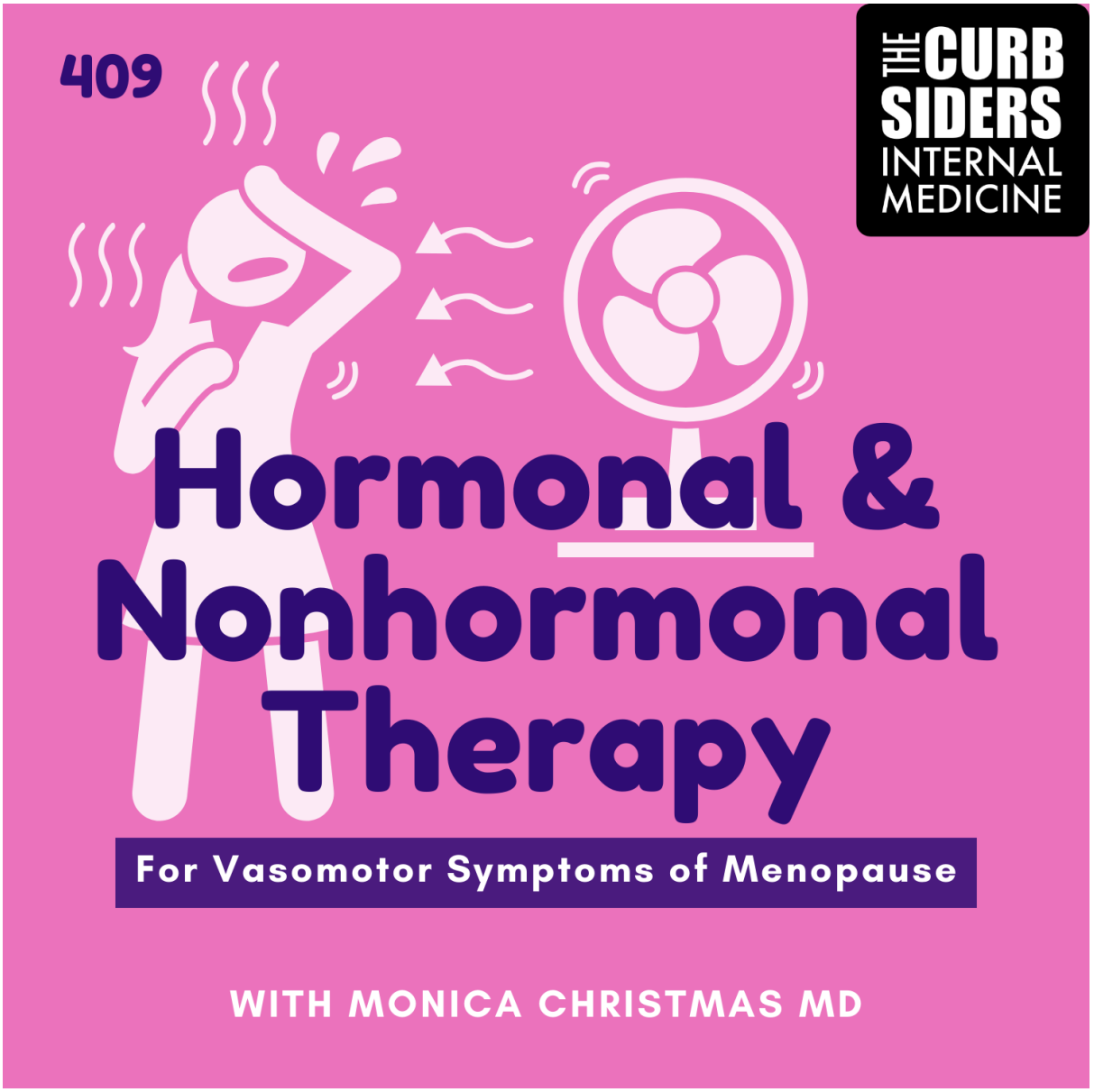
#409 Hormonal and Nonhormonal Therapy for Vasomotor Symptoms of Menopause



Matt: You know, Paul, the local high school is having a menopause seminar.

Paul: [laughs] Go on.

Matt: There will be a de-menstruation after last period.

Paul: You know, so to the listeners, we were going to have [Matt laughs] dueling puns and I'm jumping ship. I am not going to be any part of this.

[disclaimer]

[The Curbsiders theme]
Matt: Welcome back to the Curbsiders. I'm Dr. Matthew Frank Watto, here with America's primary care physician, Dr. Paul Nelson Williams. Paul, how are you?

Paul: I'm good, Matt, how are you doing?

