with the placebo group.

MR. CHEFFO: Or arguably a decrease. He would do better -- as we talked about, it's not a fair -- even though it looks good for Lipitor, it's not a fair conclusion.

THE COURT: Okay. Now, Mr. Cheffo, after that, I allowed him, over your screaming objections, to do a rebuttal report. And he -- and your expert response to that, that I

can't really figure out what data he used. Did y'all ever figure out what he did?

MR. CHEFFO: I think the best information we have is from Dr. Wade's report.

THE COURT: He said he couldn't figure it out.

MR. CHEFFO: That's the best information.

THE COURT: How did y'all get it the first time? Y'all took his deposition. Is that how you got the information? How did you -- I mean, y'all had an idea how he -- his process when he did the initial NDA data analysis. Why aren't you able -- or what -- did he not give it to you or how did you obtain the information about how he -- his process before?

MR. CHEFFO: Someone will jump in. Basically my understanding of how the process worked here is that they are using data that we provided, right? So it wasn't necessarily that he had kind of his own independent data; it was information that we gave, he used it in a particular way. We got his report and we saw it and kind of had --

THE COURT: Reverse engineering. Figure it out.

MR. CHEFFO: We were like, Here is his conclusions, it wasn't always clear, we talked to some experts, and figure it out. And we said that doesn't make any sense. How did you draw those conclusions? Some of the analysis that was done by smart folks on our side was to reverse engineer and

work with the experts. And some of them we couldn't figure out --

THE COURT: I'm concerned with data manipulation and then I don't have an explanation of the rebuttal report, exactly how he got there.

MR. CHEFFO: Yes. We don't -- and Your Honor, I mean, I think for -- I would even kind of maybe even go one step above that, which is the rebuttal report. They have now had the chance -- no one relies on it, it's just, for scores of reasons, is inherently unreliable. It, amongst everything else, should be stricken, should be disallowed.

THE COURT: Why is that? Just give me --

MR. CHEFFO: Because one is his analysis. We've talked about for, you know, the four, five or six reasons of the ASCOT data is just not methodologically sound. It's cherry picking. He doesn't follow --

THE COURT: I'm talking about the NDA data. What about the reanalysis in the NDA data is unreliable?

MR. CHEFFO: His analysis of the NDA data is drawing the conclusions that he has. I mean, you can't look at this data --

THE COURT: I'm saying he came back and he did something else and he reached -- and I can't figure out how -- I didn't know what data he used. What's wrong with the rebuttal report? Assuming that was the beginning here,

what's wrong with it?

MR. CHEFFO: I'm sorry?

THE COURT: The rebuttal report on the NDA data.

MR. CHEFFO: Michael, do you want to address that? I'll let Mr. Hogue address that.

THE COURT: As I understood, he was trying to address complaints or criticisms that had been asserted in his deposition. So what -- what's wrong with the rebuttal report regarding NDA data, Mr. Hogue?

MR. HOGUE: Your Honor, I don't have that specifically in front of me. Which of his opinions on the rebuttal for the NDA that you are referring to that --

THE COURT: Well, he came back and he made certain adjustments in his analysis and response to the criticisms that were made. And he claims he adjusted for differences between protocols and baseline glucose. The complaint was he hadn't done it before.

And he then, as I understand it, did not fully disclose what he actually did. So this Dr. Wei was sort of complaining he didn't really know what he had done. So it was hard to comment on it.

And, you know, I kind of need to know -- y'all weren't able to figure out what data set he used or whatever, or what information?

MR. HOGUE: Even at the deposition when I marked

sets of his data from his data files, he said that was not his document. So getting beyond -- getting an answer from Dr. Jewell about his -- his analysis or the way he did it beyond what he put in his report is extraordinarily difficult. So I can't specifically say when Dr. Wade could not reproduce one of his data sets, which -- which in fact in the NDA he did multiple different ones.

THE COURT: This is the situation where he did the five analyses and then he turned around and did this regression analysis. Is that the data we are talking about?

MR. HOGUE: Yes, Your Honor.

THE COURT: Hold on one second.

(Pause in proceedings.)

THE COURT: I'm looking at Dr. Wei's record, page 9, he -- in paragraph 27 he said in the original report, he reported -- "he" being Jewell, Dr. Jewell -- reported the total exposure was 80 patient years and a placebo group of 342 patient years in the atorvastatin group. Then he goes on in the rebuttal report it's now 74 patient years, smaller than the 80, etcetera. He doesn't know how he changed the data. And I take it y'all don't really know the answer to that any more than --

MR. HOGUE: Your Honor, I don't know that he explained the difference between the 80 and the 74. That was part of his time analysis.

I think that the bigger issue with his analysis of the data is, what he claims it to be, is this glucose abnormality that these patients already had. And when they already had the glucose abnormality at baseline, he didn't exclude any of those patients. So when he says that these patients had glucose abnormalities, I'm just going to run the statistics on those numbers without excluding the patients who already had that problem.

THE COURT: Preexisting.

MR. HOGUE: That creates the issue.

THE COURT: Yes. I understand. Thank you.

MR. CHEFFO: I almost hate to ask you if you have any other questions.

THE COURT: I'm looking through my notes here. Thank you. I think we've done -- I think that covers it. I want to hear from the plaintiffs on this, if I could.

Ms. Bierstein? Do they give you like battle pay for being --

MS. BIERSTEIN: I should get battle pay, Your Honor. I really should. You probably heard, since we had to ask for more time, my lunch was very late in arriving. Yes, I'm going to ask for a combat pay.

I think with Dr. Jewell, we are starting at the beginning with what I believe is a fundamental misconception about his opinion. We hear from some of defense counsel

about all the things that Dr. Jewell didn't look at. He didn't look at JUPITER, and he didn't look at this, and he didn't look at that. And here is my problem: Dr. Jewell, as they keep telling you, is not a medical doctor. He's not offering an opinion about diabetes. He's not offering an opinion --

THE COURT: What are his opinions?

MS. BIERSTEIN: Well -- excuse me?

THE COURT: What is he -- if he's not offering an opinion regarding -- what is he actually offering?

MS. BIERSTEIN: So starting on page 3 of Dr. Jewell's report, we have the summary of opinions. This tells us exactly what Dr. Jewell's opinions are because Dr. Jewell's opinions are a data point that is, you know, is relevant for various things. And some of them were used by some of the other experts; some of them are not. But the point is he doesn't give an opinion about whether Lipitor causes diabetes. He gives a statistical opinion about specific studies.

Each of his opinions says, It is my opinion that the data in this study showed X. Those are his opinions. So the first opinion is an opinion about the NDA. And I'm going to come back to the NDA because I think the NDA opinion is quite different from all the other opinions and I'm going to want to go through that pretty carefully.

When you look at the next opinion, paragraph 7, it's a specific opinion about what the numbers in SPARCL -- that when you do the analysis of SPARCL, this is what the relative risks were. So this is a raw sort of statistical computation. If you do the analysis in SPARCL, here are the relative risks. It's going to be for somebody else to look at what he did with SPARCL and look at it in the context of JUPITER and in the context of TNT and the context of Navarese, all the studies. That's what Dr. Quon did. That's what Dr. Singh did. That's what Dr. Roberts did. That's what Dr. Gale did.

That was not Dr. Jewell's task. It was to look at the data and do the statistical calculations. That's why he doesn't look at the other studies because it's not Dr. Jewell's job to tell you what the significance of this study is. His job is to tell you what the numbers are. Somebody else, a Quon, a Singh, a Roberts, a Gail not only will tell us, and does give opinions about the significance of each study, but more important, what they do is they give an opinion about the totality, when you look at all the studies together, what you will see.

So, yeah, they are going to plug in Dr. Jewell's analysis of SPARCL or Dr. Jewell's analysis of TNT, but they are going to plug that in into a universe of all of the evidence.

Dr. Jewell does not pretend to do that. And you will not find in his summary of his opinions -- it begins on, as I mentioned, on page 3, it tags over just a little bit on to page 5, it's paragraph, 6, 7, 8 and 9 -- well actually, even -- 9 is not one of his opinions. He's offering three opinions in this report: One about the NDA, one about SPARCL and one about what you will see in TNT. And all of his opinions are not -- they are not opinions about causation, they are not opinions about what happens, you know, they are -- these are -- if you run the numbers, this is the association you will see in this particular study. So that's the first thing I want to clear up.

THE COURT: So you leave it to the doctors to say, Okay, this association, the significance, or lack of it, that the group, like in SPARCL, had a prior stroke, other risk factors, had 80 milligrams, all of that, that's not his business. He's not -- he's just saying in this group that's the result and it's for someone else to extrapolate the significance of that.

MS. BIERSTEIN: Exactly. It's for someone else to evaluate the significance of each study and all the studies together. That's where you will see Dr. Quon, Roberts and Gale doing, This study showed this and this one showed this, and so it is -- that is somebody else's job.

And the other thing that they do, Your Honor -- and

I think this goes to this last point -- is they look to see Well, you know, how strong is that paper? Is there something wrong with the protocol? I mean, it's up to the causation people to decide what weight to give to each analysis. And that's true for Dr. Jewell's analysis, as well. That is, it's up to them to evaluate, you know, what they think about that; not to evaluate the statistical part of it. Because the statistics is Dr. Jewell's business. But the rest of it, to understand, Well, how do we square SPARCL with, you know, JUPITER? How do you square A with B? That's for the other doctors to do. Dr. Jewell's work is quite limited.

THE COURT: So the NDA data, he combines the placebo and the Lipitor group into one, and he combines the people with diabetes preexisting with -- or more than 125 with those --

MS. BIERSTEIN: That's not right, Your Honor. I have to say this: I know that's what they keep telling you and it's just not correct. And let me tell you why it's not correct.

THE COURT: I mean, I saw the numbers about 40.

MS. BIERSTEIN: I understand, but -- numbers are fine unless -- but if you don't know what they mean, it's a little bit of a problem. So let me try to explain what was really going on here.

First of all, the thing I said to you earlier, Dr.

Jewell -- the 3:1 ratio is not Dr. Jewell's number; it's Pfizer's number.

THE COURT: I'm talking right now about specifically of combining the placebo and --

MS. BIERSTEIN: I'm getting there. Just if Your Honor will be patient, I'm going to get there, okay?

So let's start with what Pfizer did. Their protocol called for the investigators to pull out and report lab abnormalities. It was up to the investigators to use their judgment. They had certain lab values that they took. And the investigators were charged with reporting abnormalities that they find -- that they found.

Pfizer's investigators identified 40 subjects in the trial. This is Pfizer -- well, it was Park Davis at the time, but it's Pfizer, Pfizer is the successor -- it's Pfizer who identified 40 subjects as having clinically meaningful deviations from baseline, okay? And it was Pfizer that divided them, ultimately 37 in the Lipitor arm, three in the placebo arm.

And now because the number of patients was different in the Lipitor arm and placebo arm, you don't just say 37:3, but it was Pfizer that did the computation. That the increased risks of these clinically meaningful deviations from baseline, Pfizer said Lipitor compared to placebo 3:1, 3 percent to 1 percent. That was Pfizer's computation.

And Dr. Jewell did not redo that computation. He didn't revisit it. This is a place where Dr. Jewell accepted the Pfizer analysis. Somebody, you know, at Pfizer, somebody on the line selected these people. And somebody there did the ratio computation. And Jewell said, Great, I accept that number.

And that's important for two reasons: One, because the NDA trials are 10-milligram trials. And so to the extent that the NDA trials are showing something -- and we are going to talk about what they are showing in a minute -- they are showing it at 10 milligrams, and it's unaffected by Dr. Jewell because he's not doing that analysis. He just accepted Pfizer's word for it. The 3:1 is right out of a Pfizer's chart.

THE COURT: Explain to me again what 3:1 is. I want to make sure I'm understanding.

MS. BIERSTEIN: 3 percent versus 1 percent. What they did is --

THE COURT: Milligrams increase?

MS. BIERSTEIN: No, we are not there yet. We are just talking about the number of people with clinically meaningful deviations from their baseline.

So there were 37 of them on the Lipitor arm, there were three of them on the placebo arm. So we want to know what's the ratio of people on Lipitor? Were there more on

Lipitor than there were in the placebo arm?

THE COURT: I got you.

MS. BIERSTEIN: You can't just say 37:3, that would make you think it was a huge difference for Lipitor because there were many more people on the Lipitor. See, here the placebo is only 270 people.

THE COURT: Right.

MS. BIERSTEIN: There is a whole bunch more to combine -- atorvastatin is 11:22. So when I want to know what is the ratio of 37:3, 37 atorvastatin, three placebo, what is the ratio among the people with -- this is Pfizer, this isn't Dr. Jewell's table, this is in Pfizer's integrated safety survey study, ISS. Clinical abnormalities, okay? So here it is.

