Birth Control Pills in PCOS Treatment - Benefits, Risks & All You Need to Know

Birth control pills or oral contraceptive pills (OCP) can be used for long-term treatment in women with PCOS who are not planning pregnancy. These pills have been shown to help regulate many PCOS symptoms such as irregular periods, extra hair growth and acne.

However, due to the association of PCOS with metabolic syndrome, there is a controversy regarding the risks versus benefits of birth control pills in women with PCOS.

Many women experience various side effects as well as withdrawal effects of birth control pills.

Dr Carolyn Alexander of Southern California Reproductive Center will help us understand the science behind use of birth control pills in PCOS treatment, the risks and benefits involved, and other alternatives touching upon recent research in hormone combinations more effective in PCOS management. PCOS patients advocates Lisa Rosenthal and Tatiana Alafouzo will guide the discussion from the patient panel.

Full Transcript:

Shweta Mishra: Good Evening everyone I'm Shweta Mishra I welcome you all to this session on birth control pills in PCOS treatment in association with the PCOS Tracker app that aims to help women keep track of their PCOS symptoms more information about which is available on the website pcostracker.app. Today I am beyond excited to welcome our eminent guest expert Dr. Carolyn Alexander of Southern California Reproductive Center, to educate us about the risks benefits, and everything we want to know about the use of oral contraceptive pills in the management of PCOS. Winner of numerous awards in medicine and teaching and featured in several media outlets Dr. Alexander is board certified in Obstetrics and Gynaecology as well as in Reproductive Endocrinology and Infertility. She has done extensive research on PCOS and specializes in dealing with patients facing infertility as a result of PCOS. Dr. Alexander, welcome to the show. Thank you for finding time to talk to us today.

Dr. Carolyn Alexander: Thank you so much for having me. It's an exciting topic, important topic.

Shweta Mishra: Thank you, Doctor pleasure is all ours. On the patient panel, we have PCOS advocates Lisa Rosenthal, who has been advocating for 30 years in this field now and Tatiana Alafouzo, who is a

PCOS warrior and PCOS researcher joining us from the UK. Lisa, Tatiana, welcome to the show and thank you for joining the panel today.

Lisa Rosenthal: Thank you for having us.

Shweta Mishra: Thank you. So, Dr. Alexander, I know you want to get back to your patients as soon as possible. So, I'll just jump right in and to set the stage and give a little bit of background to our audience could you please begin with talking a bit about the mechanism by which birth control pills help in preventing conception?

Dr. Carolyn Alexander: Sure, oral contraceptive pills are combination of estrogen with progesterone. The progesterone is the majority of the mechanism of action, but there is a little bit of estrogen in there, which helps keep the uterine lining stable so that people don't get spotting when they're in between placebo weeks. The interesting thing about what that does is it tells your pituitary, which is your master control gland that there is plenty of estrogen here please don't send follicles stimulating hormone down to stimulate a follicle and ovulate. In addition, it also tells LH, which causes the egg to come out of the shell when you ovulate to be suppressed. So typically, most people on the birth control pill, if you're taking it every day at the same time, will have suppression of those two master hormones and it increases your liver production of SHBG or Sex Hormone-Binding Globulin which then can bind to the free testosterone which is floating around. So, a lot of people with acne or hair growth or hair loss on their head, can start to see some improvement with that because of the rise that SHBG drops the free testosterone. In addition, it blocks the Corpus luteum or the ovulatory remnant that makes hormones and so people tend to have less chance to get pregnant and it thickens up the mucus at your cervix so that sperm can't really swim as freely through. But if we skip a birth control pill, there is a chance to spontaneously ovulate, and some patients can get accidentally pregnant if they're not consistently taking their pill at the same time, especially if they weigh over 200 pounds, there's quicker absorption in your system and the opportunity sometimes to spontaneously ovulate.

Shweta Mishra: Right, okay. Thank you so much for explaining. And how do these pills help in PCOS treatment? Could you elaborate, what mechanism is played there?