Matt: I'm great. Obviously, based on the pun that we opened with, we are going to be talking about menopause specifically.

Paul: It'd be so weird if weren't. [laughs]

Matt: [laughs] Tonight, we're going to be talking-- [crosstalk]

Paul: [laughs] Ankle pain exercise.

Matt: Ankle pain? Yep. There you go. We'll be talking about hormonal and nonhormonal therapy for vasomotor symptoms of menopause. We have a great returning guest, Dr. Monica Christmas. She is an expert on all things menopause and really just had so many great tips. So, really excited for people to hear this. But Paul, before we get to that, could you tell the audience what exactly is it that we do on The Curbsiders?

Paul: Sure, Matt. As a reminder to our audience, we are The Internal Medicine Podcast. We use expert interviews to bring you clinical pearls and practice-changing knowledge. As you mentioned, Matt, we had a great conversation with Dr. Monica Christmas. Shall I remind our audience who it is that we talk to?

Matt: That would be fantastic, Paul. I'd love to hear her bio.

Paul: She is an associate professor and director of the Menopause Program and Center for Women's Integrated Health in the section of minimally invasive gynecologic surgery at the University of Chicago Medicine in Chicago, Illinois. I think I got all the words in there.

Matt: [chuckles] You did.

Paul: She is on the Board of Trustees for the North American Menopause Society and is on the International COMMA, which is Core Outcomes in Menopause and the capitalization there is surprising. Also, the MAPS, the Menopause Priority Setting Partnership, which she talks about later in the episode steering committee. She is a tireless advocate and a pioneer championing the need to better understand unanswered questions about the optimal management of menopause in racially and ethnically diverse populations. In this episode, Dr. Christmas talks us through various options for the symptoms of menopause. So, the vasomotor symptoms and even the genitourinary symptoms of menopause and when to consider hormone therapy, which might be more often than you think, how long to treat, what formulations to go with, what our options are, what the contraindications are.

So, I feel like I don't know about you, Matt, but I feel like I have a much better framework overall as to approaching a topic that may be a little bit anxious, I think, before we talk to Dr. Christmas.

Matt: Paul, I did want to remind the audience that this episode will be available for CME through VCU Health at *curbsiders.vcuhealth.org.* One last thing, Paul, we have a Patreon now, and people can join our Kashlak family if they want to get bonus episodes, if they want to hear all the episodes ad free, our whole catalog Paul and we also have a Discord, which is a place where it's a private forum for Curbsiders superfans. We're on there answering questions, interacting with the audience. People should join if that sounds like something that would be fun to them or if they just don't care for the ads in the episode, or if they just want bonus content. Two extra episodes a month on the Patreon there. Anything to say about that, Paul?

Paul: I mean, the Discord part is cool. It's nice to be able to interact with our listeners, and I think they run cases past each other. We talk about a lot of nonmedical stuff in terms of book and movie recommendations. It's a fun space to hang out. So, if that's appealing to you at all, I would strongly encourage you to sign up.

Matt: All right. With all that, let's get to the episode.

[music]

Matt: All right, Monica, we've been talking for a while here. You're a previous guest on the show. We're so glad to have you back. But in case people didn't hear the first time around, tell people what's a hobby or interest that you have outside of medicine that you wanted to share with them.

Monica: I am a yoga enthusiast and I love reading on the beach, nothing medical, of course.

Matt: Good choice.

Monica: Yeah, and adding to my beach time, I love walking on the beach and listening to audiobooks in addition to my yoga.

Matt: Yeah. How about a recent audiobook that you've enjoyed?

Monica: I am thoroughly enjoying it, but I have to say, it really is impacting my mood and making me sad. [Matt laughs] But I'm listening to the *Goldfinch* right now.

Matt: Oh, yeah.

Monica: I love reading, so if a book makes it to my bookshelf, that means I've read it already. But I have the ones that I haven't read yet in my room, and the *Goldfinch* has been one that I've been meaning to read and hadn't. So, I decided oh, it's warm. I've been walking every night. I'm going to listen to it. But, man, it's gut wrenching, but it's so beautiful.

Matt: I had the same feeling, I was reading it on Kindle or something, and I didn't realize how long it was. I was like, “I feel like I've been reading this for months. When is this thing--” But it is, yeah, if you are prone to melancholy, that book is just like it may add to your mood, but it's a beautiful book I agree.
Paul: Longtime listeners may remember there was a year where I was trying to watch a new movie every single day. As part of those, I was actually trying to include the movies and American film institute's top 100. I never made it to *Sophie's Choice* for that very reason. I've

just been like, “I know. I'm sure it's fantastic, but I'm waiting until I have the emotional reserve for it, and that day has yet to come, that was, like, six years ago." So, Sophie's Choice, sorry, but I know how it turns out. Anyway, this is not about me. This is about you. Dr. Christmas. Different type of question, let me ask you about a piece of advice or feedback that you either given that you loved or that you love to give to your learners.