The glucose abnormalities we have three in placebo, we have 37 -- and I don't have on this chart, but I know -- it's somewhere else -- Pfizer does the calculation that if you adjust for the difference between the 11:22 here and the 270 there, what you see is that the ratio 37:3, 1 percent of those people -- you can see that sort of roughly 3 out of 270, 3 percent, 37 out of 11 --

THE COURT: That 37 includes 25 of them have preexisting diabetes.

MS. BIERSTEIN: I'm getting there, Your Honor. I really want to do this slowly because there are a lot of

separate points and I want to go step by step. This is not Jewell. This is nobody. This is Pfizer.

THE COURT: I hear you.

MS. BIERSTEIN: I'm going to get to the diabetics. I am. I promise you. If you let me go step by step, I will answer your question.

So the problem is Pfizer says 3 percent to 1 percent.

Now I'm going to take a little detour here into Dr. Jewell and we are going to come back to your problem with the diabetics. What is Dr. Jewell doing with the NDA if he's not doing this? And this comes back to your issue about him combining them.

So what -- what Pfizer said in the ISS is that when they pulled out the abnormalities, what was the standard? How did they decide who counted as having an abnormality, okay? And the term that they used was clinically meaningful deviations from baseline. But the problem is we don't know what that means. What is a clinically meaningful deviation from baseline?

So Dr. Jewell wanted to get a feel for what's the magnitude of a clinically meaningful deviation from baseline? So what he did is since Pfizer tagged all 40 of these people and Jewell assumed that Pfizer used a consistent definition of clinically meaningful deviations from baseline, because

they did it while it was still blinded, so he said, Well, if I want to understand how big a deviation you needed to get pulled out as clinically meaningful, I better look at all 40. Because those are the 40 that Pfizer tagged.

So since they tagged 40 people, using what we believe was a consistent definition of clinically meaningful deviation from their baseline, then Jewell says, Well, let me figure out from those 40 how big a difference were we talking about. So he looked at all 40 to understand what Pfizer meant by clinically meaningful. That is, how big a difference did you need?

So the only purpose of combining the two was to understand Pfizer's criteria for what's a clinically meaningful deviation. We don't know what the exact criteria were, but we got a feel for what the average amount was.

So that's what he was doing. Whether or not you accept that that was the right thing to do --

THE COURT: Let me ask you this: Did anyone take -- if we took out the 25 who had 125s at baseline or above, more than 125 at baseline, and the two out of three who had more than 125 at baseline in the placebo group, did anyone do an analysis of whether there was a statistically significant increase in that 12 versus the 1? I mean, the difference between 25 and 37?

MS. BIERSTEIN: I'm not aware of that. But I'm

going to tell you two things that may give you a different feeling about this.

The first thing is, I think as you know, the NDA trials were multiple --

THE COURT: Let me understand. You don't think he did that?

MS. BIERSTEIN: I don't think Pfizer did it. I don't think anybody did it.

THE COURT: I'm just saying, if you are trying to tell me that there is something meaningful that people who already had diabetes got diabetes or that people in the placebo -- on the placebo group are counted in there, I mean, other than saying, Well, that's what Pfizer did -- and I'm sure they weren't using it the way you are using it --

MS. BIERSTEIN: Your Honor --

THE COURT: -- is there a scientifically valid basis to analyze this?

MS. BIERSTEIN: Yes, there is. Let me tell you what that is. There is two points I want to make on this, and there is a scientifically valid way to do this.

So the first issue is this: Among the NDA studies -- there were many different studies -- there were two of the studies that had some very interesting results on precisely this subject. In two of the studies -- this is buried 600 pages in in the ISS, this is Pfizer's analysis --

they looked at the subjects who began with low or normal glucose values at baseline. That is people under 100 at baseline. In these two studies by the end of the trial 26 percent of them had high glucose.

THE COURT: High glucose over 100.

MS. BIERSTEIN: Over 100. 26 percent of the people who started with low normal at baseline were over 100 at the end of the study. You are going to see that in, I think it's chart 25-A in the ISS, table 25-A, but -- I can't remember the other one -- 31-A. Exhibit 25 -- Exhibit -- well, that's not Exhibit 25 or 31.

MR. SUGGS: They referred to in the deposition --

MS. BIERSTEIN: We may need to supply that. So that's one point.

But I think, Your Honor, the other point is much more fundamental. Pfizer keeps telling you -- and they are quite correct on this -- that what the NDA trial showed was not the development of diabetes; what the NDA trial showed was elevation of blood glucose.

THE COURT: Yes.

MS. BIERSTEIN: Okay? So what does that mean? It means that, say I have a 140 glucose, I'm diabetic. Lipitor can increase that by an average of 30 milligrams per deciliter during the course of the study.

THE COURT: But that doesn't tell you it causes --

your theory is is that Lipitor causes diabetes.

MS. BIERSTEIN: Sure.

THE COURT: But I want to -- you know, remember now, you've already got -- in the NDA, were there studies done that concluded that there was no increase in the risk of diabetes?

MS. BIERSTEIN: The NDA didn't study the diabetes question, Your Honor. In the NDA the issue was glucose elevation.

THE COURT: Let me rephrase the question. Did they conclude that Lipitor had any affect on glucose elevation, the original authors?

MS. BIERSTEIN: There were no authors, Your Honor.

THE COURT: This is the NDA.

MS. BIERSTEIN: There were no authors. They decided that the Lipitor may not have been the explanation for the 3:1, but there was no published study. They submitted the data. They said --

THE COURT: Who is "they," by the way?

MS. BIERSTEIN: Pfizer. This is not published data.

THE COURT: I got you.

And then Dr. Jewell comes in and he analyzes these 40 people. I'm asking you: For those who did not have preexisting glucose above 125, did he analyze the effect of

Lipitor on that pool of people?

MS. BIERSTEIN: He did not do that.

THE COURT: Okay. And --

MS. BIERSTEIN: He did that in terms of he analyzed -- no, he did not separate out those people. But Your Honor --

THE COURT: Did Dr. Wei separate them out?

MS. BIERSTEIN: Not that I know of. No, Your Honor. Nobody has done that.

Because, Your Honor -- the reason nobody has done that is I think everybody understands that the putative mechanism here, how is Lipitor causing diabetes? It's elevating blood glucose. And this is what Dr. Gale is telling you in his report, it's what the studies are showing you, it's elevating glucose.

THE COURT: Why would you put placebo into that pool?

MS. BIERSTEIN: Okay. Because Dr. Jewell wasn't deciding the placebo issue at that point. He was trying to understand by how much. But what he was really trying to understand was what criteria did Pfizer use when they said clinically meaningful elevation?

THE COURT: I'm trying to get --

MS. BIERSTEIN: I think we are mixing apples and oranges.

THE COURT: It just seems to me unimpressive that you are trying to determine the impact of Lipitor on a group of -- a pool of people and you include people that did not get Lipitor.

MS. BIERSTEIN: Okay. But that's not what Dr. Jewell was trying to do in that particular computation. In that particular computation he wasn't trying to understand the effect of Lipitor; he was trying to understand what criteria did Pfizer use? So you've got to ask what question was he asking before, you know, if he got the wrong answer.

THE COURT: What is his opinion arising out of the NDA? What is his opinion?

MS. BIERSTEIN: Well, this, I think, Your Honor, is where I'm going to pull up his report again. The part about the 3:1 was not Dr. Jewell's opinion; that was Pfizer's opinion. Dr. Jewell's opinion was that the average elevation among people identified by Pfizer as having clinically meaningful deviations was 30 milligrams per deciliter. And maybe we don't care about that.

THE COURT: You say that on an average these 40 individuals, almost all of them statin, experienced a very significant increase in blood glucose levels following initiation of treatment; is that accurate?

MS. BIERSTEIN: Say that again?

THE COURT: On average, of these 40 people,

including the placebo group, almost all of them on Lipitor experienced a very significant increase in blood glucose levels following initiation of treatment. Is that --

MS. BIERSTEIN: Yes, Your Honor, that's accurate.

THE COURT: I'm reading from his report.

MS. BIERSTEIN: I'm agreeing with you.

THE COURT: And in that group he's including the placebo.

MS. BIERSTEIN: Yes, Your Honor. But the point is at what ratio? There were people in placebo who had clinically meaningful elevation, but what was the ratio? Three times as many in the Lipitor group. We are always going to see it in the --

THE COURT: The 40 included -- I mean, I thought we were trying to prove that -- I mean, your theory is that Lipitor causes diabetes. And we have the huge majority of the people being studied already had diabetes.

MS. BIERSTEIN: Your Honor, the point of this study, from our perspective -- now remember, again, our experts, Dr. Quon and Dr. Singh, Dr. Roberts, Dr. Gale, looked at all of the studies; they didn't just look on this.

THE COURT: But they relied on Dr. Jewell. And if his methodology is flawed, then their opinions are flawed.

MS. BIERSTEIN: Your Honor, they didn't rely on Dr. Jewell for their use of the NDA because it was Pfizer that

determined that three times as many people taking Lipitor had clinically meaningful deviations from baseline as people taking placebo. That is not Dr. Jewell; that is Pfizer. So when Dr. Quon says that the NDA confirms this because three times as many people had elevated glucose on Lipitor as on placebo, he's not getting that from Dr. Jewell; he's getting that from Pfizer.

And if -- and the way you get -- but Your Honor, the way you get the ratio, you've got to compare those on Lipitor to those on placebo. That's how you know the effect of Lipitor. Some number of people are going to have elevated glucose without Lipitor.

How do we know how bad the Lipitor is? We do a ratio. How many on Lipitor versus how many on placebo? Who did the ratio? Pfizer; not us. So of course they counted the placebo people because they had to do the comparison. But Jewell did not do the 3:1; they did. Jewell didn't conclude that three times as many people on Lipitor had elevated glucose; they did.

But I want to come back to this business about diabetics, because if the mechanism here is that we increase blood glucose, even a diabetic can get their blood glucose elevated. The problem with Lipitor is that it seems to have this effect on the glucose-regulating mechanism. So the issue is it elevates glucose. In the NDA we saw that result

most strongly in people who already had diabetes. But as I said, in some of the studies, we saw it in people who didn't have diabetes. We saw it in 26 percent of the people who were low or normal ended up with high glucose. So the question of what does the NDA mean is what the NDA tells Dr. Quon, Dr. Singh, Dr. Roberts and Dr. Gale. What the NDA says is Lipitor at 10 milligrams seems to be elevating glucose in a clinically significant way. It's doing it across the board. That is, it's doing it -- we notice it most strongly in people who are already diabetic, but we notice it as well in people who are not diabetic.

THE COURT: What about people who are not diabetic? Does it tell us anything about people -- because I'm trying to deal with this group of people who are in my MDL --

MS. BIERSTEIN: Well, but Your Honor --

THE COURT: -- and don't have preexisting --

MS. BIERSTEIN: Not every data point goes to the ultimate question. So we do need to ask ourselves the ultimate question in this case: Did Lipitor cause diabetes in a woman who didn't already have it? But the scientists build their case brick by brick.

So when a doctor is -- you know, you asked the question about 10 versus 80 milligrams. Let's say we have lots of studies that show that Lipitor causes diabetes at 80. And now we want to ask our question, where does the effect

begin? Scientists think it's interesting and significant that it elevates glucose even beginning at 10. That is, this noticeable effect of raising glucose by an average of 30 milligrams per deciliter, you see it even at the 10 level. Even if the study doesn't run long enough to test diabetes --

THE COURT: So long as you include preexisting diabetics.

MS. BIERSTEIN: No. The 3:1 is -- as long as you include -- well, as long as --

THE COURT: As long as you include the existing 25 of the 37.

MS. BIERSTEIN: It's elevating glucose, yes. In people in whom it elevates glucose, it elevates glucose a lot, and a bunch of those are diabetic.

But as we said, Your Honor, 26 percent of the subjects in two of the studies with low or normal at baseline, under 100, they are not only not diabetic, they are not even prediabetic.

THE COURT: You are moving the goal line here. I'm just trying -- you have people who aren't yet over 125.

MS. BIERSTEIN: I'm talking about --

THE COURT: That's 12 people in the Lipitor group who have new onset and one in the placebo group.

MS. BIERSTEIN: Right.

THE COURT: But when he's analyzing -- he's

analyzing 40 people, not 13. And you are saying -- and it may inform us -- I'm just amazed that no one has done the analysis on how about is there -- is there a statistically significant increase? Probably because it's just too small. So he has to -- isn't there a question to Dr. Jewell, Why did you do this? And he said, I had to to get statistical significance? Isn't that in a deposition?