Dr. Carolyn Alexander: Sure, it's similar to the increase in SHBG or Sex Hormone-Binding Globulin, that will help us find the free testosterone. There's a little debate about whether DHEAS which is a male hormone from your adrenal gland, if that will slightly be suppressed. I've had patients over the years, asked me to check that when they're on the pill and we still do see it pretty high. The way that the birth control pill helps PCOS is to protect the uterus from endometrial hyperplasia, which is a pre pre cancer issue that comes when the lining thickens because we're not getting our period every month to shed the lining, the uterine lining can get very unhealthy inside and so it's really important if you're not getting your period by the 40th day to talk to your doctor about either plain progesterone or a birth control pill combo, which is estrogen with progesterone. The other thing with PCOS that I found is some people if they feel their mood swings, go up and down there's a group of PCOS patients that when they go on the birth control pill, it's a steady-state of a hormone compliment and they feel a little better in their mood, but there's a subset that then also, sometimes feel the blues and feel down, and don't feel like themselves. Then right away, switch that type of pill. We're blessed here to have so many types of progesterone types in the pills. Even myself I felt different on different types of combination pills, and I can say that I can recollect the one that I felt like totally good on it and when I was younger. So, it really can affect mood in a good way, in a not a good way. And some women with PCOS, it does make their metabolism get better and some patients they feel very bloated and kind of water retention with the pill, so we change the brand for that, that changes the type of progesterone. Usually, we can kind of tailor and figure out, which pills going to help the most.

Shweta Mishra: Right, Okay. You have to kind of take it on a case-to-case basis, right? Thank you, doctor. With that, I will move on to the patient panel now. And first on the panel, we have Lisa Rosenthal, who has been advocating in the field of quality for 30 years now. Motivated by her personal journey, she is determined to help others who are undergoing fertility treatment. She is the founder and teacher of the fertile

yoga program. And is also a certified grief recovery specialist. Lisa, thank you for joining today and the floor is all yours.

Lisa Rosenthal: Thank you for having me and for being here with you and I also have PCOS myself. So, there's a lot of personal at stake. So, Dr. Alexander, if birth control pills are controlling the symptoms of PCOS, right? And it's really, they're working. Well, how can somebody try to get pregnant without kind of resuming those symptoms?

Dr. Carolyn Alexander: Yeah, that's a good question. Sometimes when people say in about six months, I want to try what we'll do is, we'll discuss proper nutrition, prenatal vitamins, strategies to avoid insulin, yo-yoing of insulin. And right, when they stopped the pill, I usually have them start to try because there's a blessing of three months that decrease in testosterone as well as the AMH if it's really high sometimes after the birth control pill, it will be a little lower, so less inflammation in the system. And there's sort of a blessed time where people can get pregnant. Even for myself when I stopped the pill, I started trying a night, I conceived. But there are some in the past we used to say, you have to take a month, breather off the pill, then start to try, but it seems to me that there's a lot of patients who conceived in that window of that three months where you're in a better opportunity. If the patient is on spironolactone, I usually have them stop it six weeks ahead because it blocks the Androgen receptor. And we don't want that right before, the person's going to get pregnant, even though the half-life is debatable on it. But I usually have them stop at a month or more before they start to stop the pill and start to try. I warn patients that they may have to be a little more cognizant of eating and exercising and mindfulness to kind of keep your cortisol down so that they don't get, all the explosive symptoms. Some patients, get a little bit of acne that when they stop it. It takes a little time for that to pop up from stopping a pill. And a lot of people who are over 35 years old are coming in saying, I may stop the pill at six months, please help me figure out what to do. So, we check the semen analysis. We check if we need to check their fallopian tubes. We talk about making sure the thyroid and vitamin D levels are healthy, their pap smears up to date. So, there are a few checkpoints before we stop the pill that we can do so that you're not taking too much time off the pill and not and then realize that we should have been working hard on the sperm. Dr. ___ from Hershey, Pennsylvania, he did a study looking at women with PCOS and what was interesting is a third of the time, there was a malefactor. And so even though in our mind for, like oh man, it's going to may be hard to get her to ovulate, we got to get her as healthy as possible. We don't want to forget that, about a third of the time, it can be a malefactor, too.

Lisa Rosenthal: Really fascinating answer. I had no idea about that sort of lovely three-month, period, That's amazing. Really helpful. Thank you. So, the second question is sort of twofold did birth controls stop or help me ovulate. And if so, what were they doing and why did I experience bleeding? I think the question sort of goes to the idea that the patient got regular periods, but were they ovulating? Just because you bled.

