**Episode 15: Journal Club May 2017**

Dr. Joe Chappelle: Hello everyone, and welcome back. I’m Joe Chappelle and you’re listening to the OB/GYN Podcast. Today, we’re going to do something a little bit different. Hopefully, the start of a monthly series of journal clubs. Every month we’ll be choosing an article that is free online so everyone can read it. And this means that likely we’ll be choosing articles from either The Green Journal, The Gray Journal, or even the New England Journal of Medicine. That being said, if you have a great article that you want to see reviewed please send it my way and we’ll put in on the show. Today, I want to introduce my co-host for this episode and hopefully a lot more to come. His name is Jerry Ballas. He is an MFM at Baylor University and I am very happy to have him here.

Dr. Jerry Ballas: Going to correct you there, Joe. It’s Baylor College of Medicine.

Dr. Joe Chappelle: Duly noted.

Dr. Jerry Ballas: Baylor University is in Waco and we don’t go there.

Dr. Joe Chappelle: Okay. So, there you go. Baylor College of Medicine. I apologize to all the Baylor people out there. In any case, let’s get started today. I chose an article from The Green Journal, the April 2017 issue. It was written by Mohammad Maher and it was from Menoufia University in Egypt. The title is *Sildenafil Citrate Therapy for Oligohydramnios*. The way we’re going to structure this is we’ll start with some opening remarks and then we’ll start at the intro, go through the paper and then we’ll circle back to the abstract. A link to the paper is in the show notes so you can either read it ahead of time, follow along or just sit back and listen as we go through it. Whatever works for you. So, to start off, Dr. Ballas, do you have any opening thoughts on this paper?

Dr. Jerry Ballas: I got to say, when I saw the original content, the original theme of the paper in terms of dealing with oligohydramnios, as an MFM, you know we’re always trying to find ways to deal with the placenta, which is a big mystery to us. The use of a vasodilator like sildenafil isn’t a new concept. A lot of us have been looking at whether we can help with growth restriction or other problems that we assume are due to lack of blood flow or lack of… you know, uteroplacental insufficiency. So, looking at something like sildenafil to deal with potential uteroplacental insufficiency is an area of interest to most MFMs.

Dr. Joe Chappelle: I have to agree. First thing I do when I look at a paper is, does this apply to me? Is it interesting? And I would say, certainly oligohydramnios is something that we see in clinical practice on a regular basis, so it’s certainly of clinical interest.

Dr. Jerry Ballas: Correct. And they’re attacking a very specific offset of oligohydramnios, the idiopathic oligo. Typically, when we think of oligohydramnios, we’ll look to see any other abnormalities, whether it’s fetal growth restriction, whether there’s Doppler abnormalities, uterine abnormalities, some sort of secondary cause, one of the most frustrating things is when you have the idiopathic variety that you can’t quite put in the backburner. But at the same time, at say 32 weeks, you’re not really going to act upon. So, this is definitely an interesting study population that I give them credit for.

Dr. Joe Chappelle: Yeah. I couldn’t agree more with everything you just said there. That idiopathic oligohydramnios, and I think is going to become important in this paper, is a very challenging one, especially when you’re extremely preterm, because when you get to 38 weeks, fine, deliver. But at 30 weeks, what do you do? How long do you watch them? Can you do anything for it? So, I definitely appreciated the gist of this article.

Alright. So, why don’t we move into the intro. And one of the first things that I like to think about, or how I like to organize it when I go through this is a couple of questions. Which is, what are we talking about? Why is it important? Is there any background I need to understand about the question being asked? And then, most importantly, what question is being asked? And so, I’m going to try to go through it with those kind of things in mind. Some of this journal club is about the actual research, and we’re going to talk a whole lot about their methods and inclusion and exclusion, how they analyze it. But another part of journal club to me is the art of scientific literature and how do you write a paper and how do you convey your thoughts to other people. So, sometimes I might go a little bit into the weeds on that, so I apologize, but that’s the stuff that fascinates me.

In the first one, I think that we already kind of determined, is what they’re studying, which is the pathophysiology of oligohydramnios and what can we do about it besides just watch it. Next part is, why is it important? And this they don’t do such a good job of saying why oligohydramnios is important. I don’t know, what do you think, Jerry?

Dr. Jerry Ballas: Yeah, no. I think they kind of kept it a little light on the background. As an MFM, just day to day, I know the importance of fluid level in terms of telling me a little bit about placental function, fetal renal function, fetal wellbeing. We use it as part of our biophysical profile, so it’s almost second nature to me to know that a fluid level check is almost like a vital sign to the pregnancy and to the fetus and the uterus, and even maternal status as well.

Dr. Joe Chappelle: Yeah. Absolutely. I think in some ways the readers of The Green Journal probably know exactly what you just said. But when you’re trying to make a case for an intervention on something, it would be nice to say why it’s bad, and therefore why you think it’s important that you’re trying to correct it. So that would’ve been nice here. I don’t think it significantly affects the paper, but I do think it would’ve been nice to mention. And then for background they talk to us about sildenafil and how it works. And there’s something very interesting in here, so I want to bring it up. And that is in the second paragraph here where they state the pathophysiology of oligohydramnios is not well understood, but when detected in the absence of rupture of membranes has been considered to be a sign of chronic suboptimal placental function. They have a reference here. One of my things I love to do is go read people’s references and see if the reference actually says what they are using it for. And so, I did that here. What they’re quoting here is a paper from Sherman et al. in 2005 in the Journal of Perinatology. And while it does state that fluid levels are a sign of placental perfusion, all that data comes from sheep. Not to say that it’s not true, but it’s kind of a strong-ish statement for only data from animals.

Dr. Jerry Ballas: Truth be told, a lot of our understanding of placenta in general is extrapolated from sheep data. Only now are they really starting to come up with true human models and better in vitro studies using functional MRIs and newer technology. But a lot of our assumptions and underlying presumption is from sheep data and well antiquated sheep data.

Dr. Joe Chappelle: Alright, well, there you go. And again, I don’t want to make it seem like I’m saying they could’ve done better here. Sometimes you just have to work with the data that you have available and the references that are there. And it can’t be done a different way. But I do like to know what they’re quoting from. In the next part here, they tell us about Viagra, which is sildenafil citrate, and the fact that it’s a vasodilator which is presumed to lead to vascular relaxation and increase uterine blood flow. And again, they have a reference here. So, of course I went and looked it up. This particular one is an interesting reference. They took myometrial biopsies from women with and without growth restriction affecting the pregnancies and they incubated those biopsies with Viagra and they found that the biopsies from the women with the growth restriction dilated and that the other women didn’t, and so they’re presuming that at least in cases of growth restriction that Viagra can cause vasodilatation, or dilatation, I should say, of the myometrium, and therefore increase blood flow. Which is interesting, but I’m not really sure that it allows them to say that Viagra leads to vascular relaxation and increase uterine blood flow.

Dr. Jerry Ballas: They make a leap. They definitely do make a leap. And if you read the title of that paper quickly, you may read it as Viagra helps with growth restriction, but you have to look at the next level down where they took a part of the pathophysiology they believe leads to growth restriction and showed some improvement. One brick in the wall possibly, but again, not a causal relationship just yet.