MS. BIERSTEIN: I -- again, we could ask Dr. Jewell if we had him here. And I think he might be a better --

THE COURT: I'm going to --

MS. BIERSTEIN: But Your Honor -- but I want to make the point, the NDA analysis is not -- I mean, the issue with Dr. Jewell and the NDA is simply a question of him measuring the magnitude because this 3:1 business and this 26 percent of the subjects with low/normal has nothing to do with Dr. Jewell. That's not his analysis.

So even if you say, I don't like what Dr. Jewell did with the NDA because I don't like him computing the 30 on all 40 people, you still have the 3:1 ratio.

And you still have to ask a clinician, a scientist, someone like Dr. Quon, Dr. Singh, does it matter that it was showing that in people who might have already been diabetic? And that's -- you've got to ask them, does it matter?

THE COURT: Did that 3:1 have statistical significance? I thought it -- I thought that was the one

that had a confidence interval from .9 to something.

MS. BIERSTEIN: It was statistically significant. My understanding is that Pfizer reported it as statistically significant.

MR. MARCUM: Pfizer did not.

THE COURT: I'm again referring to Dr. Jewell's report and it says the 3.0 with a 95 percent confidence interval of .9 to 9.6. So it wouldn't --

MR. SUGGS: Your Honor, I'm not sure where you are reading from --

THE COURT: I'm reading from Dr. Jewell's report. Page 9, paragraph 17.

MR. SUGGS: Do you happen to have it there?

MS. BIERSTEIN: I think it was a mistake --

MR. CHEFFO: Just to highlight -- I mean, just to -- Dr. Wade did address this in paragraph 140 of the report. I can talk more about it, but I think you asked if there was an analysis, and I think he looked specifically at the issue that you raised.

THE COURT: Will you make a note to do that? Because I want to let Ms. Bierstein have her --

MR. CHEFFO: Absolutely, Your Honor.

MS. BIERSTEIN: He says based on this data was three with a 95 percent confidence interval.

THE COURT: Did I misread the report?

MR. SUGGS: Yes, Your Honor, you did. At the top of page --

THE COURT: I was reading it verbatim. I was wondering how I misread it.

MR. SUGGS: Page 9 at the very top: "Based on this data, the estimated risk for an abnormal glucose measurement associated with atorvastatin was 3.0" --

THE COURT: Which is the number Ms. Bierstein has been giving me.

MR. SUGGS: And he goes on to say: "With a 95 percent confidence interval of .9 to 9.6 and a statistically significant two-sided mid P exact P-value of .04."

So it is statistically significant, Your Honor. If you keep on reading the rest of the sentence --

THE COURT: I mean, every time -- the goal line just keeps getting moved. That's the problem here is -- and you know, Dr. Jewell is sufficiently thastle with all of this, that he can do all these manipulations, and when you say, We have been looking at confidence intervals and statistical significance, and he goes to another test because that one doesn't suit him. And it sounds terrible 3:1, but you realize, you know --

MR. SUGGS: Your Honor, he says it's statistically significant.

MS. BIERSTEIN: I don't understand where the moving goalpost is, Your Honor. He's using a 95 percent confidence interval, and the interval goes from .9 to 9.6.

MR. SUGGS: And, Your Honor, that number that you were talking about there, that is when he was doing a comparison between this 1 percent and the 3 percent given these numbers. If you combined them together -- his whole reason for combining those 40 was not to see if that was a statistically significant difference between those two. His only purpose in combining the 27 and the -- I'm sorry -- the 37 and the -- yeah, the 37 and the 3 was to define this.

When you see that word clinical laboratory abnormalities, what does that mean, Your Honor? There is nothing on this table that says what they mean by clinically -- clinical abnormalities.

So he took those that they identified and he looked at the data that Pfizer produced and said what was the change in the glucose? And on average for those folks, it was --

THE COURT: Those 40.

MR. SUGGS: Those 40, the placebo and the atorvastatin, it was 30 milligrams per deciliter, so --

MS. BIERSTEIN: That told us what Pfizer's criteria was. They picked the 40.

THE COURT: I understand what your position is.

MS. BIERSTEIN: But Your Honor, I think it's

important to see that the 3:1 here, the percentages --

THE COURT: I see it.

MS. BIERSTEIN: But that's not -- that's not Dr. Jewell. And I think that's important to note. It's not Dr. Jewell who is coming up with the 3:1. And I think on this issue of the people who already had diabetes, that doesn't mean that Lipitor isn't raising glucose.

And if Lipitor is raising glucose in diabetics and nondiabetics, then -- and this is something Dr. Gale testifies to -- it's taking diabetics and making them worse. But we are not suing over those people because they already had diabetes. It's taking people who don't have prediabetes and giving them prediabetes, and it's taking people with prediabetes and giving them diabetes. Because what it's doing is, in some subset of people who are sensitive to it, it is elevating glucose by a large amount. And in the people in whom Pfizer picked out, that large amount average is 30. So if it's --

THE COURT: So what does he do in the rebuttal report on the NDA data?

MS. BIERSTEIN: Let me grab the rebuttal report which I have here in hard copy. I don't have the rebuttal. I don't have it with me.

THE COURT: Yes, sir, Mr. Suggs?

MR. SUGGS: What Dr. Jewell did in his rebuttal

report was in response to criticisms made by Dr. Wade. And basically he said that he should have done a Cox proportional hazard model, which is what he did. And when he did that, he found out that the risk is even higher than it was before. And now they have told us that they are not even going to call Dr. Wade to testify.

THE COURT: I'm only concerned about, right this moment, about Dr. Jewell.

MS. BIERSTEIN: So did you have a specific question? I did find the rebuttal report.

THE COURT: I'm confused. I'm sitting here trying to get -- and I know I'm into the weeds now. I'm looking at Dr. Jewell's report and he's explaining that -- he has to drop a footnote about the use of this P-value and he admits it is not statistically significant. But then he has, well, you know, maybe the odds ratio is -- this is really --

MS. BIERSTEIN: Which page?

THE COURT: He's doing a lot of back flips here.

MS. BIERSTEIN: Which page are you on?

THE COURT: Page 9 of his report. I was looking at footnote 15. "Although the lower bound for the 95 percent confidence interval for the relative risk is below 1, this is not the case for the odds ratio."

I mean, you know, it's just -- he's -- I mean, he's just -- if the standard we have been using for everything

else doesn't work, he'll go to another standard. And he admits -- he says: "This indicates imprecisely that atorvastatin subjects were estimated to be 3 times."

I mean, it's just -- you know, he's got a conclusion and he's going to get there one way or the other. I mean, that's the way I read this.

MR. SUGGS: Your Honor, he did three different analyses -- three different P-values there because he knew if he picked one he was going to get criticism from that side over there, Well, you should have picked this one. He did all three of them.

THE COURT: Y'all's explanation is it's Pfizer's fault or Dr. Wade's fault. But when he doesn't like the result, he will throw out the panel and he'll do whatever. He didn't rely on any of them --

MR. SUGGS: He's showing all of his work.

MS. BIERSTEIN: In fairness, he's disclosing this. He puts in a footnote, he's not picking one, he's giving you all the data so that you, or more importantly, our other experts can assess the significance.

This would be different than if he picked one and didn't tell you that he ran the other ones and they came out differently. He's telling you, you get this if you do relative risk; you get this if you do odds ratio and you get this if you do absolute risk difference.

Your Honor, if you look in the reference manual on scientific evidence, if you look at the epidemiology textbook, they will all tell you that there are three -- at least three different ways to look at these comparisons. Sometimes you use relative risk; sometimes you use odds ratio; some of the calculations are hazard ratio; sometimes you use absolute difference.

If you look at the various papers that are reported across the board, they use different ones. Sometimes they are using odds ratio; sometimes they are using hazard ratio. I've got to tell you my eyeballs spin and I don't know how Dr. Waters picked whether to use odds ratio or hazard ratio or relative risk. I don't know how any of them pick which to use. Even when I look in the textbook, it doesn't tell me which one to use. When I look in the reference manual on scientific evidence -- which I mention because it's a resource that is very accessible to lawyers and judges -- they tell you here are the three. They don't tell you which one to use.

I'm having trouble with the idea that because Dr. Jewell didn't pick one, because he did all of them and he gave you the numbers that he got for all of them, that that's somehow a little shaky because I don't know of anything that tells you which one to pick, so he didn't. If he had picked one, I think Mr. Suggs is right, we would hear, Well, if you

looked at hazard ratio, you would get a different result.

THE COURT: I think we've kind of talked the NDA to death. What else have you got? What else do you want to share with me on Dr. Jewell?

MS. BIERSTEIN: I think also I feel like this morning we talked the ASCOT study to death.

THE COURT: I think we did a good job on ASCOT.

MS. BIERSTEIN: We talked ASCOT to death.

THE COURT: Before and after.

MS. BIERSTEIN: So I don't have anything on SPARCL unless Your Honor has specific --

THE COURT: No. I thought --

MS. BIERSTEIN: -- questions. I think we are pretty clear on that, unless Mr. Suggs has anything to add on SPARCL.

I want to come back to your first question about, well, you know, if you have an issue with Dr. Jewell, what does that do to the rest of my experts? And I told you I didn't think it did very much. Mr. Cheffo suggests I've back peddled from that and I haven't at all. But we did start to talk about Dr. Jewell more because Your Honor focused on it.

But if you look at the expert reports, despite the pretty graphic with everybody pointing at Jewell, you won't actually see that much of it in their reports. You will see

it with SPARCL. As I said, the NDA, the 3:1, I know Dr. Quon attributes that to Dr. Jewell, but the point is, it's Pfizer; it's not Dr. Jewell. And nobody used the ASCOT analysis.

So I think that on the issue of what effect does Dr. Jewell have? There is some important insights that we get from Dr. Jewell about the magnitude and about the scope and some of the -- you know, I don't want to minimize his role, but in terms of our four causation experts, they are looking at a wealth of scientific information, and Dr. Jewell is a tiny piece of it.

THE COURT: So it won't be of any great consequence if I keep some of his opinions out.

MS. BIERSTEIN: I think if you keep some of his opinions out, it would not be any reason for you to knock out any of the four causation experts.

Now, Your Honor, there are some other things -- and I don't think this is the time to do it -- that I wanted to say on the whole 10-milligram/80-milligram issue that don't relate specifically to Dr. Jewell. And I'm thinking maybe there is going to be another point in our back and forth.

THE COURT: I'll give you a chance to talk on that. I've got to say that that is an area which I don't really have an answer in my own mind right this moment. I'm trying to sort it out and what underlying evidence there is to

support it. I mean, is there a -- is there sufficient data to say that it doesn't matter or that it is statistically significant at all levels? I mean, those are the kind of questions I have in my mind. And I tell you the stuff is so voluminous, it's hard to sort through what you actually have. It's just in my own mind the SPARCL study is probably the strongest data I see in support of plaintiffs' position, and it's 80 milligrams. I mean, that's just -- you know, whether that tells us anything is another issue. But --

MS. BIERSTEIN: Your Honor, I think some of that is putting together questions that maybe should be separate. We have a question of is there causation? And we understand that in the question of is there causation do statins cause diabetes? Does Lipitor cause diabetes? That the randomized clinical trials are the best evidence. But we know -- I'm not at all being dismissive of the observational studies. I think they are very important. I just don't think they would necessarily stand alone.

When we ask ourselves --

THE COURT: Here is my point: The answer might be -- does Lipitor elevate, cause new onset diabetes in women? The answer might be yes if the dosage is X amount. That might be the answer. And it might be no if it's below, or unproven if it's below that amount. And then I've got to sort out if that's where the data is. What does that mean

for the case where the plaintiff doesn't have the evidence to prove? I just don't think just because it's 80 I should just assume dosage is irrelevant.

MS. BIERSTEIN: I'm not asking you to assume that based on that. And this is why I say I have more to say about it. I was going to marshal all of the evidence for 10-milligram, but I thought maybe in the context of Dr. Jewell it's not the place to do it because it's not really about Dr. Jewell. There is a lot of evidence below 80, but I think it is very possible, Your Honor, that the answer to the question, you know, may be a sort of depends on the woman; depends on the circumstance. Could this dose --

THE COURT: Maybe that's -- maybe that's the answer.

MS. BIERSTEIN: But I think, you know, again, TNT, IDEAL, the NDA, there are a number of trials that are below -- that are below 80 milligrams.

THE COURT: Well, TNT and IDEAL show a slight increase but not statistically significant.

MS. BIERSTEIN: Here is what is interesting about TNT: TNT is not showing a difference. TNT is comparing 10 to 80. And it's showing such a small difference that what it would tell you is that whatever effect Lipitor at 80 has, it's not much different from Lipitor at 10.