Dr. Carolyn Alexander: That's a good question. So, the uterus, I think of it when I teach medical students as bricks with mortar. So, there's like kind of glue between the bricks and so for your body to shed the lining, you just need a withdrawal of progesterone and a little withdrawal of estrogen. So even at 50 years old and let's say I'm not getting my period at all, and I think I have menopause. If I give you a little bit of estrogen and progesterone for even two weeks and stop it suddenly you'll shed the light. So even though it seems like it's a period and they're ovulating. It's not ovulatory periods with the birth control pill. It's because those bricks and mortar are therein, the mortar comes away and the bricks shed. I don't know if that's a good explanation. But that's the way I think about it and then you're not necessarily ovulating. There are some people who can ovulate on a progesterone-only pill. And so that's why that pill has to be taken sharply within exact 24 hours. Because if you even go, a few hours later, your body can spontaneously ovulate.

Lisa Rosenthal: So, if I'm understanding you correctly and that was a great analogy. I love the visual if I'm understanding you correctly. What you're saying is that ovulation and bleeding actually don't have that much to do with each other?

Dr. Carolyn Alexander: Not really.

Lisa Rosenthal: Excellent. I think a lot of women assume that if they're bleeding that they are also ovulating. I think that was what that question was trying to get to. So, the next one you've really answered which is how long do I need to be off birth control before I start fertility treatment?

Dr. Carolyn Alexander: Yeah, we use birth control pills to optimize the hormones prior to fertility treatments. So, there's a little debate on that when you're freezing your eggs, if you're thinking to freeze your eggs, and some people may respond better to the injectable IVF medications. If they've been off the pill for a few weeks, but there are some people that are better coming right off the pill. It depends on your AMH and your ultrasound, but in general, if you're going to try like naturally, I would start trying when you stop the pill.

Lisa Rosenthal: I love that. It's so individualized. So, what about diagnostic testing for fertility. Well, if a patient is on birth control, will the birth control pills and hormones mask the PCOS? Will they mask any other fertility problems?

Dr. Carolyn Alexander: That's a good question. So, it's very hard to tease out congenital adrenal hyperplasia from PCOS when someone's on the pill because the test differential is an adrenal gland hormone called 17 hydroxyprogesterone, and that's normal when you're on the pill. And so, to really get a sense of what's going on, especially in LA, with our Ashkenazi population, our Mediterranean patients, they sometimes are told you have PCOS, but then when we see them and we check, we catch pretty often non-classical adrenal hyperplasia, which can look exactly like PCOS, but it's very important to differentiate that because if her partner has a CH Gene than a baby has a one in four chance to get both copies and that can be pretty dramatic and affect that baby. And so, it's important to differentiate some hormones. So sometimes we do have to say stop the pill come back in five to six weeks, and then we'll do a panel. But interestingly, when you're on the birth control pill, the textbook answer, is that the Anti-Mullerian Hormone level-AMH is still predictable and helpful and that in Europeans are using AMH to diagnose PCOS. And at ASRM, which I'll bring up at the end, they had a really interesting paper showing that if the AMH was over six, you have a high probability, that you might have PCOS. Here we don't use it as our diagnostic criteria, we use it as a red flag to see that there might be PCOS, but we don't use it as a diagnostic criterion.

Lisa Rosenthal: Does it affect FSH?

Dr. Carolyn Alexander: Yes. It'll make it normal.

Lisa Rosenthal: Interesting. Okay, so that's certainly a big thing. Thank you. Great answer really, so helpful. So, my last question is what could or should I be on instead of birth control? Because obviously the birth control pills as you've been saying really do help so many different symptoms and challenges, we face trying to if we have to be off birth control because you are trying to get pregnant. Is there anything else that a patient can do?

Dr. Carolyn Alexander: Yes, Spironolactone is helpful.

Lisa Rosenthal: Okay, it's really interesting to hear this Shweta. And my understanding in the United States is AMH, is really being used as a predictor by most board-certified reproductive endocrinologists. ____ Connecticut, that is our predictor. It is not just a red flag. It is what we look at, but it is fascinating to hear that it may be a connected to PCOS as well.

Shweta Mishra: Right, right. Yeah, and I think different practices may follow, different criteria for diagnosis, a part from the Rotterdam criteria that is like the three steps that they follow, right. In addition to those different clinics may be using different criteria.

Lisa Rosenthal: Yes, but AMH, the Anti-Mullerian Hormone I think is one of the biggest predictors for infertility and for ovarian aging as well.