Monica: Oh, my. So, you switched up the question a little bit, so I'm going to give you two answers. So initially, I think I thought of it as what is a pearl about menopause and this menopause transition. It takes me back to that expression that says health is wealth. I always tell my patients, you cannot eat yourself out of no exercise, and you can't exercise your way out of a bad diet. So, that is my menopause pearl. We'll talk more about why I'm saying that later. Then for me, especially as a physician, you too will appreciate this. My first year out, I had just a colleague that was a mentor to me, actually a general surgeon. He said to me after I was really just struggling with a patient case that I had, it was an outcome that I hadn't anticipated.

He told me that medicine was humbling. No matter how perfect you are or how perfect you think the medicine is, things happen. Patients will understand if you are humble. I've taken that with me now over the last 20 years. I think he was right.

Matt: Yeah. That's fantastic advice for all the perfectionists listening.

Paul: [laughs] Which is all of you.

Matt: Yeah, yeah. All right, well, this is off to a great start. But, Paul, we got to get to the topic of the day, so why don't you read us a case from Kashlak to get things started?

Paul: Sure. So, Monica, we're going to talk about Ms. Jay She is a 48-year-old female with pure hypercholesterolemia with an ASCVD risk score of about 1.4% like a [unintelligible 00:08:05] story specific. [Matt laughs] She also has obesity with a body mass index of 33. She's presenting with 12 months of amenorrhea and five to seven daily hot flashes, often accompanied by sweating. These symptoms have been really disruptive to her work and sleep. She knows that she doesn't want hormone therapy because she's read so many scary things. She did see a commercial about VMS on TV and she'd like to discuss, all right, everyone, wish me luck here fezolinetant.

She has no personal or family history of venous thromboembolism or breast cancer. She does not smoke tobacco. She reports that her father had an MI at age 72. So, we were talking a little bit before we got started, Matt and I, I think there's sometimes low-grade terror among people at this point to even prescribe any medications. I shouldn't say any medications, but hormone therapy specifically for vasomotor symptoms for menopause. So, I'd like to see here to start your general take on where we are in terms of the world in medicine in terms of thinking about prescribing hormone replacement therapy for these symptoms. Is it good, bad, and different and where in the pendulum swing are we right now?

Monica: Yeah, excellent question. So, for this patient, I always like to go into, these are what your options are, and we can talk about the good, the bad, the ugly, and then I let them know that you can pick one and you don't actually have to be married to it. If it doesn't work, you're going to let me know because I'm going to bring you back in a few weeks. I think usually eight weeks, eight to 12 weeks is a good time point to bring people back. If we need to change, we can. So, usually we'll tell them, “Hey, we're going to start with lifestyle modifications, me counseling you.” Now, you may decide that you want to jump straight to a prescription option, but we'll talk about what are the lifestyle modifications, what are some nonhormonal options, and then we'll go to the hormonal options.

I think, thinking about things, especially with somebody that has some fears about hormone therapy, gives them some autonomy, some power in the conversation. So, many of the things that people are going to come in and ask you about, “Black cohosh, various vitamins, soy, all of the herbal things,” and there're lots of stuff on the market. The reality is that really none of that stuff has been shown to better than placebo. So, if they come in and they're saying, “I started this thing and I feel great,” then as long as there're no contraindications, I'm not going to burst their bubble and take it away from them. But if they're not using something, I have a hard time telling somebody to go spend their hard-earned money on something that probably isn't going to work. I'll explain to them what the placebo effect is and why it may not be as beneficial.

Weight loss has been shown to help minimize the severity and frequency of hot flashes. Although, exercise hasn't been. But you need the exercise to get to the weight loss and exercise is good for so many other things and then I counsel them about just healthy eating. The Mediterranean diet has been found in numerous studies over many years to be not only a great way of eating and is associated with decreased cardiovascular, decreased risk of diabetes, decreased risk of osteoporosis even. It's even associated with decreased risk of dementia. So, I usually will give them some information about that and we talk about an exercise regimen and then I start moving also to cognitive behavioral therapy and hypnosis. People look at me like, “Well, how would cognitive behavioral therapy work?” I tell them, “Well, you know part of it is that as soon as you have that hot flash, many of us start to get worked up.”