Dr. Joe Chappelle: Yeah. And again, I don’t want to say they shouldn’t have used that reference, but I think that the line that they wrote when they referenced doesn’t really go together and they could’ve written that a lot more transparently. And again, I don’t know that they’re actually wrong. It makes sense that Viagra would increase blood flow to the uterus because it works on smooth muscle, so that makes sense. But I don’t know that it’s as ironclad as they made it seem.

Dr. Jerry Ballas: But there is a world of difference between the uterus and the placenta. And that’s the part we still don’t quite understand.

Dr. Joe Chappelle: I think that that is a very, very good point. I had not thought about this paper in that light, where we’re trying to affect the uterus to affect the placenta. It’s just that those two things don’t necessarily go hand in hand. I hadn’t thought of that.

Dr. Jerry Ballas: What’s good for the uterus isn’t always good for the placenta and vice versa.

Dr. Joe Chappelle: Okay. This is why I have smart people like Dr. Ballas on.

Dr. Jerry Ballas: And we should also have a disclaimer that we are not sponsored by Viagra nor take any money from them.

Dr. Joe Chappelle: That is a good point. We’re not sponsored nor take money from anybody. There’s our disclaimer. Now, we get into probably the most important sentence in the entire paper and that is their aim. They state, and I’ll quote it, “The aim of our study was to compare sildenafil hydration therapy with hydration alone in improving the AFI in pregnancies complicated by idiopathic oligohydramnios and to assess pregnancy outcomes of both groups.” Alright, so let’s unpack that a little bit. The aim of our study here, they’re saying, was to compare giving Viagra with hydration versus just hydration alone and see does that affect the AFI. Sounds pretty simple. And they also tack on this last thing, which is pregnancy outcomes. One of the things, and Jerry, I know you read a lot too, is you’ll see in most papers they’ll tell you what the primary outcome and what the secondary outcome is, here. And so, I’m going to assume, as they said it first, that seeing if the AFI improved is their primary outcome. Would you agree?

Dr. Jerry Ballas: Yes.

Dr. Joe Chappelle: Okay. And that becomes important when you’re reading papers because most of the time, or I would say maybe 100% of the time, if anything can be said to be 100%, that the study is powered to the primary outcome and nothing else. And so, any time you have a secondary outcome or a subgroup you really have to consider what their numbers were in those groups to see if really they can even make a statement about it. Whereas their primary outcome hopefully is powered so they can make a real statement about it. And, we’ll get to it in a second, but in their small study here, I’m surprised they even talk about pregnancy outcomes because it’s such a small group.

Dr. Jerry Ballas: Right. Well, I mean, in a way, this day and age you kind of have to if you’re going to submit an article, because the next question from the reviewers always is going to be how does this help us? And so, they made the attempt, they took a swing, and well, lo and behold as we’ll reveal later, there is a couple of significant p values. But we’ll talk more about that in a little bit.

Dr. Joe Chappelle: Alright. So, then I guess we’re done with the intro there. And I think, overall it wasn’t a bad intro. I do appreciate brief intros in general. I do feel, I think you agree, that they could’ve had a little more background, maybe another paragraph to tell us a little bit more about the bad effects of oligohydramnios and what they’re trying to prevent. But overall, I think it was a pretty well-structured intro without too much fat.

Dr. Jerry Ballas: Agreed.

Dr. Joe Chappelle: Okay. So, let’s move on to the methods then. This was an open-label randomized controlled trial. The reason it is that way is because they gave some of the women a pill and some women not a pill, so they did not do a placebo here. They just either gave them– so, the women know they were given a pill or weren’t given a pill. I’m not really sure why they decided not to do a placebo.

Dr. Jerry Ballas: That’s actually high on my mind. I was going to bring it up a little later, but we’ll circle back to that.

Dr. Joe Chappelle: Okay. We’ll put a pin in that for later. It’s not really that much harder to do a placebo, so it’s an interesting choice. Then they mention that it was IRB approved, which is kind of standard these days. Anywhere in the world, when you’re doing, especially a trial like this, when you’re giving an intervention. And then they registered it with clinicaltrials.gov, which, for those of you who are international who don’t know, that is a U.S. registry of clinical trials. Pretty much, these days, if you’re doing any kind of interventional trial and you are not registered with clinicaltrials.gov before you start the study, you will not be published. Jerry?

Dr. Jerry Ballas: I agree.

Dr. Joe Chappelle: That seems to be the impression I get.

Dr. Jerry Ballas: Oh, absolutely. And your individual local institution could come down on you pretty hard.

Dr. Joe Chappelle: Yeah. And it’s interesting. I guess for people who do tons of research they know about this. I do a little bit of research, which you guys have heard me talk about a little bit on the show before. So, the first time I did a real study kind of like this I just came across the fact that I really needed to be registered on clinicaltrials.gov and I knew nothing about it. So, anyway, public service for anyone out there who’s going to be doing clinical research.

Alright, so then we get into their inclusion criteria. And again, I said the aim was the most important part of the paper. Well, this is going to be our second most important part, our inclusion and exclusion. So, they decided to include singleton pregnancies at over 30 weeks with an amniotic fluid index of less than 5 and that sounds appropriate for what they’re looking at, right?

Dr. Jerry Ballas: Mm-hm.

Dr. Joe Chappelle: And then, this is interesting to me. They say that all these women were discovered after having a routine ultrasound. Obviously, Jerry, you’re an MFM, and so your practice is different than mine, but we don’t routinely do ultrasounds at 30 weeks.

Dr. Jerry Ballas: Right. Well, you’d be surprised, and I’m learning this more and more, in Europe and a lot of parts of the world they are starting to add the third trimester growth scan as part of a routine evaluation. So, I actually have a lot of patients that come in from overseas, and we’re talking everywhere from Europe, to Middle East, to Africa, whose practitioners would scan them every six weeks if they wanted. So, there’s a lot more ultrasound going on, you’d be surprised, in other parts of the world, than there are here. So, between 20 and 32 weeks there’s a lot of women getting routine scans overseas.

Dr. Joe Chappelle: Alright. Well, there you go, then. For our listeners out there, and those of you who have joined the Slack, if you are working someplace outside of the States or even some place in the States where the routine is for your to do those ultrasounds at say, 28 or 30 weeks, then please write in and let us know. Would love to hear from you.

In any case, moving on to the exclusion criteria, they excluded the following women: any women with fetal anomalies, abnormal Dopplers, which also goes along with IUGR which they also excluded, which I’ll talk about in a second, women in labor with ruptured membranes, which is kind of obvious and then other chronic maternal medical conditions such as kidney, lung or heart disease. Jerry, I’m sure that you’re going to agree with me here. For a study that’s looking at placental perfusion, it’s interesting that they excluded the women with IUGR.

Dr. Jerry Ballas: I think because other trials have not shown an effect on that large outcome of IUGR. I think they wanted to avoid that population, because I think we’re learning more and more that there’s just another level of complication that isn’t going to be addressed by a simple vasodilation. And so, typically, the IUGR will come with a comorbidity of some sort that then you start having the control for. So, they really, I think, were trying to parcel down to the idiopathic oligohydramnios just for clarity of outcome and to avoid having either over-control for factors or have to explain too many confounding issues.