Shweta Mishra: Yeah, that's right. Yeah, there are all these outliers. I know that my personal experience is

that when I was diagnosed with a low low amount of AMH once. And everything happened in between, and after 2-3 years again, when I was diagnosed, it was all normal. So, I was totally confused there, and one doctor said that, yes, you are low on your reserves you should hurry up and the other one was like, okay no, you're all good. So, good that the normal AMH levels came closer to when I got pregnant, so I'm happy about that. And I know there are technicalities that I don't understand but good for me.

Lisa Rosenthal: Tatiana in terms of that with patients it's what makes things so confusing. All the individualization is wonderful because patients are being treated like unique people, but it can be very confusing when you have one respected clinician saying one thing and one another.

Shweta Mishra: Absolutely.

Tatiana Alafouzo: I mean, that's why there's really no universal like criteria for diagnosing PCOS. And also, I think why so many like, Dr. Alexander was saying so many cases either get miss diagnosed or undiagnosed. I mean, 70% of the patients, go undiagnosed because it's like you're saying, the personalization is great, on the one hand, but on the other hand, it's like so many people look different from one another that there's or have different test results that it's almost like we're not really sure what's going on or maybe one clinician has something that they look at and another one has something else as you were saying.

Lisa Rosenthal: I literally got diagnosed in my 50s. I'm in the field, but even when I got diagnosed, it's like maybe yes, maybe no. It's hard, the reputation PCOS has as it's hard to diagnose or it's easy to diagnose and again because it's not a disease and it doesn't follow sort of the same path.

Dr. Carolyn Alexander: I was listening in. So, I felt that was really interesting.

Lisa Rosenthal: And so, the question was, what could or should I be on instead of birth control for PCOS. So, for a patient who has to go off birth control to try to get pregnant and has that re-emergence of some of those symptoms. What could they do instead or beyond instead?

Dr. Carolyn Alexander: Metformin will lower testosterone. Some people get GI upset with Metformin. I've become a more of a fan of myo-inositol and I've even tried it myself. I think it's interesting and helps improve insulin resistance too, and you could take that, so you get a positive pregnancy test. And then the other thing is that the exercise, diet, acupuncture. I'm a big fan of mindfulness and acupuncture too.

Lisa Rosenthal: Well, thank you so much. That's it for me. I'll send it back to you, Shweta.

Shweta Mishra: Thank you. Thanks, Lisa. Great questions. Next up on the panel, we have Tatiana Alafouzo. Tatiana who is a PCOS warrior passionate about empowering women with PCOS, take control of their symptoms. She is a registered associate nutritionist with the Association of Nutrition in the UK and is currently working on her Ph.D. focusing on complementary and alternative therapies for PCOS management. Tatiana, please go ahead.

Tatiana Alafouzo: Hi Dr. Alexander.. Thank you so much for taking the time to answer my questions. So, I just was curious. What are the most common side effects that women with PCOS on birth control experience or come to you about and do these differ from those who do not have PCOS?

Dr. Carolyn Alexander: That's a really good question. I was thinking about that a lot, and I feel that the mood changes on the pill, seem more noticeable in women with PCOS than I feel like I've heard a lot over the years. I do think a lot of patients with cystic acne or acne on their back see improvement with the pill, but there's this subset of some patients is their adrenal androgens are high that it doesn't improve or sometimes it worsens for a short amount of time. The way it changes are it's really hit or miss. I noticed in puberty in the younger women there are some people that seem that their ___ improves when the testosterone goes down with the pill. And I think again because I think of the birth control pill as having 8

types of progesterone types and some people are just so much more sensitive to norethindrone versus levonorgestrel versus ___ versus desogestrel versus norgestrel. So, I think of it, as I have to sort of figure out, which one's better for them, from the bloating, headache, nausea, weight gain. If the patients take the pill at night, they have less nausea. A lot of patients say that they also don't forget because everyone brushes their teeth, hopefully, so I tell them to put it with your toothbrush. If you're going to brush your teeth, take your pill at night. And then the heaven forbid, the blood clotting risk, which I was reading articles last night to prepare for today and I was interested to see that there is sort of an association in some women with PCOS that there's a higher predisposition for blood clots, but it's hard to tease out as that and a weight thing like because of apple-shaped body and maybe having more of our tummy weight which I have too but or is it actually what's called plasminogen activator (PAI-1) that the levels were may be different in someone with PCOS. I started adding PAI-1 mutation to my patients who have recurrent pregnancy loss with PCOS, and I've caught it like a few times and it's not a common thing to catch. So, there are some blood clotting things. So, drospirenone, which is in Yaz and Yasmin may have a higher risk of blood clots. So, it's important to think about that, again it is an individual care situation to each patient.