And that's what was so interesting -- and I do have to bring this back up about Dr. Waters' e-mail to

Mr. DeMicco -- and I really did not give Your Honor some crucial pieces of information about this when Dr. Waters wrote and said he thought there was -- that the study showed no difference between 10 and 80. Mr. DeMicco, who was at that time the medical director -- I guess it's Dr. DeMicco -- Dr. DeMicco was the medical director at Pfizer and he wrote back and said, I agree. So the problem is that the doctors, the scientists, are agreeing among themselves that one of the things --

THE COURT: Did you take their depositions?

MS. BIERSTEIN: Yeah, I think so.

MR. MARCUM: Dr. DeMicco; not Dr. Waters.

MS. BIERSTEIN: One of the things that TNT is showing us is that there is not a difference between 10 and 80. The lack of statistical significance there is the plus, not the minus. Because although it wasn't statistically significant in whether it was causing it, it was -- what was interesting -- the point is it wasn't comparing to placebo; it was comparing 10 to 80. So if you don't get a difference, what does that mean? It means the effect of 10 and the effect of 80 are too similar to tell the difference.

Now, I think that's a pretty important piece of evidence. And if you add that to this NDA trial, not this -- these numbers, the 26 percent of the people in two studies, one was a 10-milligram trial and the other was a

trial that began at 10 and then increased to 20 for people who didn't get an effect at 10. 26 percent of the people with low or normal glucose end up with elevated glucose at the end.

So when you asked me what's the evidence that this is happening below 80? I'm saying look at TNT. Look at these NDA trials. Not only the total summary, but in particular these two important ones because they are not about people with diabetes; they are about people who don't have diabetes or prediabetes and we are seeing the effect. We are seeing it even at the 10-milligram dose. And I think -- and Pfizer's medical director is agreeing that he's seeing the effect at a 10-milligram dose.

So I think those are important facts for Your Honor to consider in deciding whether there is enough here for us to go ahead on an opinion that's not qualified at 80. Because we are -- and then if you add what I referenced this morning, that we see it in less potent statins, so a less potent statin is not exactly the same as Lipitor at a lower dose. But if you are trying to understand, how does this effect work? Does it matter how big a hit of the statin you are getting? Well, to some extent it's going to matter.

The fact that you are going to see it in a lower dose statin confirms what we see in the NDA and what we see in the particular -- these two particular studies in the NDA,

the 26 percent, and confirms what we see in TNT.

So I think --

THE COURT: Thank you, ma'am. Let me -- anything further, Mr. Cheffo?

MR. CHEFFO: Just very brief. I can't comment on all these.

I mean, Your Honor, I think the question was, if there -- this comes down to the core issue if there is an absence of evidence, I wrote down or it's unproven, that doesn't pass *Daubert*.

THE COURT: Correct.

MR. CHEFFO: The other thing is I would just say this: We've heard, like, what amounts to be kind of just trust me testimony about e-mails and things. That's not going to get past *Daubert*. There is a lot of data in this case, and it's not going to be talking about what people said or Pfizer didn't say or did say because that's not true.

Second -- third, I would just refer Your Honor to, I think it was a statement that Dr. Wade didn't cover it. Paragraph 140 of his report specifically looked, I think, at the issue that Your Honor asked about. This idea that, you know -- which I find interesting -- that, you know, Well, you don't have to rely on Dr. Jewell because Pfizer keeps saying we admit it, we admit it, we admit it. Of course we don't.

Putting that aside, Dr. Jewell is the only one who

deals with this data and analyzes it and then gives it, I think as Your Honor knows.

And perhaps even more importantly, let's talk about something that -- again, another kind of Hemingway Ground Hog Day, let's maybe -- apparently the plaintiffs, if you say it enough it will become true -- but here is the problem: This data was looked at by a guy named Dr. Black, right? Dr. Black at the time was a medical monitor for Pfizer -- for Park Davis. He looked at it and found that there was no issues with respect to the data and glucose metabolism.

I think I put this up on a slide earlier with Dr. Singh. It's not like no one looked at this. The FDA specifically -- because I think you asked -- found in looking at all the data not just a piece, there is little evidence for an effect on Lipitor on glucose metabolism.

You've probably seen these things, the tractor trailer fills with information on all of the data that they had before them. That was the FDA's conclusion back in 1996. You've heard kind of this whole explanation about why he combined the 37 and 4 and --

THE COURT: I still can't figure it out.

MR. CHEFFO: I can't really, either. But I tell you what, what I think they keep pointing at is they say, Well, it was clinically meaningful. They need to figure that out. I have no idea why that would do it.

Let me cut to the chase here, because if you see deposition transcripts, it's the same thing again over and over, until they finally get to Dr. Black, who was the medical monitor. And Dr. Black tells us under oath -- no longer a Pfizer employee, he's off to something else, he's the guy who knows this data -- and he says, you know what? In order to get on this chart you just had to be over 125 and over baseline. That was it. That's it.

So all of these kind of --

THE COURT: So you had people already diabetic, already over 125?

MR. CHEFFO: Exactly.

THE COURT: It's just interesting to me no one has analyzed -- and it may be just the data percentage is just too small -- it's the 12 people get elevated who did not have previous glucoses above 125 took Lipitor and got glucoses above 125 in the Lipitor group, and one of the three got it in the placebo group. That's what we know, right?

MR. CHEFFO: That's right.

THE COURT: Those are the people who are supposed to be plaintiffs in this case.

MR. CHEFFO: If this was a causal connection, sure, right? But we all know that is not what this is looking at.

THE COURT: Because then we know that -- anyway, it's just to me an odd way to come at it. And every time the

inclusion of certain data is suspect, I'm being told it's Pfizer's fault. It's Pfizer's fault because -- but the one commonality I see regarding different definitions and different approaches and different methodologies, the one common thing is it produces an opinion supporting the plaintiffs' view, that's the one common feature of all these, it would seem to me, questionable methodologies.

MR. CHEFFO: On that we can agree, Your Honor. And I guess my final point is really this, is, you know -- and I'm certainly not going to reiterate it, but I just -- I'm still not really clear -- we've had a few hours now, and counsel keeps saying, We have four causation experts. I will just say it once and the last time, but I know that they can say they are causation experts. We agree on Singh to the extent he wants to deal with it. But I think you've asked the questions, you've kind of highlighted the fact that someone's opinion is that there is an increased risk is simply not a causation.

THE COURT: That's not enough.

MR. CHEFFO: So in our view, at best they have one person, Dr. Singh, who says, you know, looking at the 80-milligram SPARCL data, relying heavily on Dr. Jewell for FDA and any kind of gender efficacy -- I'm sorry, gender safety analysis -- it's Dr. Jewell.

THE COURT: If he doesn't have Dr. Jewell to rely

on, other than SPARCL, assuming he just has the SPARCL opinion from Dr. Jewell, what effect does it have on Dr. Singh?

MR. CHEFFO: Well, Your Honor, I think -- so Dr. Singh, we had those buckets, right? Dr. Singh relies on SPARCL, you know, and he relies on that, I think himself in that information. He relies on the FDA data but only as it comes through Dr. Jewell. He relies on observational studies. And his own meta-analysis, the 1.09 small risk. And he does do the Bradford Hill.

I think in fairness, in purposes of Dr. Jewell, you couldn't have Dr. Singh relying on anything on this NDA analysis. He would then basically be in a situation of saying, I've looked at SPARCL, one study, I didn't look at ASCOT, and, you know, what conclusions can you draw from that? At best, as we said -- which we don't agree with -- at best, all those studies talk about are 80 milligrams.

THE COURT: That's cross-examination. That -- to me that's cross-examination.

MR. CHEFFO: Understood. But the dose issue I think is something that is not cross-examination.

THE COURT: Okay.

MR. CHEFFO: Thank you, Your Honor.

THE COURT: Thank you. Let's take a break here. I'm going to kill Ms. Diaz if I don't give her a break here.

And let's come back in 15 minutes.

(Thereupon, there was a brief recess.)

THE COURT: Okay. Let's go to Dr. Quon, if we could.

Yes, sir? Is that okay?

MR. CHEFFO: It is. I was going to do Roberts. It's really quick.

THE COURT: If you are ready to do Roberts, we can do Roberts. If you've got the computer set up and everything, let's do it.

MR. CHEFFO: Thank you, Your Honor. Because I really do think, at least from my end, this will be short.

I have two slides. This is Dr. Roberts' opinions. And I think plaintiffs probably -- you know, we do challenge all of them; not necessarily all of this motion here. It's her second opinion, I guess that we are focusing on, increases the risk of diabetes in women. And --

THE COURT: She relies on what for that?

MR. CHEFFO: She relies on Dr. Jewell's analysis.

And I guess this comes back to this point of this increased risk, right? So it's, in our view, not even a causation opinion. And then I guess the only part --

THE COURT: Well, it increases the risk. Does she say -- does she reach the opinion that it is a proximate cause or a cause --

MR. CHEFFO: No.

THE COURT: -- of -- well, that's a problem.

MR. CHEFFO: I agree. And in fact, there is not a new onset here, Your Honor. When you look at her deposition, which is actually my second slide.

So, you know, the first box was created about of -- we have been here for a number of hours, so I'm not going to address those issues -- but the point is she's not a person who has experience with diabetes and dose and knowledge of the ADA criteria. It's not just an absence. She kind of admitted that.

And oddly, she takes a number of very, very medically and scientifically contrary views. I don't think anybody on either side of the V, other than Dr. Roberts, would tell Your Honor or a jury that observational studies are better evidence than clinical trials.

In fact, I think --

THE COURT: She's a true believer.

MR. CHEFFO: She is a true believer. That I will give it to her.

This is the point -- I will sit down after I read her testimony -- she was asked, you know:

"Question. Is Lipitor the cause of diabetes?

Answer. I'm not sure what you mean by that.

Question. So you don't know whether Lipitor causes

diabetes?

Answer. I think Lipitor increases the risk of developing diabetes.

Question. But you've said there is a difference in increasing the risk and being a cause, right? The two are not synonymous."

THE COURT: They are not synonymous.

MR. CHEFFO: That's exactly the point.

THE COURT: I mean, increasing the risk increases the chance. The chance.

MR. CHEFFO: Exactly.

THE COURT: Increased chance is not proximate cause. It is not a reasonable degree of medical certainty, etcetera. It is just not. More likely than not. She's got to do better than that.

MR. CHEFFO: If she comes in looking like that, wearing her stethoscope -- we hope she won't because --

THE COURT: I won't be disappointed. I would let her do it.

MR. CHEFFO: The point really, all seriously, Your Honor -- I think you made this point earlier -- this is not a causation issue; this is a, Trust me, there is an increased risk. And it is not something that passes *Daubert* and should pass *Daubert* in any regard.

THE COURT: She is not a statistician, doesn't

pretend to be. Relies on Dr. Jewell's --

MR. CHEFFO: That's my understanding, Your Honor.

THE COURT: So what happens if Dr. Jewell is only able to talk about SPARCL?

MR. CHEFFO: Well, I think frankly, I would say no matter who she relies on or what she is relying on, at least as to Dr. Roberts -- and I've tried to be relatively narrow -- but she's basically telling us she doesn't even --

THE COURT: She doesn't get there even with all this testimony.

MR. CHEFFO: That's right.

So you can leave it all in or all out. But this is not a doctor who is going -- who should get up -- I mean, she can't even tell us in a deposition what diabetes -- what causation means. And then says, I'm only offering an opinion on the increased risk.

And again, then after having a lot of time and effort, the plaintiffs say, not that Dr. Roberts is going to come in and offer a causation opinion -- this is what they tell us in their brief at page 15 -- that it's an increased risk. It's just not a causation opinion. And that's what *Daubert* is for. And she shouldn't be able to get up and say it increases the risk. A lot of things increase the risk. That's why juries would be confused. That's why we have *Daubert*.

THE COURT: Okay. Ms. Bierstein, go at it.

MS. BIERSTEIN: I'm going to go at it, Your Honor. I'm not sure where to start.

I'm going to start with increases the risk and proximate cause, Your Honor. Proximate cause is a case-specific analysis. The point of a general causation analysis is do we have a reason for a case-specific doctor to rule in diabetes as a potential cause in order for them to then go through their differential diagnosis to figure out if they can rule out the other things?

Dr. Roberts, none of these experts, could ever give you proximate cause because proximate cause is case specific. When Dr. Roberts tells you that it increases the risk, she's telling you that it is among the factors that a doctor doing a differential diagnosis should be ruling in and that it's one of the things that can be a substantial contributing factor --

THE COURT: But can be is not -- can be, may increase the risk, if it -- if she has a 1 percent chance before and a 3 percent chance afterwards, that increases the risk, but it doesn't tell us very much more than it increases the risk.

MS. BIERSTEIN: Well, Your Honor, that's where -- I mean, there is an issue about the magnitude, and we'll get to that.