Dr. Joe Chappelle: Yeah. I think that actually raises an important point. When you are arranging your own study, it’s that you want to make the inclusion and exclusion criteria narrow enough that you can say something about what your intervention is without, like you said, too many confounders. And at the same time, you want to make it inclusive enough that you can apply it to a large group of people.

Dr. Jerry Ballas: And that you can find people.

Dr. Joe Chappelle: Exactly. So, if you say that yes, for women who are missing a toe on their left foot, we can give them this medication, their babies will be better, well that’s nice and I’m glad that we proved that but it doesn’t really help me in my usual daily clinical practice.

Dr. Jerry Ballas: One little caveat I would have liked to have seen also with AFI versus the deepest vertical pocket is a long time debate going on in the MFM world, And for those of you listening, deepest vertical pocket being greater than 2 cm versus AFI of 5. There are some camps in the MFM world that debate which one is a better assessment of fetal wellbeing. Some feel that the AFI is a little more of a confounded measurement since it’s subjective four times over. So, I would’ve liked to have seen perhaps a little more delineation as to whether they included women who didn’t even have a deepest vertical pocket of 2. So, not just saying AFI of less than 5, but what did they do with women who had a deepest vertical pocket less than 2, because there is some thought that that’s a different breed altogether in terms of oligo. But just a little caveat in terms of inclusion-exclusion.

Dr. Joe Chappelle: Again, I have to agree with that. When looking at IUGR the definition most commonly used is less than 10%, but we all know that by definition, less than 10% of babies will be less than 10% because that’s how we got the definition, right?

Dr. Jerry Ballas: Correct.

Dr. Joe Chappelle: And I think we found, in the last 10 years or so, that it’s really the less than 5% or even sometimes less than 2 or 3% that are the real pathologic pregnancies. And I think that’s what you’re getting at here, that and AFI of 5, although it’s “low”, might actually not the that pathologic.

Dr. Jerry Ballas: Correct.

Dr. Joe Chappelle: Okay. And so, even despite their best efforts here with their inclusion and exclusion criteria they still may be lumping together some women with different etiologies for oligohydramnios.

Dr. Jerry Ballas: Correct.

Dr. Joe Chappelle: Okay. So, then going on to their protocol, they had one ultrasonographer, which was nice. That gets rid of at least some of the variation. Although, as you just said, ultrasound in general is relatively subjective. And even the same person doing the same ultrasound a few hours apart might get a different number. So, there is that even though they did use one person, which is nice. They measured the AFI twice in each occasion and the mean AFI was obtained by averaging the two, so that was their attempt to get rid of some of that variability, so I applaud them for that. Then, they took all women and they admitted them to the hospital. They gave them all two liters of IV fluids over 4 hours. Then, the women in the experimental group, they gave them the Viagra 25 mg. every 8 hours. Now, just as an aside here about that 25 mg. because I kind of wondered where they got that from. And I mean, in some sense they’re doing a new trial here so they’re kind of making it up, but I still wanted to know where they got it from. And it looks like this is the same dose that is given to adults with pulmonary hypertension and so I think maybe that’s why they chose it, because they at least knew it was safe.

Dr. Jerry Ballas: And it’s been used in pregnant women with pulmonary hypertension, so they probably have some pregnancy-related exposure studies that make them a little more comfortable using it.

Dr. Joe Chappelle: Okay. Well, there you go, I didn’t know that. That’s good. Anyway, it seems like a fine dose, I’m always curious how they choose these things.

Dr. Jerry Ballas: You know it’s not the male dose because that would be interesting.

Dr. Joe Chappelle: I don’t even- do you know what the male dose is off the top of your head?

Dr. Jerry Ballas: Not at all. Moving on.

Dr. Joe Chappelle: Yeah, me either. Okay. Alright, that got awkward quick. So, then they found that women who had a 20% or higher increase in their AFI in 24 hours were sent home either to continue hydrating, and they recommended two liters a day, or to go home and do the two liters a day plus take their Viagra. One thing I should mention here, and they mention it later, is that they didn’t actually check to see if their patients were either taking their Viagra or drinking what they’re supposed to be drinking. And again, I don’t know how you would actually do that, so I’m not saying that it’s a fault of theirs but it’s something to keep in mind.

Dr. Jerry Ballas: And this actually where I got to mention the use of the placebo would’ve been ideal. So, here’s where a huge bias can be introduced to your study, when you do not make your groups as equal as possible in the intervention. So, now you have a group of women who are taking a pill. They are prompted to intervene with the pathology you told them they had. So, not only are they taking the pill, but you’ve also told them to drink two liters of water. Meanwhile, you have another set of women who you just told to drink at least two liters of water a day. So, without a prompt, that pill, that magical pill that many patients look for, is there a strong of a prompt to drink the liquid as well? So, this is where I think a standardized placebo pill could’ve taken at least a little of that question out of the mind, because it’s a strong desire to correct what you told was wrong in a pregnancy. A woman is going to use every means necessary, and if you give them a pill as a prompt, they’re going to drink that water as well. So, that’s one question I had about not using a placebo pill.

Dr. Joe Chappelle: I couldn’t agree with that more and stress the importance of why most of these kinds of studies are done as a double-blind study, where neither the doctor nor the patient knows if they’re getting the medication or not. And especially I agree with you, you know, it could be either way, but probably women who were taking the pill were more likely to drink because they’re being reminded every 8 hours to drink more. But you could also envision a situation where women are saying, well, I’m taking the pill, so I don’t have to drink that much. So, you could see it both ways. I think yours is probably more correct because every pregnant woman I know who has a situation like this is probably drinking 4 liters a day instead of 2 liters a day.

Dr. Jerry Ballas: With each pill.

Dr. Joe Chappelle: With each pill, right. Exactly. But there’s still bias in there from the patient side. Then they go on to say that women were monitored twice a week with a nonstress test and then once a week with an AFI and biophysical profile. Then women were readmitted if they had persistent decreased fetal movement or if they had abnormal testing, which makes sense. And they recommended bed rest and daily kick counts for all the women. Again, they don’t know how many women actually did that, if they actually rested or not, but they did recommend it. Then we get to the primary outcome, yes!

So, they tell us the primary study outcome was the amniotic fluid volume at 6 weeks or follow up or the final volume before delivery, whichever occurred first. Now, I’m going to state that again because it’s very important to the results. So, the primary study outcome was the amniotic fluid volume at 6 weeks or the final volume before delivery, whichever occurred first. We’re going to come back to that so stick a mental pin in that as well, we’ll get back to it. The secondary outcome measures were randomization to delivery, so basically from the start of the study, how long until they were delivered, the mode of delivery, gestational age at birth and neonatal outcomes including neonatal weight, Apgars, pH and admission to the NICU.