Tatiana Alafouzo: Thank you so much because my next question was actually going to be many times those with PCOS are prescribed low dose or an ultra-low dose pill like Yaz and Yasmin including myself and just as you said about the potential blood clotting factor, so would any family history of a stroke or any kind of cardiac issues come into that when you're sort of making that decision of whether or not to prescribe a pill like that?

Dr. Carolyn Alexander: Yes, I think what I've been doing which is a teeny bit of ___ is if they say their dad or mom or sister or cousin, or anybody had a blood clot at a younger age than we can do, what's called the thrombophilia panel, which is like a blood panel of genetic mutations that cause us to be predisposed to blood clots.

Tatiana Alafouzo: I think you muted.

Dr. Carolyn Alexander: Yaz and Yasmin to start them. But if they come in and they say, well, I was on it for years and I felt great. Then I noticed that once they've been on it for at least a month and heaven forbid didn't really get a blood clot. Then the likelihood that, that will pop it is low. It's the same risk is if you're going on a long flight or a long car ride, take an aspirin, maybe an aspirin, maybe or talk to your doctor and think about that just and keep your calves moving. Don't just be dehydrated and sitting in place for hours and hours. Because anybody on the pill could get a blood clot from that.

Tatiana Alafouzo: Thank you. Thank you so much. Lisa my goodness just going back to your story, I cannot believe that you were diagnosed so late.

Lisa Rosenthal: I was diagnosed because two of my daughters were diagnosed actually.

Shweta Mishra: Oh my god, that's like a reverse diagnosis.

Dr. Carolyn Alexander: ____ I've noticed that there are Anti cardio like antibodies which increase the risk of blood clots as very high especially if they have like, even if they had a symptomatic covid, so, I think we're seeing something interesting about post covid patients, and that were noticing that too.

Tatiana Alafouzo: My goodness. I didn't even think of that. That's so crazy. It's like a whole another layer to even add on to the whole blood clot situation or something to think about when you have PCOS. What composition of birth control pills have you found to be the most effective for your patients with PCOS, which you found both tolerable and safer? They've kind of maybe not had as many mood issues on or things that you had mentioned before.

Dr. Carolyn Alexander: Desogestrel has been really good. I've noticed it it's even though some of the progesterone say androgenic and patients call and say oh what about that? Any type of pill will still improve

PCOS in patients. So, Loestrin can be helpful and also Ortho-Cyclen and ___ all the types of pills. I have a lot of patients who love NuvaRing, because they can leave it in for four weeks then take it out, put a new one and they can pick when they want to have their period.

Tatiana Alafouzo: Oh, well, do you mind, please explain the pros and the cons of progestin-only pills?

Dr. Carolyn Alexander: Sure. Some people cannot tolerate the estrogen effect of the pill. A patient today she said that when she was in college, she got like severely depressed when she was on the pill. She didn't feel like herself. She tried different types. She couldn't tolerate it. Another patient of mine really had bad headaches and nausea. If someone has migraine with aura, they should consider a progesterone-only pill because the aura has some risk factors also for blood clots. If their blood pressure is high, in our young PCOS patients, we noticed the lower number, the diastolic blood pressure is higher in a lot of them it's not always the top number and so is ___ from a progesterone-only pill. And breastfeeding, we encourage a progesterone-only pill, so we don't suppress milk production in that window after having the baby.

Tatiana Alafouzo: Thank you so much. I didn't know all of these things. And lastly, do you have any advice for a PCOS patient, who has been on birth control for a very long time and now is looking to come off of it after many years, please.

Dr. Carolyn Alexander: Sure. I would check a hemoglobin A1c to see if you need to be on Metformin. I would like to plan ahead. So, try to eat really healthy, lots of vegetables in your diet, exercise, and then keep a little log when you stop the pill if you're really starting to notice fluctuations and acne, growth, hair loss, things like that. Keep a login. Then you could discuss it with your doctor. What would be the best kind of course of action that helps each of the symptoms?

Tatiana Alafouzo: Dr. Alexander, thank you so much for answering all my questions. I really appreciate it.

Dr. Carolyn Alexander: Good to see you. Yeah.