But I think the point is she's not saying it -- that it -- maybe it increases the risk; she's saying it does increase the risk. And that means that it is one of the things that can be a substantial factor.

Now, you still need a case-specific expert to tell you whether in any particular case having ruled in Lipitor on the basis of an opinion like that you can now rule out the other factors as being sufficient alone in combination to have done it without the Lipitor. That is a case -- that has to be to a reasonable degree of medical certainty.

But her reasonable degree of medical certainty is simply that Lipitor, when she says increases the risk, what she means is if you -- in the people who don't take Lipitor from an epidemiological point of view, you are going to see X cases of diabetes. And in the people who do take it, you are going to see some larger number.

THE COURT: X plus something.

MS. BIERSTEIN: And then you are going to make the inference, which I'm going to show you she makes, that in fact that distinction is causal, the reason you saw more is causal.

And her opinion -- and I will go through this, but I need to touch on something else first -- her opinion is full of all the factors we would look at. She also -- she talks about statin-induced diabetes. I think she's quite clear

that she's giving an opinion that -- that --

THE COURT: The terminology doesn't establish causation.

MS. BIERSTEIN: I understand that.

But there is quite a difference between whether it's established, which I'm going to get to, or whether she purports to do it. And I'm saying she -- when she's talking about increased risk, she's saying that increased risk was caused by the Lipitor. She's not simply talking about an association. So I think -- you know, I want to be clear, I think she is offering that opinion.

THE COURT: Does she rely on Dr. Jewell?

MS. BIERSTEIN: That's the interesting thing, because Mr. Cheffo says yes, and I'm going to tell you no, or at least only in one very small place.

And here is what I want to do. I want to look at her report. Her discussion of statin-induced diabetes begins on page 8. She starts with an overview about some articles that have accepted this conclusion, this Goldstein article and the Mascitelli article. She goes through the JUPITER trial. She talks about the WOSCOPS trial. She talks about the WHI study. She talks about the PROVE-IT Study. She talks about the CARDS analysis. She talks about a study in the U.K., a 2014 published paper. She talks about Navarese. She talks about the Chen study. She talks

about a Canadian study. She talks about the Price Study, which I believe that Dr. Waters was one of the -- one of the collaborators on the Price Study. She talks about the Pie Study. She talks about this Aiman Study from the *Journal of Pharmacology and Pharmacotherapeutics*.

So in her basic discussion of statin-induced diabetes generally -- this is before she gets to some more specific issues about Lipitor in women -- she doesn't even mention Dr. Jewell's name. Her analysis of the relationship, the causal connection between statins and diabetes is entirely independent of Dr. Jewell.

THE COURT: You are telling me she's basing it on these various studies?

MS. BIERSTEIN: She's basing it on a review of scientific literature.

THE COURT: Is there some criticism of her that she doesn't consider the full literature; that she cherry picks her studies?

MS. BIERSTEIN: I don't know of any criticism of her in that regard. And I have to say, given the broad range of studies that she did, if there is some particular one that is not in there, maybe we should talk about that.

The Lipitor specific ones she talks about separately. She talks about a paper that Goodarzi and colleagues published, which looked at a group of studies,

including ASCOT and SPARCL. She does talk about Dr. Jewell's SPARCL analysis. That's why I said she does except in this one particular place. She looks at data from a Framingham Study analyzed by a Dr. William Kannel. She looks at another study published in *Diabetes Care* looking at gender differences in statins and diabetes. She goes -- so there is -- she keeps going through a number of these studies. And as I say, the one part --

THE COURT: Let me ask you this: Isn't she one of the experts who says, I think it increases the risk and then she -- but she does not know how you would ever establish specific causation?

MS. BIERSTEIN: Um, I don't recall. It is possible that she does, Your Honor, but that wouldn't --

THE COURT: I mean, I thought all of your general causation experts when asked basically said I don't have a clue how you would get to specific causation?

MS. BIERSTEIN: Well, sure, Your Honor, because epidemiologists don't deal with --

THE COURT: She's not an epidemiologist; she's a cardiologist.

MS. BIERSTEIN: She's a cardiologist, which would mean on the issue of why you would know somebody got diabetes, I'm not surprised she couldn't tell how.

THE COURT: This is an issue we are going to be

really struggling with the next time we are all together, the next round of this.

MS. BIERSTEIN: I think primary care doctors are the front line in diagnosing diabetes, but cardiologists like Dr. Roberts are not. So it doesn't surprise me that a specialist like -- she's looking at a lot of studies and she can read them. She's coming at this from the other side.

THE COURT: I thought Dr. Quon, who was a diabetes expert, also said he didn't know how you get there.

MS. BIERSTEIN: It may be he doesn't know how. And I think the focus is he's not a case-specific expert. And the question is he may not know how to do it --

THE COURT: This is always a problem in cases. I had it as a litigator. You would sit there, you would want to use an expert for one purpose and then they just kill you on some other purpose, okay? I think it's pretty damaging for your general causation experts all to say, Beats me how you would ever prove it in any particular case.

MS. BIERSTEIN: But, Your Honor, they were asked it in a vacuum. They need a patient. I don't think any of them were saying, If I had full medical records, this, this and this, I still couldn't give you an opinion. When you are asked in a vacuum, Well, how would you do it? And this is a similar problem with the case-specific people when asked about hypotheticals. You need a patient to do it. So when

a general causation expert said, Well, how would you go about this --

THE COURT: You are telling me you didn't ask any of your general causation experts to look at specific causation?

MS. BIERSTEIN: That's correct, Your Honor. That's my understanding, that we did not.

THE COURT: They get on the stand and say, Beats me how you would ever prove it. That's not helpful for y'all.

MS. BIERSTEIN: As I said, I think they were asked it in a vacuum. If you were to ask them -- if you gave them a file and said, what would you need to do? I mean, you know, differential diagnosis is what you do. And that's not certainly something --

THE COURT: We'll get into that. The differential diagnosis is just what's possible. You've then got to have a meaningful way to rule out other causes, right?

MS. BIERSTEIN: You do need a meaningful --

THE COURT: Because otherwise it's just a possibility.

MS. BIERSTEIN: I agree with you. And I think you will see that when we go to the case specifics. But I think Dr. Roberts' opinion is that we should be ruling it in. And whether or not she thinks it's possible to rule other things out, you know, they want to bring that out --

THE COURT: She said it increases the risk -- in a

large pool it increases the risk and she's relying on these various studies to demonstrate. That is what you are telling me?

MS. BIERSTEIN: That's what I'm telling you. She's relying on an enormous body of scientific literature.

And what I did with Dr. Gale before, I'm going to do again -- well, in fact, you know, she goes one better in her discussion. I was giving you her opinions from the summary of opinions. This is from page -- I'm going to give you the page in a minute. First I'm going to read you the quotation: "Taken in sum" --

THE COURT: This is her report?

MS. BIERSTEIN: This is her report.

THE COURT: What page?

MS. BIERSTEIN: I've got to -- I can't scroll down to it, can I? I've got to look at the page and then I've got to find the quotation again. It's page 9.

THE COURT: Thank you. Keep going. I'm sorry. I interrupted you.

MS. BIERSTEIN: On page 9 she says: "Taken in sum, multiple lines of evidence from both RCT" -- that is randomized clinical trials -- "and epidemiological observational studies support the fact that atorvastatin can be a substantial factor in causing" --

THE COURT: Can be.

MS. BIERSTEIN: "Can be a substantial factor in causing new onset diabetes."

THE COURT: Can be is not more likely than not. Can be is possible.

MS. BIERSTEIN: No. I think, Your Honor, the point is can be means that your case-specific doctor can put it on the ruling in and then they have to do the ruling out. But if it can't ever --

THE COURT: I just can't imagine these people wouldn't come in and be prepared to say, I can say with a reasonable degree of medical certainty that Lipitor causes diabetes.

MS. BIERSTEIN: I think she -- I think that is what she is saying.

THE COURT: She said increased risk.

MS. BIERSTEIN: No, there -- she said substantial factor in causing.

THE COURT: May. May.

MS. BIERSTEIN: Not may, can. I think it's different.

THE COURT: Can. Okay.

MS. BIERSTEIN: Can is physically capable of. Let's not confuse may and can. Can means is actually capable of. So Lipitor is actually physically capable, substituting the definition of can, of substantially --

THE COURT: You read can to read more likely than not?

MS. BIERSTEIN: Um, I believe that a causation, a generic causation opinion is not a more likely than not. A general causation opinion is an opinion that is a substance is capable of causing the injury. The more likely than not is whether it caused this plaintiffs' injury. But before we can talk about whether it's more likely than not that it caused --

THE COURT: A causation expert has to say anything --

MS. BIERSTEIN: It can cause it.

THE COURT: Possible. Possible is enough.

MS. BIERSTEIN: Because -- because for example, Your Honor, there are some things -- if I wanted to say I drank a glass of water and I -- and I developed diabetes, I don't think you could find anyone to say you can put that on your rule-in list for differential diagnosis because water is not capable of producing that effect. The question is: Is Lipitor capable of producing this effect? That is what Dr. Roberts is opining on. And she's telling you, Yes, in my opinion, Lipitor is capable of substantially contributing to -- as a causal factor, a substantial factor in causing diabetes. It can do that.

THE COURT: It seems to me we are really watering

down proximate cause here.

MS. BIERSTEIN: I don't think we are watering it down, Your Honor. We are putting it where it belongs in the case-specific expert where it is as strong as it ever was.

Reasonable degree of medical certainty, although I will tell you that's not the standard in Colorado --

THE COURT: What is the standard in Colorado?

MS. BIERSTEIN: I wrote that brief, and it's a month ago and I'm trying to remember. It's a little different than a reasonable degree of medical certainty.

THE COURT: Anybody know that?

MS. BIERSTEIN: It's funny in Colorado.

THE COURT: I'm going to be the world's expert in every state.

MS. BIERSTEIN: We are going to have by preponderance of the evidence, we are going to have proximate cause, we are going to have all of that, but we are going to have it in a case-specific context. What the general causation experts are doing is different. They are simply telling you, is it even possible that this could happen? Because if it's not, then when Dr. Murphy and Dr. Handshoe do their differential diagnoses, they couldn't even put it on the list. Dr. Roberts is telling you, yeah, it belongs on that list because it can do it.

I did want to take a minute, Your Honor, if we are

done with that, just to give you the pages where she does the Hill factors. Because again, I think she, in going from association to the fact that it's causal, I think she did consider the Hill factors. So she does the strength of the association. You will see that for every study that she talked about on pages 8 to 17 -- the same with consistency and replication, you will see that in 8 to 17. Specificity. That's the one where we know that in this case it's not as specific as some other things. That is, Lipitor diabetes is not a single-cause disease. And she recognizes the role of alternative factors. She talks about that on page 10. So that's a factor that weighs the other way, but she takes that into account.

Temporality. We have a disagreement with Pfizer in terms of consideration of new onset. And I know Your Honor understands this that if that's the point at which Lipitor made the difference, it happens in the right time. She talks about biological gradient expressly at page 12.

She discusses the plausibility factor at pages 17 to 19.

I think on the consistency with other knowledge, this is kind of throughout the report, she places her opinions in the context of knowledge of other statins, knowledge about other diabetes risk factors, knowledge about how statins work to lower cholesterol, which is really her

field, and the effect of statins on blood glucose.

I think I mentioned before this experiment item doesn't really apply here because that's when you can sort of do a D challenge. You take it away, you see if it stops. We don't have that here.

And on the analogy that Dr. Hill thought might sometimes be useful, I think she's analogizing between other statins and diabetes. So I think Dr. Roberts is incorporating the Hill factors into her analysis. She's drawing on the wealth of scientific literature. She's bringing her expertise as a doctor and she's giving a causation opinion limited, as I said, to general causation, to the fact that Lipitor is capable of causing diabetes.

She's not purporting to tell you anything about its affect on Wilma Daniels or its affect on Juanita Hempstead, she's telling you it can do this. So when those doctors come in to do the differential, when they put it on the list to rule in, there is a reason for it because it does -- it is capable of causing that effect.

THE COURT: So your view is what -- she shows it's capable, then your entire case hangs on the specific causation expert?

MS. BIERSTEIN: I think it always does, Your Honor. A particular case depends on the case-specific expert.

THE COURT: We have one expert testifying in

Daniels.

MS. BIERSTEIN: That's right. One in *Daniels* and two in *Hempstead*. And I think that's -- in order for either of those plaintiffs to prove that their diabetes was caused by Lipitor, those are the experts you are going to look to is are the case specifics.

THE COURT: Very good. Thank you.

Mr. Cheffo?

MR. CHEFFO: Thirty seconds, Your Honor. A few points.