Then, they tell us their power calculation, which is actually based on a decent study using just on maternal hydration therapy alone, so they assume that Viagra, when combined with hydration would increase the fluid levels from a 30% increase in this trial they quoted to 45%, so there’s an increase of 15% difference in AFI by adding the Viagra, which is made up, but sounds like a reasonable made up. So, doing that calculation out, they got a sample size of 167 women and then they included an extra 10% for losing women due to drop out for whatever reason. All of that is a very smart way of going about designing their study.

Dr. Jerry Ballas: Yeah. I think the authors did a very good job at this point, very clean, straightforward explanation of their statistical outlook and what they were planning on doing. Pretty standard fare. The data that they were collecting, the categorical and continuous variables, they have pretty-well covered with what they were planning on doing so, yeah, they’re on the ball with the statistical analysis and planned analysis for the group that they have.

Dr. Joe Chappelle: Yeah. Then looking next at their stats, I’m not going to go through all their stats. Neither Jerry or I are statisticians, but we know enough about stats to look at this and say that it seems like they used the appropriate stats, or at least they know what stats to write down that they used. This is one area of scientific research, and I don’t think you’re going to get any arguments from anyone else when I say this, that is really probably the weakest part of literature, because there are many ways to examine data. You need to make sure that the data is normalized if you use certain tests, or if it’s not normal use other tests, so on and so forth. And we have no way of knowing if these authors did that. I’m not saying this is against them. I’m saying in general in scientific literature we don’t know how the data was analyzed and whether it was analyzed correctly. And that is one of the black boxes of scientific literature which I don’t really know how to get around, but it is concerning.

Dr. Jerry Ballas: I mean, I can tell you from experience, my background is from years and years ago in epi and biostats. And I can tell you a strong research institution or at least a smart researching team will get a solid statistician to look at their data and make sure– because you’d be surprised if you try to sneak something through, either at the poster presentation to a letter of the editor when your paper gets published that somebody will look at this and say “your data’s not normally distributed, how did you use that statistical analysis for that?” So, I do agree. There is a lot of a black box component to this but man you’d be surprised, people waiting to catch you on stuff.

Dr. Joe Chappelle: Fair enough. There you go for crowdsourced stats.

Dr. Jerry Ballas: Exactly.

Dr. Joe Chappelle: Alright. So, I think that we’re at a pretty good point here to move on to the results. I agree with their little mini conclusion there on the methods. I thought it was well-written, it was straightforward. You can disagree or agree with some of the choices they made but they stated their choices clearly. Let’s move on to the results. They screened 184 women who were randomized, and they ended up with 166, which was exactly 10% dropout rate, which is what they had figured. They had 82 in their Viagra group and 84 in the hydration group. And then they tell us about their demographics, which were relatively the same.

Dr. Jerry Ballas: One quick I’d like to take back and I realize I wrote the word “N” and I circled it next to this. “N” with a question mark. I’d like to know what their total volume of patients it took to find these cases. That’d be my one curiosity. Idiopathic oligohydramnios overall, I got to say, is fairly rare, it’s not uncommon. But I’d be curious to see what their overall volume was or delivery volume, how many women on average they see to get a number of 196. It kind of gives you an idea of the scope of the problem that they’re looking at.

Dr. Joe Chappelle: I think what you’re getting at there is interesting. It’s about looking at the population that they’re dealing with if, say, in our population the incidence of idiopathic oligohydramnios at 30 weeks is, say, 2%, and theirs is 10%, we have to ask ourselves is there something else going on in that population?

Dr. Jerry Ballas: Correct.

Dr. Joe Chappelle: And I think that’s an interesting point.

Dr. Jerry Ballas: And then I also say bless them that their average BMI is 24.9. Jeez. They obviously do not practice in Texas.

Dr. Joe Chappelle: I can say in most places, they don’t practice in the U.S. because you are not alone in having a high average BMI, although definitely the south has been known to be slightly higher. But I mean, otherwise their demographics are relatively similar. I will note the large range in a lot of the values there. Even maternal age, 20 to 46. And I’m surprised they found enough 46-year-olds or some 46-year-olds with no chronic medical issues who were pregnant, but God bless them.

Dr. Jerry Ballas: I almost consider over 40 a chronic issue of its own, because we do monitor over-40 differently towards the end of pregnancy and, in our institution at least, advice delivery between 39 and 40 weeks. And so that does bring up an interesting point. I didn’t see anywhere… I know they gave us the average and the mean but I wonder how many of those patients were over 40. Question for another day.

Dr. Joe Chappelle: Yeah. Agreed. And then the only other thing I want to bring out here is the mode of conception. There were… I don’t want to use the word significant, but there were definitely a few more of the reproductive-help women in the hydration group only than in the Viagra and hydration. Again, they don’t give us p values here. I’m assuming if it was significant they would have told us that. But there certainly are a few more there, so that’s interesting. And the last thing there is the gestational age at randomization, which is identical in both, and even the ranges are pretty identical, although I will mention that the top 35.3 and 35.9, it’s interesting to include a woman like this at 36 weeks with oligohydramnios, because I’ll tell you at my hospital if she was 36 weeks with oligo, she probably wouldn’t be pregnant too long.

Dr. Jerry Ballas: This also brings into the deepest vertical pocket, because we will start at that point even dividing it out even more. If I can get a 2 by 2 pocket at 36 weeks, I’m comfortable forging ahead. Not much longer, but at least can get her into the early term category. So, that’s why I would’ve loved to have seen that little breakdown as well.

Dr. Joe Chappelle: Agreed. And actually, that brings up something that I didn’t mention in the methods, because they don’t really mention it. They mention it somewhere in the paper, though. It’s about why these women were delivered. There is no criteria for delivery. So, what I’m guessing happened here, because again, they don’t really tell us, is that these women weren’t necessarily under their care, that they had a primary obstetrician who was responsible for delivery timing and delivery decisions and that they weren’t involved in that decision-making.

Dr. Jerry Ballas: That would have to be my assumption.

Dr. Joe Chappelle: Okay. And so, that definitely, when we get into their primary outcome, which I’ll talk about in a minute, that definitely confuses things because we don’t know whether they delivered because their fluid went down further, whether they delivered for non-reassuring tracing, were they delivered because they were 36 weeks and their doctor said I’m tired of dealing with this, let’s deliver them? We don’t know. And it makes it difficult to interpret their outcome because their outcome was either delivery or at 6 weeks. Especially when we talk about some of their secondary outcomes.

Alright. Moving on to the next table, which is table 3, where they tell us the AFI for both groups and they break it down by each week. And they also tell us the number of readmission and how long they were admitted. Do you have any initial thoughts on this table?

Dr. Jerry Ballas: Well, right off the bat they really are impressing with showing their significant p values which every researcher wants to put on their first big table. And so, right off the bat you’re looking at this and you’re saying obviously sildenafil helps. That’s your initial reaction here.