Shweta Mishra: Thank you. Thank you, Tatiana great questions. So, Dr. I'll be mindful of your time. I have just a couple of questions before we wrap up this show and I think you talked a little bit about this thing that I'm going to ask you. Just wanted to understand if you have observed, any differences in the ease with which your patients conceive between the ones who were on birth control pills compared to the ones who were off the pill before they came to begin fertility treatments with you.

Dr. Carolyn Alexander: That's a good question. I think it has a lot to do with how high their testosterone is, the total and free testosterone as well as AMH if they come in and they've had regular periods and have not been on the birth control pill and their Androgen panel is normal, hemoglobin A1c looks good, and their AMH is between 2 to 8, I feel like it's doable. I think the patients who come in and say I haven't had a period in six months, I don't feel like myself, there's something off, something is wrong, I can't sleep very well, I'm not feeling like myself. That's where I find it, where it's a little more difficult plus the uterus has been bombarded by unopposed estrogen because they haven't ovulated and had a shedding of the lining. Sometimes that uterus needs a kickstart with some progesterone to really, like start fresh so that we don't have an increased risk of miscarriage we want to optimize that was a lecture I gave a few weeks ago, on optimization of hemoglobin A1c before pregnancy, and less congenital anomalies in the babies plus if your hemoglobin A1c is above 5.7, you start to have an increased risk of anomalies in pregnancies which are malformations when the early embryo is forming. And so, it's really important before you start to try to get a check-up, check that your vitamin D level is 30 to 50, your TSH is normal, your thyroid level and that your liver and kidney function is the normal lot of women with PCOS, get NASH, which is non-alcoholic like liver enzymes bumps, and now my new question with a lot of patients is, do you snore? Because there are some people with sleep apnea and that lowers oxygenation to the pregnancy and can cause IUGR- Intrauterine growth deficiency. And so, it's important to check on a lot of the whole person. And now since covid, a lot of people don't go to the doctor much. So, we are their sort of primary care doctor as well as OB and all that.

Shweta Mishra: Right. Thank you. Thank you for that explanation. And lastly, I think I'll just take a couple more minutes if you could briefly share some of the interesting research updates from ASRM 2021, right? You just visited the conference, and it would be great if you could discuss a little bit about the research papers that were discussed about PCOS and the use of birth control pills and treatment.

Dr. Carolyn Alexander: And yeah. Well, there was a lot of talk about AMH, there was well-done poster on that, using it as a diagnostic criterion. I think, what was really an echoed thing through the lectures was with IVF and PCOS is to freeze the embryos and put them in later because they had less OB complications, pregnancy complications. If they froze the embryos, here we mostly do frozen embryo transfers, but some patients want a fresh transfer. We don't do it if their estrogen goes over 2800. So, if your estrogen is very high at the time of the retrieval, the uterus isn't as fresh and ready for the embryo. So, it may be better to freeze the embryos for the future. The other thing they talked a bit about was the protocols for PCOS patients and ways to avoid hyperstimulation using Cabergoline and Metformin, and Lupron only triggers, which is a GnRH Agonist trigger, which has essentially made hyperstimulation syndrome really very rare. I have knocked on wood, had one in a long time. So, we used to see it so much more frequently over these 20 years of doing this, but now it's been so rare to see hyperstimulation.

Shweta Mishra: Right. Thank you. That's very interesting to hear and I'm particularly interested in the frozen versus fresh embryo transfer resource that you just discussed and would be great if you can in another talk, we can totally discuss that right. Yeah, that's it. All right. Thank you so much for your time, Dr. Alexander. I think that's a wrap for today and it was wonderful listening to all the information shared that you. And I'm sure this talk will be having helpful for women of all ages who are either planning to use birth control pills for PCOS treatment, or they are using them right now. So, thank you very much for all the information shared, and thank you for finding time from your busy schedule to educate us today. Tatiana and Lisa thanks for joining the panel today and guiding us with your very relevant questions. I thank you all for whatever you do for the PCOS community. And I request everyone in the audience to check out the PCOS Tracker app that has been downloaded more than 51000 times now. I would appreciate each and every feedback from you guys, and it will help only to make the app better for women to use. Please send your feedback to shweta@trialx.com, and to listen to our other upcoming talks on PCOS and other topics, please visit our website Curetalks.com. So, until next time, thank you everyone, and have a great day and stay safe. Thank you.