Possibility, not enough under *Daubert* by any stretch. Does Dr. Roberts rely on Dr. Jewell? Page 13 of her report, of course she does.

And specifically with respect to the gender issue -- in fact, I think that's primarily the only significant reliance that Dr. Roberts places on her opinions in connection with Lipitor, relying specifically on Dr. Jewell's analysis there.

Your Honor asked about Colorado law. It's a but/for analysis there. So I don't think some of --

THE COURT: But/for is pretty similar to most probable and -- I mean --

MR. CHEFFO: Yeah.

THE COURT: -- more likely than not. Those are all fairly close to each other.

MR. CHEFFO: It's a pretty high standard, Your Honor.

We come back to -- what we keep hearing, right, is first it's, you know, it's likely and it's more likely or increase risks. But the bottom line is she said, Well, it's the job of these kind of people -- who in our view are not even talking about causation -- say it can do this, right? So we are back to it can do this. What caused diabetes or any dose, any length of time, any woman, anywhere.

So that's what this is all about is Dr. Roberts would say, Hey, it can do this. And in every individual trial we are going to have to run through all this massive amounts of work. It's not the way general causation works.

THE COURT: Remind me on what these general causation experts -- none of them were -- were prepared to do a specific causation opinion?

MR. CHEFFO: No. I mean, in fact, it was quite telling, people who -- now, in fairness, right? So there were two phases of this. They offered general causation opinions. But certainly, we've worked well together, as Your Honor knows, if someone offered a specific causation in this or other litigations, you would say, We are going to do the deposition on general causation, a few hours on specific causation; things like that.

THE COURT: There is nothing -- I mean, in most

cases if you were trying to prove causation in a medical situation, your ideal situation is to have one person do it all. I mean, you know, to go all the way, both general and specific. Not required. Nothing wrong with doing them separately, but the fact that four experts opine on general causation and each also says, I don't have a clue how you get to specific causation, that -- you know, that just got my attention.

MR. CHEFFO: And there is a reason for that, Your Honor. You know, it's -- I think -- again, I don't say this without platitude, they are good lawyers and they know that would be better. More is not better when it comes to experts and testimony.

THE COURT: You never know when you start losing control.

MR. CHEFFO: You want to find that expert who is great on general causation. And not only that, I'm going to be a specific causation, man or woman.

But the problem comes back to what they have kind of created. They have this massive kind of unregulated cases. And if they were to ask anyone to put any of these criteria, they would have to admit, Well, that may be John or Mary's case or this case. So what they have done is specifically avoid the issue.

And even now they are coming and saying, We are

going to continue to play this game and kick the can down the road and hope we can get to specific trials. That's exactly not what an MDL, not what *Daubert* is supposed to do, because they don't want to answer any of those questions.

Thank you, Your Honor.

MS. BIERSTEIN: Your Honor, I understand that you have some concern about why we didn't ask the general causation experts to do specific causation. I would like to shed a little bit of light on that.

Your Honor, for our general causation experts, we went and hired research scientists who were already doing work on statins and diabetes. We didn't want to get made for-litigation opinions. What we did was we went and got the research scientists who were already in the lab: Dr. Quon, Dr. Singh, Dr. Roberts had already done research on these issues. They were practicing scientists and we knew --

THE COURT: Dr. Quon, is he in a clinical practice or is he only a researcher?

MS. BIERSTEIN: I think he's just a researcher. He has -- his field was endocrinology, but he's just a researcher. Dr. Roberts does both. Dr. Singh is just a researcher.

And I think what's important, Your Honor, is that by getting experts who could bring to this analysis the same

rigor they bring to their own scientific work, because they were already doing the scientific work, we were trying to get the best people who were in the lab.

But I think Your Honor can understand those are not going to be the people you are going to ask to do a case-specific analysis because it's not what they do.

As I said, Dr. Quon is not a clinician. Dr. Singh is not a clinician. Dr. Roberts is neither primary care, which would put her on the front line with the sort of people, nor an endocrinologist.

THE COURT: I don't doubt you have every right to split this, but if someone has enough expertise to offer an opinion that a drug is capable of causing diabetes and who, like Dr. Quon, is boarded in internal medicine, is a specialist in endocrinology, he would normally have the ability to go to the next step and apply it to the facts of a particular matter. The fact that you didn't do it -- you have every right to use different experts.

But, you know, on a -- before I was on the bench I handled a lot of medical-related litigation, and I hired experts, just like everybody in this courtroom has, and I just sort of know, you know, it's the only -- there is an old Fourth Circuit case that I often quote which says -- if you excuse the gender reference -- You seek to persuade us -- persuade us as judges what we know to be untrue as men, okay?

And you just -- just doesn't ring right to me why these people, who seem to have very strong opinions about general causation, are helpless to address specific causation. It's all one basket to me. But you have every right not to do it. It's just when four people say, almost identically, I wouldn't have a clue how to do it, then I'm going to look with -- obviously, I'm going to scrutinize the opinion of your specific causation person. I really haven't gotten into that. It certainly raised a question in my mind hearing that.

MS. BIERSTEIN: Your Honor, I expect you to scrutinize them.

And Mr. Hahn wants to add a comment. But before he does, I want to say in an individual case there are really good reasons maybe to use the same expert. But in an MDL where general causation, is this capable of, is a general question, the specifics -- you know, a lot of times you want an expert who is better tailored to a particular plaintiff, a particular venue. It's a different sort of decision.

THE COURT: I get that.

MS. BIERSTEIN: So I just don't like the implication that we were pulling a fast one.

THE COURT: I don't think you are. I think you are dealing with the --

MS. BIERSTEIN: The experts weren't prepared on it

because we never asked them to do it. And we didn't ask them to do it, as I said, because we picked the top notch research scientists so that these would be the bulletproof people whose opinions were never litigation driven because these were opinions formed in the lab. So I think that explains it.

But I know Mr. Hahn is going to say something I didn't.

THE COURT: Yes, sir. Mr. Hahn?

MR. HAHN: The other reason, which is very important, is that we are in an MDL. And the Plaintiffs Steering Committee in the MDL is charged with producing the playbook for a general causation trial, and that's it. We are not charged with anything but that unless there is a bellwether trial. And so we, as MDL lawyers -- which is all any of us do -- is that we put it in different boxes. And we've got a package with general causation experts that if this case does not resolve, will be sent out all over the country, and those individual lawyers can rely on that and then get their specific causation expert separately. And the general causation experts would have their testimony done via deposition and via video and not necessarily live. And that's the process.

And so we couldn't cross-pollinate because then Dr. Roberts would not be available to go all over the country.

So that's the biggest reason why. And so they can't answer --

THE COURT: I can understand that part. It's just when they are asked, How would you do it? And they say, I can't imagine a methodology we can use --

MR. HAHN: I don't think that's -- that's 100 percent accurate. What they are saying is, I can't answer that question because I don't have a patient in front of me, so I can't do the analysis.

THE COURT: Everybody will have their own. But in the end if you have an expert that can meet the standard it won't matter.

MR. HAHN: Yes, sir.

THE COURT: And I understand the --

MR. HAHN: There is a very specific reason and we are very methodical in doing it the way we did --

THE COURT: I hear you.

MR. HAHN: -- for that reason.

Thank you, Judge.

MR. CHEFFO: Just to correct a few things.

Again, it doesn't make sense to me -- but it doesn't really matter, it matters if it makes sense to you, Your Honor -- but if they are going to come and testify, the idea that you have these world class, top notch people, you wouldn't ask them about a specific case if they are going to

testify anyway.

But more importantly, you heard that these are world class, top notch researchers. They are not the right people. I think we heard only one of them. But in fact, Dr. Singh is a practicing internist. He's certified. We heard he's kind of a bench scientist apparently. And in his own clinical practice he doesn't distinguish between men and women in prescribing statins. Dr. Gale has been a practicing diabetologist for 40 years and Dr. Roberts is a practicing physician.

So these are not just people who would not otherwise, if asked, kind of say -- and the idea that there is no one before you. So you can't talk about general causation, you can't make a causation opinion or even a specific -- you know, if there is a methodology, you don't --

THE COURT: I understood y'all are asking them. What is the method by which you would do it? Because obviously you didn't have the case specific in front of them. And they said, I don't know how you do it. I can't figure out how you would do it.

MR. CHEFFO: Mrs. Daniels, in the records you have never seen, tell me what happened. We didn't hide the ball. You are now saying that Lipitor can cause diabetes.

THE COURT: You would think they would say, Well, this risk factor, you ruled it out by a certain method.

You've got this risk factor, you rule it out by this method. And the -- and the differential would start -- it would start rising to the top. And then at that point you would be able to offer an opinion that it was with a reasonable degree of certainty it was a substantial cause of -- that would be the process.

MR. CHEFFO: That's right.

THE COURT: And you don't need a case-specific for that. And, you know, these so-called world class experts, not one of them has done a peer-reviewed article on this subject, which is just one of those *Daubert* factors I've got to consider.

MR. CHEFFO: Thank you, Your Honor.

Should we now turn to Dr. Quon?

THE COURT: Let's do Dr. Quon.

MR. CHEFFO: I think at least on my side, mercifully, we are going to be short.

So Dr. Quon. This is what -- the plaintiffs tell us he's going to testify a little bit different than the increased risk. Dr. Quon does not specifically provide a discrete causation opinion, although he does opine on the topic.

THE COURT: What does that mean?

MR. CHEFFO: Gosh, I don't know, Your Honor. I wish I did. I kind of -- I was assuming that this meant

that we weren't going to have to talk about him today because he's not offering a causation opinion. But, I mean, look, here is what I think the point of Dr. Quon is, trying to put the best, you know -- I'm not going to play a plaintiffs' lawyer.

THE COURT: There is some background information for which he could be helpful, I think, for the jury.

MR. CHEFFO: He's a mechanism person, I think, right? And the point is he has a very specific, narrow, you know, piece of information on, you know, mechanisms or something. But that's not, again, a causation opinion.

THE COURT: He helps -- doesn't he sort of help with biological plausibility?

MR. CHEFFO: Well, I think in -- kind of in theory he does. I don't think he actually does because, you know, in order to deal with it, he basically said this is the problems with his methodology. Even to the extent there was a causation analysis, he didn't make, you know, any kind of efforts to look at the 10-milligram dose.

We have the same issues on gender that we've talked about throughout the day here.

THE COURT: Does he offer opinions on gender?

MR. CHEFFO: He basically relies on Dr. Jewell for the gender analysis.

And he -- so -- you know, in the beginning of the

day, I kind of highlighted for you this acceleration theory, and we saw it in the briefs. And then I showed you -- pulled out some statements or some allegations from the Complaint, and there is nothing about acceleration. So I'm just going to spend a minute or two talking about that.

And then he does purport to offer an opinion on mechanism. And we think that that is kind of unsound, particularly in light of what he's said outside the courtroom.

Let's just talk for a minute about acceleration. So even if there was a theory, right? We can -- you know, we've talked, I think, through that, but it can't be just the plaintiffs' counsel getting up and saying, well, it could be.

First of all, as I've said, you've now seen all of the causation experts' opinions about what they are going to offer. They don't say a word about acceleration, exacerbation. But we wanted to be fair and we said, Well, you know, can we get up here and say, well, the plaintiffs have never said anything about acceleration, not in their Complaint and not in their experts.

So we looked -- and if you look there is two pages in a 50-page report, and it's titled "acceleration". I will tell you if you read it -- if you haven't already -- it actually -- to me, my fair takeaway was it was like an exacerbation. It was either it caused diabetes or it was a

contributing factor, whatever they said, or once you had diabetes. So it wasn't an acceleration; it was more like an exacerbation. But it's only two pages.

THE COURT: But it might -- if you exacerbated someone who was not diabetic into being a diabetic, then you could have both acceleration and exacerbation.

MR. CHEFFO: It depends. But I think the studies that they've talked about talk about once you have -- once you have diabetes --

THE COURT: I understand. But I'm saying, I don't think they are mutually incompatible. The question is: Does he have a scientific basis to make that opinion?

The second quote, though, which I had noted was it appears that the rate of conversion to diabetes is higher, appears is not enough. I mean, that is not -- that is not a sufficient standard.

MR. CHEFFO: Exactly. And I think if you read that two pages, Your Honor, it's kind of --

THE COURT: What pages of the report are you talking about?

MR. CHEFFO: It is on pages 14 and -- well, I'm sorry. It's -- his report is 24, and it's at pages 14 and 15 of their opposition brief. So, you know, we are just trying to, you know, be -- I think present it in kind of the fairest way we can.

THE COURT: Then he says "additional analyses are needed".

MR. CHEFFO: This is from his deposition, right? We say -- okay. We asked him how much Lipitor accelerates the diagnosis of diabetes depends on a population. It hasn't been studied carefully. This is really, at best, a hypothesis. The exact math acceleration hasn't been studied. It goes back to these points.