Dr. Joe Chappelle: Right. So, they’re looking at number of readmissions. Almost none of the patients in the Viagra group were readmitted. So, then we’re assuming that their NSTs were normal and their AFI was normal, whereas… I’m trying to look at it now. Half the women were readmitted once or twice in the hydration alone so there’s something there. The AFI after the first treatment, so I guess that’s the admission, was similar between the two groups. And remember that their average AFI at admission was 3.4 and they showed basically a doubling of the AFI in both groups. So, interestingly, the Viagra didn’t really seem to make a difference at least in the initial treatment. It’s 2.8 and 2.9 so it’s pretty much the same. And then they go in by week by week. One of the things to look at looking at this table is how many women are still pregnant at each one. In the Viagra group, up to week 3, pretty much all the women are still pregnant. And then you start seeing a fall. It goes from 82, 82, 82, 76, 65, 33. And then in the hydration alone group, there’s a pretty steep fall off over the weeks, so it’s 84, 83, 67, 28, 6 and then 2. And so, this is going to become important when they look at their primary outcome, because again, that was either at 6 weeks or at delivery. There’s a big difference in the number of women that were delivered there.

So, that’s their primary outcome data there. And I’m going to ask that we delay talking about their result for primary outcome for a minute, and I want to move on and talk about their secondary outcomes first, which I know sounds a little backwards but bear with me. So, for table 3, which is their secondary outcome, again, as Dr. Ballas says, they really like their p values here and they have a lot of significant p values. Now, of course one of the things I always teach my residents when we look at papers, is you have to remember that there’s a difference between statistical significance and clinical significance. So, you can have a statistically significant difference of a few points but clinically that’s irrelevant. And we get into some of that here. Some interesting things that they found, or I thought were interesting anyway, and Dr. Ballas you can chime in… One is, not surprisingly from the last data, the gestational age at delivery was much higher in their Viagra group, which we could have guessed based on at how many weeks they were delivered. And again, going with that, pregnancies were prolonged much further in the Viagra group. But here’s where it gets interesting to me. And the first one is the meconium staining. So much higher in the hydration only group. What do you make of that?

Dr. Jerry Ballas: I kind of look at this all as group, the meconium staining, the abnormal tracing and the… c-section being for abnormal. I mean, all of this in one way does look like the classic sequalae from a fetus without a lot fluid around, maybe having a lot of variables going through fetal distress causing meconium staining. That’s kind of the classically taught triad of fetal distress, which is low fluid, cord compression, repetitively meconium staining.

Dr. Joe Chappelle: I agree. Two things come to mind when I’m looking at this data. One is either the populations are actually much more different between the two groups than we think for some reason, which I find unlikely, because I actually think they did a pretty good job randomizing. Or maybe the Viagra… let me go back and say this again. With increased fluid like you’re talking about, it seems to me that fetal distress and all that kind of stuff, obviously that usually goes with poor prefusion to the fetus, right? You can see that in the abnormal tracing and the abnormal Dopplers. So, is the Viagra… I mean, we’re using fluid as a proxy here, but maybe their statement in the introduction really is true and that Viagra really does increase blood flow to the fetus.

Dr. Jerry Ballas: So, you’re thinking it’s more of a placental effect than a uterine effect?

Dr. Joe Chappelle: Right.

Dr. Jerry Ballas: Interesting theory.

Dr. Joe Chappelle: Well, I mean, it’s just these outcomes here, these are the things we see in babies with IUGR and things like that as opposed to your run of the mill oligo. I don’t know, it was interesting to me. We have no way of proving that, they have no way of proving that but food for thought. Moving on to the neonatal outcomes and I will tell you that in general, I’m going to use the word “detest”, and that may be too strong a word or not strong enough a word, but I usually detest neonatal outcomes because in order to find significance in neonatal outcomes, generally the end up pulling them and making a neonatal composite score, something like that. They didn’t do that here thankfully, but the thing they also didn’t do was control for gestational age, and I’m going to imagine that a lot of these differences here are due to the fact that they were much more premature in the hydration only group.

Dr. Jerry Ballas: Yeah, no, I could definitely see a three-week difference in your average gestational age. Obviously, the neonatal weight, you’re always going to get a great p value out of that if you have a group that delivers three weeks earlier, admissions to NICU… Yeah, so this is all, I agree, related to gestational age.

Dr. Joe Chappelle: Which isn’t obviously to say that… Obviously the experimental group here got a benefit from the medication because their pregnancies lasted longer and that all goes with neonatal outcomes, so I’m okay with that. And I can’t actually remember, we’ll get to the discussion in a little bit, whether they make a statement about the Viagra for neonatal outcomes but I could see someone saying “oh, look, well Viagra improves neonatal outcomes” based on this data and that’s not necessarily true.

Dr. Jerry Ballas: To go back to an interesting point you made, you got my brain going here. When you were talking about could the Viagra be having its primary effect on the fetus through the cord, maybe the placenta itself. Another group that’s notoriously known to have a high rate of meconium staining are cholestasis kids. So, our cholestasis pregnancies, which we still don’t know what the exact pathophysiology behind demises or abnormal tracings in labor or the abnormally high meconium staining that comes along with it, but it’s always been proposed that there is a vasoconstrictive effect of these bile acids on both placental and umbilical cord circulation. So, could the Viagra effect actually be an effect on placental and cord vasodilation that’s protective to the fetus and labor? Fascinating. Just a thought off the top of my head.

Dr. Joe Chappelle: Absolutely. The further we get into that sort of stuff in many ways the baby and the placenta are still a black box to us. We don’t really understand how that all works, right?

Dr. Jerry Ballas: Correct.

Dr. Joe Chappelle: And I think this paper actually hinted at a lot of things that are a lot more interesting to me than just fixing the AFI.

Dr. Jerry Ballas: I would have loved if they’d gotten cord blood samples and measured the level of Viagra in the cord blood. That would have been a nice caveat to this study.

Dr. Joe Chappelle: Yeah. Agreed. Alright, so now let’s circle back to their primary outcome. I do want to mention, by the way, that their entire results section is only three paragraphs long. And they are three very short paragraphs. And again, like I said in the introduction I’m all for brevity, but this is a paper that probably could have benefited from maybe a couple more paragraphs in the results.

Dr. Jerry Ballas: I’m telling you, it’s a p value showcase, and so they really just direct you to the tables. I think that was their aim.

Dr. Joe Chappelle: Yeah. And there is two schools of thought when it comes to writing, and I shouldn’t actually say two schools of thought, because really the one school of thought that is the right one is that you should be able to read the paper without tables and understand it. However, that runs up against publishing realities of how many pages that they want to publish, because each page in a journal costs money, and a lot of money, especially in a very large journal like the Green Journal, which is distributing I don’t know how many thousands of copies every month, and so they try to keep the papers as short as possible, and in places like the New England Journal of Medicine now are publishing a lot of supplemental stuff online with the full methods and things like that. But in any case, it’s still kind of a short results section.

But let’s go back to their primary outcome. You will remember, because I said it twice, that their primary outcome was the AFI at delivery or at 6 weeks, whatever happened first. So, I’m going to read the paragraph where they discuss that primary outcome in the results section. They state the amniotic fluid volume was higher in the Viagra group at the final assessment, 11.5 versus 5.4 cm with a p value of 0.02. That is not the same thing as their primary outcome. They’re just telling you that 6 weeks. But of course, if you go back to that table with the weeks in it and who has still delivered, there were only two patients left in the control group. And so that’s why their primary outcome to begin with was we want to know at delivery or at 6 weeks, but they only reported at 6 weeks.