I know I did when I was having them. It's like, “Oh my goodness, it's happening again. I start fanning myself. Woe is me. This is terrible.” Especially if it's happening in the middle of the night, “Oh my goodness, my sleep is disrupted. Now I'm only going to have three hours of sleep and my hair is soaking wet. I don't have time to do it over in the morning.” That anxiety around it really does incite more of the hot flashes versus taking a deep breath, maybe drinking some cold water, throwing the covers off or wherever you are. When I'm in the office, I like putting a cold pack on my chest or my neck, but just saying, I know what this is, it's going to pass. If my heart is racing a little bit, I know this is not a heart attack, this is what happens and it goes away.

I think those cognitive behavioral therapies and even hypnosis, that's really, it's calming our central nervous system down, it's helping us to self-soothe. So, those things actually have been shown in randomized control trials to actually help too. So, somebody is saying, “You know what, that sounds great, Dr. Christmas, but not really into hypnosis, not going to do cognitive behavioral therapy. I am exercising and I've lost some weight and my hot flashes are still kicking my butt. What else you got, lady? So, if we start talking about the nonhormone options, in particular for this patient, there are certain antidepressants that used in low doses that have been shown to help minimize hot flashes and night sweats. Now, it's not perfect. It's not going to make them 100% go away. So, we want to level set and help people with their expectations so that they don't think it's going to be 100% gone.

But certainly, if it's their night sweats that are bothering them. Many of the antidepressants that have been shown to be efficacious also may help with sleep too. As well as if mood swings are an issue, they can help stabilize the mood. So, that's a good option, especially in somebody that either has contraindications to hormone therapy or just doesn't want to be on it. Gabapentin has also been shown or Neurontin has been shown to help minimize hot flashes and night sweats as well. There are some side effects with it. So, sometimes if they've got some other reasons for needing to be on the medication, then it's a win because, “Hey, we can treat two things at once,” but if they don't, I usually do let them know, you might feel a little sleepy or drowsy, so maybe it's better to take it at night, but we could try it if that's something that especially if they really want to avoid hormone therapy.

You mentioned the newer medication, fezolinetant, that was approved in May by the FDA. It has shown to actually have similar efficacy to hormone therapy. In the past, we blamed everything on estrogen deficiency and didn't really think about what other things might trigger it. So, we have found that, yes, estrogen drives the train, just drop in estrogen, but it also stimulates the release of these neurokinins, these candy neurons, and it's actually those that seem to be disrupting our body's internal thermostat or the ability to regulate our temperature. So, it is a viable option. I think probably one of the things that's maybe a downside to it right now is that it may not be covered under people's insurance formulary, so the cost may be prohibitive, but the company that does manufacture the medication is offering a rebate program. So, that may make it a little bit more affordable. Yes, Paul?

Paul: No, that was more so the silent signal to let Matt know I was going to talk next, but that's okay. I wondered if we could, since we're on the subject of some of the nonhormonal options, if we get maybe a little bit granular.

Monica: Yeah.

Paul: So, I guess you mentioned the antidepressants. I feel like, I see paroxetine as a favorite even though I hate that for almost every other intent and purposes [Matt laughs] in terms of discontinuation symptoms and the libido crushing and some of the other issues with it. I wonder if you would mind going through your menu of the antidepressants that you would recommend. I know I feel like some of the SNRIs I feel like, doctor UpToDate at least recommends for these symptoms. But what is your approach for the psychotherapeutics for the vasomotor symptoms?

Monica: Yeah, well, paroxetine is the only one that has FDA approval for managing hot flashes and night sweats. I usually tell people you know we're using it at a lower dose than what people typically would be on for depression. So, that means that the side effects may not be as severe. But I think you're right. If I have somebody who's one of their main symptoms is decreased libido and it's stressful to them or bothersome to them, then that's not the first thing that I'm pulling out of my bag of tricks. Venlafaxine is another that's used quite frequently, one of the other things with paroxetine, if you have somebody that has a history of breast cancer and they're on tamoxifen, the paroxetine may affect the efficacy of their drug that they're on so that's a consideration. So, for those patients, venlafaxine is usually my go to, but that one also too can cause decreased libido.

So, it's always weighing the pros and cons. So, some people will say, “Oh, my goodness, if these vasomotor symptoms were better and if I could sleep better, I think I could get it together with my libido. I'm willing to chance it.” Then there are other people that say, “Oh my goodness, if that's even a potential that it could be a side effect, weight gain is another one. If it's even a potential that it could make me gain weight or make it harder for me to lose weight, then I don't want it.” So, it is things that we have to talk about. Some of the other antidepressants that don't cause weight gain or may not have the libido side effect, don't work as well for the vasomotor symptoms. So, if those are considerations, then it may not be that that's the option for that particular patient.