They want him to say, Judge, just pass him on. Anybody can have acceleration or exacerbation. But he's telling us no one knows. No one has looked at it. He certainly hasn't. It's not -- he is not able to estimate the average time to onset for patients taking any particular dose of Lipitor compared to patients taking no medication or a different medication. He basically says, Yeah, you could study it, but I didn't.

So that is, at best, a hypothesis. That really can't get to a jury about getting up and saying, Mrs. Smith or Mrs. Jones, Lipitor is accelerated or exacerbated. That's the sum and substance of their expert testimony in hundreds and hundreds of pages.

Mechanism. The last point, Your Honor. He claims that the Lipitor caused insulin resistance. But he has published in the literature that it's not clear why Lipitor has beneficial metabolic actions in some studies but not in

others.

And I think there is testimony all throughout that he doesn't understand the mechanism of action. Because as Your Honor knows, we've talked about Bradford Hill, it's a factor. It's not the only factor. Temporality is one of the crucial ones. But certainly, when you have this very thin amount of evidence generally, and you are starting to look at these other factors, one of them being biological plausibility, and when he's publishing in the literature, he says, We really don't understand that; and in fact, it's mixed, that certainly should be a factor Your Honor takes into account.

Unless you have specific questions, I'm done.

THE COURT: No.

MS. BIERSTEIN: I'm going to try to be brief, as well, Your Honor.

Mr. Cheffo asked what it means to say he doesn't give a discrete causation opinion. But he does opine on that subject. And what it means is that Dr. Quon's report doesn't have a section that says, These are my opinions. Sometimes it's easier if they do. Dr. Quon wrote his report. He did it differently. He didn't --

THE COURT: Does he have a causation opinion?

MS. BIERSTEIN: He does, Your Honor. If you look on page 16 of his report, you will see the statement:

"Scientific evidence demonstrating that pravastatin therapy is a substantial contributing factor for new onset diabetes." That's the legal standard for cause. "A substantial contributing factor in new onset of diabetes is obtained from NDA trials, large randomized controlled studies and observational studies, as well as small physiological studies to promote insulin resistance and glucose intolerance." And we know those are the two factors you need to have to have diabetes: Insulin resistance plus glucose intolerance.

And then his report then goes on in great detail to review the literature that he used when he says scientific evidence demonstrating it is a substantial contributing factor.

Mr. Cheffo raises a few points. I've got to tell you, they all sound like cross-examination to me. Dr. Quon is a research scientist and he -- he does his own research on topics related to this. This is his area of expertise. But he didn't limit himself to his own work. He reviewed a large body of the evidence in reaching his conclusion. Dr. Quon is also one of the experts who did at his deposition, although not in his report, speak about the 10-milligram dose versus the 80-milligram dose.

THE COURT: What's he say about that?

MS. BIERSTEIN: Well, I've got the pages here, Your Honor. He -- let me make sure I'm getting kind of the

beginning of this -- he was asked:

"Question. Dr. Quon, do you believe that all approved therapeutic doses of Lipitor cause diabetes?

Answer. I believe that they increase the risk of diabetes, yes. But like I said, there is a dose dependency. So at 10 milligrams of Lipitor you know the relative risk is going to be less than at 80 milligrams. And because it's less, it may be harder to detect" -- which is again one of the things I thought was sort of misleading and goes on about that. He said -- "We have a paper showing a dose-dependent effect, and in some of the NDA data there is dose-dependent effects. You can see it at the 10-milligram dose."

That's not the end of it. They questioned him a lot more closely and asked him a lot of other questions on it. He refers to a particular quicky study and then he talks about this one where the placebo actually went the other way. He said if you take the differential between the placebo and the 10 milligrams, you get a larger change.

He was asked about any Lipitor clinical trial that showed the statistically significant increased risk in patients taking less than 80 milligrams. He said he thought the NDA involved patients --

THE COURT: In his NDA work is he relying on Dr. Jewell?

MS. BIERSTEIN: Well, you know, Your Honor, I'm not

sure about that because the only reference in his report on the NDA is the 3:1 and that didn't come from Dr. Jewell.

As I said, we saw the 3:1 on that chart. So I'm not -- I'm not sure -- he says Dr. Jewell, but he doesn't use any of Dr. Jewell's analyses. He only uses the 3:1.

But if you look at his discussion, he just talks about the data showing the 10 milligrams had an increase -- and they did ask him specifically about the fact that it was not an analysis of new onset diabetes; that it was a glucose elevation.

And he answered that question and he talks about the fact that when you are seeing this glucose elevation, he believes that what you are seeing is an effect of the drug on elevating glucose. And he was asked, Isn't that speculation on your part? And he said it's an informed opinion. Because he looked at a study and he saw, yes, it's not diabetes, yes it's 10 milligrams, yes, it's elevating glucose, and he drew -- he made an informed --

THE COURT: Which study did he rely on for that?

MS. BIERSTEIN: This is the NDA trials. These are the NDA trials.

THE COURT: He's not relying on Dr. Jewell's analysis?

MS. BIERSTEIN: I'm not sure. In his deposition he doesn't say that he is, and so I don't know.

But he -- he does talk about that we have data that 10 milligrams is sufficient to cause what we can reasonably infer. He says there is a dose-dependent effect. He sees a continuum. There is a linear -- a relationship that you are seeing it getting greater and greater at 80. I just would commend that the pages in his deposition --

THE COURT: What are those pages? Thank you.

MS. BIERSTEIN: You asked me that at the beginning and I forgot to give it to you. I started on page 53, then I jumped to page 200. And then the longest discussion is from 312 to 319 where they kind of drove down a little more on that opinion. So he does talk about that.

I don't know if Your Honor wants me to go through, you know, like Dr. Roberts, like Dr. Gale, I think Dr. Quon also considers all of the Hill factors. I can give you the page numbers, or not if --

THE COURT: If you will give me the page, that would be great.

MS. BIERSTEIN: Okay. And then I've got one more point to make about Dr. Quon after that.

Okay. So for Dr. Quon, the strength of the association, again, you know, each study -- and again, remember strength was the first and most important criteria that Dr. Hill announced. And for every study that Dr. Quon considers, he immediately considered and weighed the strength

of the association, noting the relative risk or the odds ratio or the hazard ratio, and that's at his report pages 13 to 25.

Again, you see the consistency because his opinion is drawing on the range of studies that are among different populations and different designs. And he's finding significance in the number and replicability, specificity. He's looking at the alternative causes at pages 5 to 11.

Same with temporality.

Biological gradient is expressly discussed at pages 20 and 28.

Biological plausibility at 25 to 31.

And coherence with other knowledge, I don't have the page numbers for this. This is his discussion about -- about diabetes generally, the progression of diabetes. He has a discussion about the disease and he puts it in the context of that.

And I think, as I pointed out last time, the experiment element doesn't really apply here, and the analogy, other than the analogy to other statins and diabetes.

So I think the Hill factors are present. And I think these doctors who do this kind of thing, look at studies, I think the factors that Dr. Hill identified are the kinds of things that have been drilled into them to do even

when they don't identify. They always look at strength. They always look, how many are there? Is it consistent? Did this happen more than once? Are there other causes? So you do see it running throughout that.

Your Honor, the last point I want to make is a little bit of an outlier here. It's on a totally different subject from what we have been talking about, except that it relates to Dr. Quon. And so since this is the moment when we are considering, I think I need to make this point now. And that is this: In addressing the question of whether there is evidence of efficacy for primary presentation, Pfizer doesn't make a single argument on this topic addressed to Dr. Quon.

Now, Dr. Quon did address this issue on pages 37 to 38 of his report. His section is headed: "There is no convincing evidence that there is a clinical benefit for women using Lipitor for primary prevention." That's the section heading, so it's kind of hard to miss. He discusses some evidence and he says: "Thus, it appears there is no compelling evidence for women to use Lipitor therapy for primary prevention of CVD, cardio vascular disease." That's on page 38.

Not only is this opinion not mentioned anywhere in Pfizer's efficacy briefing, there is not a single mention of Dr. Quon's report in either Pfizer's opening brief or its

reply brief on the subject of efficacy. The only mention of his name -- and I know this because I -- using the miracle of modern technology of electronic searching -- Dr. Quon's name appears precisely once in all of Pfizer's briefing on the efficacy issue. And that's in the context on a point in which Pfizer contends Dr. Quon agrees with it.

So given Pfizer hasn't offered a single evidentiary argument addressed to this particular opinion offered by Dr. Quon -- and you know, that obviously is distinct from the other opinions by Dr. Quon, and it's also distinct from the preemption argument which it's a legal argument and it would cut across everybody. But they don't offer a single evidentiary argument addressed to the efficacy opinion offered by Dr. Quon. It doesn't appear that Pfizer is seeking to exclude that opinion. It's offered no basis for the Court to do so. It's completely limited its discussion to the opinions offered by Doctors Fleming, Roberts, Wells and Abramson.

So when we turn to efficacy, which I imagine is going to be tomorrow, I'm going to do the same. But I just want to note --

THE COURT: When y'all briefed efficacy, did you use his name?

MS. BIERSTEIN: I don't believe so, Your Honor.

THE COURT: I don't think you did.

MS. BIERSTEIN: He was not at issue. Because as I say, they don't raise him. So I don't see how that particular opinion of Dr. Quon's is at issue here because they haven't -- you know, they haven't raised it. They haven't made an argument. It's different from what I think happened in general causation where they sometimes lump the experts together.

But they made a clear statement. These are the people whose opinions on this topic we are challenging. They made a statement like that in the efficacy brief, as well, Your Honor. They break it out. I don't remember the page. I could look for it for you. They list them one, two, three, four. He's not on the list. I think that's not in front of you.

THE COURT: Okay. Thank you.

Mr. Cheffo?

MR. CHEFFO: Very briefly, Your Honor.

I don't think there is a lot of dispute that we are challenging efficacy opinions. So the potential gotcha argument that, you know, we didn't put -- I think, you know, Your Honor will be guided by the fact that we are challenging all the efficacy opinions. And to the extent I haven't looked at all the papers, there was, you know, an oversight that he wasn't recognized, certainly that's part of the challenge. I don't think that we need to stand on the

ceremony with respect to that, Your Honor.

Three quick points. 3:1, right? We've heard a few times, That comes from Pfizer, That comes from Pfizer. It comes from Pfizer. But in fact, that analysis doesn't just come from Pfizer, because Your Honor knows Pfizer said when the Medical Monitor looked at it, there is no issues, no association. When the FDA looked at the information, what comes from Pfizer is the FDA statement that there is no elevations of glucose levels.

So the only spin, the only analysis that comes in any way from the Pfizer documents come from Dr. Jewell. You were asked, Well, you know, his name is kind of in there, and he's cited a few times, but I'm not really sure if they are relying -- these experts are relying on Dr. Jewell's analysis. That didn't just come from Pfizer. There was a quote that was read. I didn't get all of it, but what was kind of in the middle of it, again, was increase the risk. The whole quote was about increasing the risk.

And I guess finally, you know, it's always interesting to me when, you know, an expert report says substantial contributing factor. That's not language you really see when you read an epidemiology study or you read papers, that's not how experts who are supposed to -- nonlitigation experts talk. They talk about association, elevations of risk, causation. So, you know, the fact that

we have someone talking about substantial contributing factor, that, again, is not a causation.

I didn't hear a single thing about why that would, you know, mean that there is a causation opinion. What we are really trying to do here is find out whether these are real experts, challenge them as real scientists and find out if their opinions pass muster --

THE COURT: Mr. Cheffo, if they say -- if the general causation says, It's my opinion that Lipitor is a substantial contributing factor in the development of diabetes, doesn't affect 100 percent of them, it varies from patient to patient, why isn't that sufficient?

MR. CHEFFO: I think we see that, Your Honor, in -- more in connection with a specific causation analysis, okay? And, you know, they kind of rule in, rule out. But you know, it gets to the whole point of, if you are talking about general causation, it's a substantial contributing factor for what? What does that really tell us? Again, what dose? What length of time? Anything else. So there is no information. There is no background. And it wouldn't even remotely be helpful to the Court -- to a jury. It's basically saying, If you took Lipitor and you got diabetes, I'm going to opine that you get to go to the specific causation.

THE COURT: Possible it's related.

MR. CHEFFO: Possible. Those are not *Daubert* standards, Your Honor.

THE COURT: Well, the question is sort of by splitting the general and the specific here. And I understand why they would do it. Usually that's not a problem because the same expert is talking about both of them, okay? I mean, you are giving this opinion.