Dr. Jerry Ballas: So, you’d like to see kind of match-by-match weeks of delivery with AFI at that time.

Dr. Joe Chappelle: First, I’d like them to just answer their primary outcome. They’re the ones who made it up, I didn’t make it up for them. So, I think they should’ve given us results based on that. And you can’t really figure it out… I guess you could figure it out from the table. They do give you the AFI and the number remaining. So, I mean you could come up with an estimation, I suppose. But that was their primary outcome. And I think correctly that was their primary outcome because… I don’t know actually. I’m a little confused. So, we’re going to assume that most of these women were delivered for either non-reassuring antenatal testing or because they were persistently oligo.

Dr. Jerry Ballas: Well, that would’ve been a nice secondary table to put in here, indication for delivery.

Dr. Joe Chappelle: Right, and again, because I think that because they didn’t control the delivery maybe they didn’t have access to that information, I’m not really sure, but it makes it hard for me to interpret that primary outcome when they don’t give us the information. I actually, amazing to myself, don’t actually think it takes away that much from the paper. Although I think it may change the way they conclude in their discussion. But I did find it odd that they chose a primary outcome like they did and then didn’t give us the data to tell us what the answer was.

Dr. Jerry Ballas: Well, I think, to tell you the truth when they were formulating the study, and again I’m trying to… at this point the defense attorney would object and say I’m trying to figure it out, but it sounds like a great outcome if you think about it, but then reality hit that not every woman’s going to be still pregnant after six weeks, and I think they realized it’s a whole lot more work, which I think would have enriched the paper and the understanding of this population more if for every individual woman they had recorded the indication for delivery, what the AFI was at the time of delivery and analyze it in that regard. I would have loved to have seen AFIs at time of delivery. And maybe create an index of some sort of AFI at such-and-such week and standardize all the women. So, all the women that delivered at 36 weeks, what were their AFIs? 35 weeks, 34 weeks, 33 weeks. So, I think that would’ve been another way to look at it and I think it would’ve been a little more clinically logical way. I would want to know that okay, I start Viagra at 30 weeks with hydration, how far can I realistically expect her to deliver and how good the fluid is going to be and how good of an outcome am I looking to affect with this intervention.

Dr. Joe Chappelle: Yeah. One of the things I took away from this is that I can actually compare this to amniotic fluid infusion during labor for a woman who has variables… you know what I mean. Which we know doesn’t actually affect the baby but allows us to allow them to labor and so we get more vaginal deliveries. The only thing it’s treating is the provider and I almost feel like we’re in a similar situation here, where we are allowing the pregnancies to go on more because the fluids are higher. One caveat to that is that we did see in the hydration-only group that there was a higher risk of meconium staining and all that stuff, so maybe there is some fetal effect that we just didn’t answer in this study because it wasn’t designed that way. But, at least in some way, I really feel like we’re treating ourselves here.

Dr. Jerry Ballas: Absolutely. I can see a definite component of reassuring physicians to continue on with an improved AFI.

Dr. Joe Chappelle: So, I think we’ve beaten the results section to death. We can move on to the discussion. This is where, as far as scientific literature, this is where this paper starts to fall apart for me. Up until here I’m with it. Like I said, I have some quibbles, maybe I would’ve done something differently, maybe I would’ve chosen a different primary outcome or secondary outcomes. But the way they presented it so far, I think has been pretty clear. And my biggest problem with the discussion is when they get into their strengths and weaknesses because they’re interesting to say the least. But before I get there I want to talk about, again speaking about literature, is the first couple of paragraphs in the discussion are essentially in my mind introduction. Because here they start telling us about the Viagra and how it may work, and they tell us finally about why AFI may be a bad thing. But that should’ve all been in the introduction. Again, as a general rule, never introduce new information in the discussion.

Dr. Jerry Ballas: I can definitely see starting with “considering the enigma” as the opening line of your discussion. That seems much more natural.

Dr. Joe Chappelle: Exactly right. In any case, again, that’s about writing and literature, it’s not necessarily about the research. But we’re here to examine it all today. After we now have moved their two paragraphs to the introduction, we can get into the rest. So, let’s talk about those strengths and weaknesses for a second here. I want to go one by one because I find them… they’re fascinating to me. I spent a long time thinking about them. Their first strength they tell us is that it was randomized with an adequate randomization method. I don’t disagree with you, but I don’t know that it needs to be listed as a strength of the paper because it’s obvious. If you didn’t do an adequate randomization… and you don’t have to tell us it’s computer-based.

Dr. Jerry Ballas: I think they could’ve easily just said randomized in order to reduce variation between… or in order to reduce potential biases between groups. I mean, that’s the definition of randomization for research purposes, so they could’ve simply said this was a randomized trial. That’s a strength… most places it’s hard to get a randomized trial up and running that gets published.

Dr. Joe Chappelle: I have now tried to do a couple randomized trials and I have published neither of them, so I can attest to that personally. The second one, this one just blows me away, a power calculation was performed.

Dr. Jerry Ballas: Well, what they’re getting at I think is actually a bit of a dig at the studies that they referenced earlier on. They kind of made them sound almost like case series in a way, like descriptive studies. And so, what separates a descriptive study or an observational study from an actual intervention study is a power calculation. They put themselves out there and said we’re looking for this difference, and we’re going to go at it rather than somebody just collecting a lot of data and saying here are the differences we saw.

Dr. Joe Chappelle: Alright. I mean, I see that. I also wouldn’t have written that in the paper.

Dr. Jerry Ballas: Yeah. That’s an interesting one.

Dr. Joe Chappelle: But I do agree with you, they’re trying, I think now that you say that, they’re trying to contrast themselves against the other studies that have come before. And they really could’ve just said a randomized study that was adequately powered, and I would’ve said okay, if they’d phrased it that way.

Dr. Jerry Ballas: Adequately powered with the stated primary outcome.

Dr. Joe Chappelle: Yeah. I’m going to take a step back for a second. So, as I’ve told all you listeners before, I’m the associate editor on a couple of journals, and it’s an international journal, it’s based out of Germany. There are lots of people who submit to whom English is not a primary language for them, and there is a lot that gets lost in translation. And so, something it’s just matter of English not being their primary language. So, I always want to keep that in mind, especially when dealing with a paper that is not from a primarily English-speaking place. So, I will give them a little latitude in there that maybe it’s just an English thing. But still interesting. You think that the reviewers might have said something here, but maybe not.

Dr. Jerry Ballas: And I’ve reviewed… I’m a reviewer for a couple of journals and I will return with a specific consider running this through an English-speaking colleague or service. A lot of places will offer services now, and actually I think if I remember correctly, The Green Journal, if you read their submission guidelines, it’s kind of a novel, but it will actually I think give a resource or tell you explicitly consider an English resource to vet your paper before submitting.

Dr. Joe Chappelle: Yeah. Definitely, especially in something like The Green Journal, where they get so many submissions that if yours is not that readable they will just kick it out right away. Alright, so let’s move on to their third determination of either persistently or just temporarily increased AFI by continuingly following patients until delivery. Again, now that you phrased it in their trying to contrast themselves against other papers, that makes a little more sense to me. To me it just sounds like good study design, but…

Dr. Jerry Ballas: Right. I think they’re, again, contrasting that this wasn’t retrospective, that they put in the leg work to follow them prospectively, which gives your paper a little more credibility.

Dr. Joe Chappelle: Yeah. And then the last two are interesting to me. Number four is that a wide range of gestational ages were included. And I actually don’t know that that was a strength, because that really depends on what they were trying to show. So, that one’s a little weird to me. And if you’re going to put that, then I think they need to justify it. And then the clinical importance of improving AFI was assessed. And a) I don’t really know what that means?

Dr. Jerry Ballas: Yeah, no. That’s kind of a throw-out sentence there.

Dr. Joe Chappelle: And b) I’m not really sure. Because remember folks, that this study was not powered for outcomes. It was only powered for the difference in AFI. That was it. And so, even though they showed all those p values there, you have to keep that in mind. Alright. So, moving on to the negative aspects. These are the limitations. Again, I would probably not write negative aspects, I would probably go with limitations, but that’s a matter of choice, I suppose. One is AFI measurement is subjective and difficult… basically it’s subjective, which I think we all agree is a limitation. Two, that normal pregnancies before 30 weeks of gestation and pregnancies with maternal and fetal complications were excluded. Again, I’m not sure what they’re trying to get at there. I don’t really know how that’s a limitation. I mean, it is in some ways in that it limits how you can apply this information to your own patients, but it doesn’t really limit the study.

Dr. Jerry Ballas: Right.

Dr. Joe Chappelle: Three, maternal position was not standardized during therapy. Again, they showed us no data that maternal position should matter. And so, it’s odd that they put this in there as a limitation. And the only thing I can think of is maybe one of the reviewers made a comment about this.

Dr. Jerry Ballas: Yeah. I was about to say that. I’m sure they got a reviewer that’s a stickler for AFI or wrote a seminal paper in amniotic fluid and put that in there saying you have to tell us the position. Are they left lateral, are they supine, et cetera. So, that sounds like a reviewer-added weakness.

Dr. Joe Chappelle: Agreed. Compliance with treatment was not assessed. That’s something we talked about already and they acknowledged it. The characteristic of amniotic fluid such as solute contents after treatment were not studied. Do you know anything about this?

Dr. Jerry Ballas: No. This maybe gets to… there are some papers out there that talk about sludge, that talk about echogenicity of amniotic fluid. Some papers have shown worse outcomes or earlier deliveries in pregnancies with notably echogenic amniotic fluid. We don’t know what the etiology is, whether it’s meconium and there’s something vasoactive going on or it’s just some of these studies are retrospective, and again you’ve got that retrospective bias creeping into some of these studies. So, that would be my guess as what they were including is perhaps there was something else going on that they didn’t assess because they didn’t comment on the appearance of the amniotic fluid.

Dr. Joe Chappelle: Okay. Yeah, interesting. Then, number six, only AFI indices and not the actual amniotic fluid volume were used to reflect improvement after therapy. Now, if someone could teach me how to measure the actual amniotic fluid volume, I’d be very happy. So, I thought that was a little weird. And again, maybe that’s from a reviewer because it’s kind of out of place and it’s not mentioned anywhere before.

Dr. Jerry Ballas: Yeah, again, I think it’s… You’ll sometimes get some sticklers… you’ll hear them correct their resident or correct their fellows about amniotic fluid index not being the actual amniotic fluid volume. And the only way you can do that is either through actual volumetric imaging or through actual volumetric subtraction by submerging women. And so, they’ll go through a whole academic discussion about the difference of AFI versus AFV.

Dr. Joe Chappelle: Okay. So, maybe they should’ve done MRIs on all these women.

Dr. Jerry Ballas: That would’ve been fascinating, expensive and really probably would’ve gotten yelled at by the IRB.

Dr. Joe Chappelle: And then the last one, and this is probably the largest, the biggest limitation, which we already mentioned, is no placebo was given to the hydration group.

Dr. Jerry Ballas: Correct. And that’s a mystery to me. Like I said, producing a sugar pill that looks like your medication is a fairly common, easy thing to do these days.

Dr. Joe Chappelle: Yeah. And so, really, I would only say, out of all these limitation, there’s probably only a couple that I would actually consider are limitations. But that’s okay. Before I get to their conclusion, which is, again, nice and brief, is there anything else you want to talk about in what they… I mean, I didn’t go through their whole discussion about what they say about the results because I think we covered it in other ways. But is there anything else you want to say about it?

Dr. Jerry Ballas: No. I was hoping to get to that concluding sentence as well, and we’re probably going to have similar takes on what they probably should have kind of framed it and said rather than the way they stated it but I will let you proceed, because we’ve been pretty much eye to eye so far. I’m curious to see what your take is.

Dr. Joe Chappelle: Okay. So, they wrote, in conclusion, our findings suggest that Viagra may offer a new opportunity to improve pregnancy outcomes for women with oligohydramnios. That’s a bold statement.

Dr. Jerry Ballas: Yes, it is.

Dr. Joe Chappelle: Yeah. So, I think that if Dr. Ballas and I haven’t done a good enough job at breaking down that statement already, then we haven’t done a good job talking about this. I mean, nothing they put here really supports this statement.

Dr. Jerry Ballas: No. I think they could’ve been much more… And I’m surprised the reviewers, because I can tell you, I’ve been rejected many a times, and a lot of the rejection comes with language and stating your conclusions, overstating the importance of your data. And this is a sentence that simply could’ve said our study suggest that sildenafil with hydration may improve fluid status of a pregnancy in the third trimester.

Dr. Joe Chappelle: Yeah.

Dr. Jerry Ballas: If you wanted to be bold, you could add a sentence that says, such improvement may aid in guiding physicians later in the pregnancy in terms of delivery and perhaps improving outcomes. Something a little more, you know, open ended.

Dr. Joe Chappelle: Something like some “may”s, some “consider”s, things like that. Because, again, remember their primary outcome and what it was powered for was to see if the AFI increased. And, again, I quibble with their primary outcome because they didn’t actually address it, but they definitely showed that they increased the fluid volume and kept it higher in the women with the Viagra group as opposed to the just hydration, so they definitely showed that, and I’m not going to argue with that. Even though we don’t know why the women were delivered, if we assume that they were delivered for non-reassuring antenatal testing and for persistent oligohydramnios, you can just see in the fact that so many more of them were still pregnant at the end of the study, that it had some effect on the fluid, right?

Dr. Jerry Ballas: Or the physicians.

Dr. Joe Chappelle: Or the physicians, or both. And so, there is something here. There’s something to sink your teeth into here, and I really liked this study. I would never had thought in a million years of giving Viagra to a pregnant woman for oligohydramnios. Now, obviously other people have and that’s why they’re here, but I thought it’s a little outside the box for most practicing providers, and so I was really taken by this, the idea of it. And their execution and their study was decent. Like we said, the limitations were already… but I really liked it, and I really wanted to like this paper. And then the discussion ruined it for me.