They have now split it and they want to say if they -- it's a -- it's a phenomena established in the studies that some subset of people who take Lipitor, a statistically significant subset, get diabetes where those in the placebo group don't, okay? And that -- they offer that with a reasonable degree of medical certainty that there is a subset within that. How is that really different from saying it increased the risk?

MR. CHEFFO: Well, I --

THE COURT: Or closer to say it's a substantial causative factor in some individuals?

MR. CHEFFO: Well, if you are looking at specific causation -- again, I have less of an issue of kind of looking at it in a specific issue. But here from a general causation, what is unprecedented really, I think, Your Honor, is again, what -- I can't remember a litigation where essentially someone is saying if you took it without any other parameters or guideposts, and you got the disease or

the injury, you are in, right? This is -- again, this comes back to our kind of core problem.

THE COURT: Of course, the screen is on specific causation on that. Because if the person comes in and they've got this -- I think one expert, am I right about that?

MR. CHEFFO: They have one expert.

THE COURT: They have one expert. He's saying, I'm relying presumably on these other experts to say that it's established in the medical literature and the data out there that Lipitor causes a higher rate of diabetes than people on the placebo group. And then he -- he says, I'm relying on that. That sticks it into the differential diagnosis. Then if he can find a methodology that credibly explains away other things, differential --

MR. CHEFFO: Again, I think, you know, no one is suggesting that they have to get down to the granular level of crazy specificity, you have to have X, Y and Z and every other factor.

Here is the problem. The specific causation factor has to be built on -- and you have to help following courts -- has to be built on some criteria. All they are saying then is every case, all they have to show to get past it is based on this testimony, they took it and they have diabetes. Now, every single case has to come with, you

know, all kinds of expert testimony and science support to find out, are there any parameters?

The point of general causation, as I've always seen it, I think the case law talks about it, is that you have to develop some guideposts, some criteria.

And also, I would just say this: If there really was evidence across the dosage -- in other words, it might be fine to say it's okay for every person if they came into court and said, Your Honor, 10 milligrams, overwhelming evidence, here is our methodology. In fact, we have a study that shows that it doesn't show, in fact, there is no risk. Navarese. They didn't talk about it virtually at all. Meta-analysis across the range.

We didn't hear a word -- this isn't a matter of can you just say it and get by, right? It's their burden to show at 20 and 40. What did you hear today or in their papers that an expert could say it's reliable? There is information that's reliable on 20 and 40 milligrams that I should get up and be able to tell a jury that this causes it.

Now, the only thing we've talked about -- and you know, Your Honor may, I'm sensing, disagree a little bit, or not disagree, but not be crediting some of our arguments on 80, but that we understand. We've talked about that. That's 80 milligrams with multiple risk factors. But that's not the case at 10, 20 and 40. And you don't get a pass by

saying it can cause it for all people at all doses at all times, we'll figure it out later. That's -- I mean, that would both be very unhelpful to litigation --

THE COURT: Obviously for an expert to get up and say you would have to do more research to get an answer on that is not helpful. Dosage levels. There needs to be further research. That's not good enough, right?

MR. CHEFFO: Right.

THE COURT: And you are right, I find, I'm more -- I'm not taking -- and who is right and who is wrong? I'll let a jury decide that. But there has got to be a threshold. And I'm just concerned about what evidence we have that the threshold is met at lower doses.

MR. CHEFFO: We don't have any, I mean any credible evidence. That's the point. That's why we have been saying all along, like there has to be some filter here. There has to be some information. And we were told and expected that there would be. And now, you know, it's kind of this is the day, and all we are told is, again, therapeutic dose. Means nothing. It means anybody who basically got it consistent with the FDA labeling, that's the limitation? I mean, it can't be that that -- that what they have put forward with these people talking about increased risk or, you know, it's possible, or it can be that, you know, whatever number of people in your MDL, that that's

enough to cover all of those people.

This is a very serious allegation, right? Your Honor is taking it seriously, the plaintiffs presumably are, we certainly are. And we spent the better part of a few years now -- and if this was -- this is a very serious case. I'm not going to get on a soap box about it, but these are folks that are saying, Here is a product that causes people to get diabetes and you shouldn't be taking it. And if you have that kind of allegation and it's clear for this mass tort --

THE COURT: They are not saying you shouldn't take it.

MR. CHEFFO: It's a warnings case.

THE COURT: That's not their claim. Their claim is you should have told us. We should have had a right to make a decision. And, you know, we'll get into tomorrow about efficacy, but efficacy sort of defeats the harmless error argument, y'all should have told them and didn't. If it didn't matter, then there is no damage. And I suppose that's why they sort of doubled down this efficacy issue.

MR. CHEFFO: Right.

THE COURT: Anything further?

MR. CHEFFO: No, Your Honor. It's been a long day. Thank you for your dedication and to your staff who has been also very patient with us. Thank you.

THE COURT: Ms. Bierstein?

MS. BIERSTEIN: I would like to save for the morning -- we do have some more evidence on the 10-milligram versus the 80, but I did --

THE COURT: I would love to hear that.

MS. BIERSTEIN: I think the morning when we are all fresh is the time to do it. But --

THE COURT: Y'all will have time tonight to figure that out. I've got to say, that's an issue that I'm struggling with, but I'm not fully confident I have all the information. That's the problem.

MS. BIERSTEIN: I think we can give you some more in the morning.

But Your Honor, I want to say -- Mr. Cheffo keeps saying, I kept thinking they were going to limit this case. And I don't know where he got that idea because I know of precisely one MDL -- and I'm sure there must be another one somewhere -- where they did that. I've done a lot of these cases. In *Yaz*, nobody was looking at that. In *Actos*, nobody -- there was no issue about which doses. In -- I mean, I could list them. The majority of the MDLs, it is true that when the defendants come to settle the cases, sometimes they make the stratification. But in terms of a *Daubert* ruling that requires the plaintiff to stratify the risks at different doses, it is not the norm.

THE COURT: If the data shows -- if ASCOT tells us that 10 milligrams, no effect, if SPARCL tells us at 80 milligrams, there is an effect, let's just say hypothetically that's the way it's interpreted, then it may be dose -- the proximate cause may be dose related, okay? It raises the spectra of that issue. And the question is: Has anyone actually addressed that issue?

Because if you -- if you want me to say regardless of dose, regardless of time, regardless of any risk factors, regardless of anything, you took -- you took Lipitor and you got diabetes, you are in the final round, nothing else, you don't have to show anything else to get to the specific causation, I think that's a tough argument to make.

MS. BIERSTEIN: Well, Your Honor, there are lots of drugs that -- I mean, I think, you know, there are lots of things if you know that if you take it, even a small amount -- I mean, there are things that are poisonous and you take it in a small -- I mean, I think we have -- there are lots of situations in which we don't stratify, particularly within this -- within this range. I don't think it's true.

Remember ASCOT. Even if you read it the way Pfizer does -- which is obviously different from the way Dr. Jewell does -- but even if you read it the way Pfizer does, ASCOT does not establish that there is no risk at 10 milligrams. ASCOT simply shows an absence of evidence that there is.

So now when we look at the NDA and we see it in 10 milligrams and we look at those two trials with the people that had below normal and normal glucose at 10 or 10 and 20 milligrams, when we look at the other statins, we have a lot of this evidence, ASCOT doesn't contradict that. ASCOT is a we didn't find it or we didn't find a statistical significance. It doesn't contradict that when we have this other evidence.

So -- and that's the other evidence that we are going to talk about tomorrow. But I think the notion that, you know, that this is something we need to do, our experts are comfortable giving an unqualified opinion on causation and they have looked at --

THE COURT: They have a very qualified --

MS. BIERSTEIN: They are qualified people. They have looked at the -- their opinion, they have not felt the need and they haven't done -- you know, not one of these scientists said, I can't give you that opinion, I can only give it to you at 80. They gave you an opinion that this is what we are seeing across -- and it was an unqualified opinion. These are the experts who I think meet all the *Daubert* criteria, and they don't --

THE COURT: But the fact they have an opinion, it's got to be data based, and I'm looking for the data that support --

MS. BIERSTEIN: I think if you look at their --

THE COURT: Come in and say, Yup, there is a -- there is an effect, and we are relying on these studies. And I go and I look at the studies, and you've got to bridge the gap between their opinion and the data.

MS. BIERSTEIN: I understand that, Your Honor. But the data wasn't only Lipitor specific. There is also statin-general data.

THE COURT: I'm looking at all. I agree with you.

MS. BIERSTEIN: And I think the statin-general -- and remember, when you look at the doses of the other statins, what you have to keep in mind is that some statins are stronger and some are weaker. And a doctor who looks at the weaker statins and still sees the effect, who says, I don't need to limit my opinion to 80 milligrams because I'm seeing this as a class of fact of all strengths, I don't think you can second guess that in these experts.

THE COURT: I mean, you know, you've got to show me where they say that kind of thing. I mean --

MS. BIERSTEIN: I think the problem, Your Honor, is that until Pfizer said, Well, you've got to stratify it, they simply looked at the totality of the data and said, Yeah, we are seeing causation in the totality. They didn't stratify because nobody said they should.

And by the way, I want to note, Your Honor, the case

is a little equivocal, and I understand the circumstances are different, but in the *Westberry* case, it's a Fourth Circuit *Daubert* opinion, one of the issues there was they couldn't show the precise dose. It's not a drug; it's an environmental exposure. And the Court didn't have a problem with that.

And I think, you know, you need to know this biological gradient. You need to have a sense that there -- you know, that there is a response. And we certainly need a sense of a threshold. But I think the -- I think *Westberry* makes clear that this business that we can peg it to the specific point, I think that's not the case. It's not true under the law.

THE COURT: Here is straight up my concern, y'all think about it tonight, I am just concerned -- I look at Dr. Jewell's testimony on SPARCL, and I say, Hum, you know, I think there is probably sufficient for most of it, if not all of it, to get to a jury. We've got to look at all the specific opinions within that. But there is something there, and you -- it's unmistakable, 80 milligrams, it seems to mean something. And I have real concerns about the substance of his opinions concerning the NDA data and ASCOT.

So then the question is once I've eliminated that, if I do that, if I reach that conclusion, then we are left with essentially a single statistical study, a statistical

analysis. And contrary to what you have been telling me when I read the stuff, everybody is relying on Dr. Jewell. So what happens to all of that?

And it seems very -- at least if you are only relying on SPARCL, then you've really got a dose issue floating on out there that at lower doses it doesn't appear, and at higher doses -- and I just need -- you need to have some opinion other than somebody saying, I have concluded across the board it's -- it has an impact. I just -- I've got to have the underlying data to show that. Just if they take from SPARCL and say, I conflate that, if you took 10 milligrams and got diabetes --

MS. BIERSTEIN: Your Honor --

THE COURT: -- if you reach that conclusion, I don't think SPARCL goes that far.

MS. BIERSTEIN: Not one of our experts bases the fact that they are giving an across-the-board opinion solely on SPARCL. And as I said, TNT shows no difference between 10 and 80. I think that's important. I think, you know --

THE COURT: 80, it says there is -- there is -- there is not significantly --

MS. BIERSTEIN: I understand, but we have other studies that says it is at 80 and then the TNT comes in and says --

THE COURT: You take that to tell me that --

MS. BIERSTEIN: I'm going to draw some inferences. Also Mr. Cheffo is running away from 3:1. I understand that the FDA and Pfizer said it doesn't mean anything. But the 3:1 was not Dr. Jewell's calculation. And it was a 10-milligram study. And it was the Pfizer people who selected the 40 cases that they identified as clinically-meaningful deviations from baseline. They are the ones who said, Hey, something weird happened to these 40 people, and guess what? It happened three times as often on the Lipitor arm than the placebo arm.

THE COURT: That 3:1 is derived from having a substantial percentage of people already being diabetic.

MS. BIERSTEIN: Sure. But it elevates people in -- including people with diabetes. The mechanism, if it's going to elevate my glucose and it's going to elevate your glucose, it's also going to elevate glucose in a diabetic because the point is it's elevating everybody. It's like the rising tide.

THE COURT: It's not elevating everybody.

MS. BIERSTEIN: Everyone with a susceptibility. There is a group of people who are susceptible to it. And those people, boom, it's raising all of them whether they are diabetic or not. And I think that's an important data point. And it's not Dr. Jewell.

THE COURT: Okay. Thank you.

MR. CHEFFO: Maybe we'll hear tomorrow who these susceptible people are and how we figure out who they are.

THE COURT: I have been waiting for that particular one. I do want to know that.

Okay, folks, we've had a long day. Thank you very much for your efforts. And without trying to exclude -- if I could ask Mr. Hahn and Mr. Cheffo to step forward.

(Thereupon, the Court was in recess.)

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

Amy C. Diaz, RPR, CRR September 30, 2015

S/ Amy Diaz