Dr. Jerry Ballas: I could see where you’re coming from. And I know, being an MFM, I’ve seen Viagra, sildenafil, being applied for maternal reasons, like we talked about, pulmonary hypertension, we’re seeing more and more of it being used. The hope that in terms of fetal growth restriction, women that we know have poor vascular disease could improve outcomes, that’s still in the works. So, for me, seeing it applied to oligohydramnios as a way of framing placental insufficiency, I actually thought it was a great next step to take. And I agree their discussion goes off the rails a little bit and then kind of just gets into this haphazard strength and weaknesses argument that they probably could’ve cleaned up a little bit more. But I think overall, great discussion generator, great idea hypothesis… Just sitting here, I thought of a couple things in terms of cholestasis pregnancies. I’d love to do a study where I actually measure the cord blood amount of Viagra to see if there’s a possible fetal effect. Could they have done things like ductus venosus studies and Doppler studies within the fetus, MCA Dopplers, that would’ve been interesting to see in order to measure fetal effects and placental effects, and even doing placental biopsies. I would’ve loved to have seen placental biopsies between these two groups and see if we can correlate with reference number three about dilated vessels in groups treated with Viagra or not. So, this study can go in many different directions, I think it’s a great hypothesis driver. I don’t necessarily think I will be inviting the Viagra rep over to my practice any time soon, but definitely some conversation starters at work.

Dr. Joe Chappelle: So, that leads us to two more things, and I promise everyone we’re almost done here, we’re wrapping up. One is, is this applicable to our patient population? And I think we both agreed that we have women like this in our population. You probably have more than I do given how you practice. So, it is applicable to our patients, but I think we can probably both agree that we’re not going to apply it to our patients yet.

Dr. Jerry Ballas: Yeah, no. I think I’ll have a little more of a wait-and-see approach. I will discuss it with patients. I do believe in picking the right patients, telling them about research, getting their consent, explaining the limitations just like we did tonight and letting them make their own decisions. I would be interested to see who would go along with this or not in my own head, actually.

Dr. Joe Chappelle: So, you would actually offer this to women.

Dr. Jerry Ballas: I would talk about it. I would talk about it and explain how it’s not a regimen that’s currently proposed by our governing bodies, but there are studies out there to show possible improvement.

Dr. Joe Chappelle: Okay. There folks, is the difference between a general Ob/Gyn and an MFM.

Dr. Jerry Ballas: I’d ask you to refer your patient to me- no.

Dr. Joe Chappelle: There you go. Exactly right. And so, the last thing I want to finish up with is I want to talk about their abstract. The abstract is usually the last thing that gets written because you are abstracting the paper, so that makes sense. But it’s also the first and usually only thing that people read. And so, I always like to look and see does the abstract adequately reflect the paper? So, I’ll open it up to you first.

Dr. Jerry Ballas: I think overall it does a pretty good job. I think it actually seems longer than the methods that I would’ve thought, having read the whole paper. The results section actually seems longer too. But I think they did a decent job highlighting what they wanted to show you. But definitely reading the paper and analyzing like we have was a must, because if all you did was sit on the toilet, read the abstract, you’re done and then go on, you may have a skewed concept that Viagra will cure oligohydramnios.

Dr. Joe Chappelle: Right. And actually, I will say that their conclusion in the abstract is better than their conclusion in the paper. Their conclusion for the abstract is that Viagra increases amniotic fluid volume in pregnancies complicated by oligohydramnios, and I say “ding, ding, ding!” They showed that. So, they should’ve taken the conclusion there and put that in the end of the paper, I would’ve been a lot happier. And I do agree, it’s humorous that their results in their abstract is almost the same length as the results in the paper, but that’s okay. Neither here or there. Any final thoughts on this paper?

Dr. Jerry Ballas: No. I think it was a great opening salvo for introducing a possible new line of therapy for high risk physicians that deal with these kind of idiopathic findings, enabling us to possibly offer new therapies to women that are theoretically low risk high reward. And I’d love to see how the literature evolves around this.

Dr. Joe Chappelle: I agree. And I want to go back, and I think both of us, and maybe me a little bit more, have given this paper kind of the rough treatment here. And I want to say that I applaud this group’s work. I think that any time you do any kind of study like this, it’s hard, and it’s years of work, and it’s a lot of hard work. And so, I really applaud the effort they put into this. I think they could’ve nipped and tucked a little bit, but I am very happy that this was done and published so that we can talk about it.

Dr. Jerry Ballas: Agreed.

Dr. Joe Chappelle: So, I think we’re going to conclude there. This is the first time we’ve done this. We didn’t know how long this was going to be, I don’t know how long the next one will be if we do it. I do hope that Dr. Ballas and I can get together and do this on an either monthly basis or semi-monthly basis, because I feel like there’s real value in one, looking at new papers and analyzing for their own clinical benefit, but also, you can take the approach that we’re using and apply it to any paper so you know whether it’s something that is valuable to you or not. And I think that there’s so little of that out there for people to listen to or to interact with that I hope that people really get something out of this maybe overly long discussion that we just had about this paper.

Dr. Jerry Ballas: And there’s something to be said about discussion these kind of works with somebody or even in a group, and I think that’s what makes journal clubs so effective, because someone will pick up on something you didn’t. So, when Joe picked out the primary outcome discrepancy between what they stated and what they actually published, that was pretty eye-opening to me. So, it’s always great to have different sets of eyes on the same data. You’d be absolutely amazed by the different conclusion that can come from things.

Dr. Joe Chappelle: So, with that I’m going to say thank you very much to Dr. Ballas for joining me in this little odyssey we did here and embarking on a new project. Like I said, I hope that you’ll be hearing from us again soon when we do this again. I am going to look to include some new people in this, so if you have an interest in clinical research or journal club type things and you want to be involved in this, please send me an email. You can find that at feedback@obgyn.fm. You can join Dr. Ballas and myself and a few other brave folks on the Slack. It’s a little quiet at the moment but we had some interesting conversations about postpartum endometritis, but we’re doing some new topics soon. So, please, again, you can send to the same email and I’ll send you an invite. And this actually was a great paper, this was not really planned, but we talked a lot here about fetal assessment and fetal wellbeing, and that’s actually going to be out next topic. So, the next three episodes are going to be about antepartum fetal surveillance, intrauterine growth restriction and, again, this was not planned folks, Dr. Ballas did not know this ahead of time, but the third one is going to be cholestasis.

Dr. Jerry Ballas: Oh, hey there. What I surprise, I like it.

Dr. Joe Chappelle: And so those will be the next three episodes coming up and then hopefully, we’ll be back again for another one of these journal clubs. Any final words there, Dr. Ballas?

Dr. Jerry Ballas: No. This was a fantastic experience and I’m hoping to see this grow. I’ve gotten the word out to my maternal fetal medicine colleagues, so hopefully we’ll see a little bump in our Slack traffic.

Dr. Joe Chappelle: There you go. Alright. Well, everyone, thank you so much for listening. And so, until next time.