Matt: Gabapentin does cause weight gain, audience we've talked about that before or can and swelling, all that's not a favorite of Paul's and mine, but I mean, for this is one of the times where sometimes I will try it, especially in the evening. It looked like the dose was fairly high, like between 900 and 2400 mg a day seems like a high dose. Do you have success with lower doses just given, like, at night, if that's when the most bothersome symptoms are?

Monica: Yeah, I usually start pretty low at just 300 mg and we titrate up if we need to and letting them know that I'm going to bring you back. I don't want to hit you with the kitchen sink right away. If you are better with a lower dose, then I don't want to start out at the top.

So, we have ways to titrate up and see how you're doing and sometimes a combination of things might better for someone.

Matt: Then, I thought it was funny and also suspicious that the paroxetine that's FDA approved is like a special you can only get-- it's like a special paroxetine salt [Paul laughs] Paul and it's 7.5 mg versus the regular that we're used to prescribing for depression, anxiety is like the 10 mg or 20 mg tablets.

Paul: That 2.5 mg, it makes all the difference. That's the secret sauce that makes only [crosstalk]

Matt: [laughs] That's a secret sauce.

Monica: Yeah, I give just the regular the 10 mg and we call it a day. [laughs]

Matt: But yeah.

Monica: Yeah [laughs]

Matt: Audience we talked about fezolinetant on another previous episode. It looked like there was another neurokinin-3 inhibitor that was like, they were studying and it had some liver damage. This one, they didn't really see that. But when I see that, I'm always like, "If patients were coming to me asking about this," my counseling would be like, "As we roll this out, we might pick up new side effects. Here's what we know so far. I'm not sure if you have any experience yet with it."

Monica: Yeah, no, absolutely. I'm counseling patients. One, I'm looking at their medical history. So, in particular, I had a patient recently that had a history of lupus, already had some renal insufficiency and a slight bump in her liver enzymes that weren't sure really what it was about. I don't think that's the right drug for you. Even with fezolinetant, there were some patients that had a slight increase in liver enzymes. So, it's recommended that you check baseline levels and then check again a few months after they've been on it, just to make sure that they're still good. So, absolutely, I think the way that you just rolled it out is how I talk to my patients too to say it's a new drug, looks safe, looks efficacious, the data was good, but again, things happen. Headaches were another one. So, people that are having issues with that have chronic migraines or chronic headaches, that was one of the bigger side effects that were reported too. So, I may not want to give somebody that's already having issues with headaches a medication that may exacerbate that too.

Matt: But this is great. I have always like when you can give the patient a buffet of options of like, "Okay, I'm going to talk to you about lifestyle changes, ways you can eat, exercise, that will improve your overall health. How losing weight can help with this. You said you talked to them about cooling techniques and maybe a little bit of like-- it sounds like almost like you're giving them a little bit of CBT tips, do you ever refer out for that? I always find CBT is like, it works for everything, but it's very hard to access in practice. So, if you have any tips but it does sound like maybe you're almost coaching your patients a little bit in how the CBT works.

Monica: I do, and I kind of coach them through the same thing when we talk about using it for sleep disruption. Because in my area, usually not only are the vasomotor symptoms bothersome to them, but if it's impacting their sleep too. One of the good things that came out of the COVID pandemic was that we really quickly pivoted to this online format. So, there're a lot of things that now are accessible to patients from a virtual format that maybe they didn't have access to before if they can't find a therapist in their area that specializes in CBT for menopausal symptoms, then there's some access of being able to find people

online too, but there're even some online resources that people can locate that they can teach the techniques to themselves too. That's not always ideal, but it is helpful and it's something that they can do and it works.

Paul: I think you've even made this joke before. But just for those of you about to take your boards, if CBT is a choice of one of the answers, [Monica laughs] if that's going to be the correct answer whatever the question is, you can probably just skip past. If you see CBT as answer, just pick that one and move on to day. [Matt laughs]

Monica: It's a mind over matter though, I call it talking myself off the ledge. [laughs] So, if you're able to really understand what the concept is, it's trying to level set of saying, “Okay, how can I self-soothe myself out of whatever the troublesome thing is that's going on right now with me?”

Paul: I should probably explore CBT. [laughter] I will say I can tell that Matt wrote this script in part because we got to the treatment before we got to the history of the examination. [Matt laughs] So, I wonder before we delve into the hormone replacement part or get too much deeper into the therapies, if we could maybe take a step back and I would love to hear how you take a vasomotor history from a patient. Are there any scales that you use to quantify things and track? Because I think so much of our treatment actually depends on the severity of the symptoms as well. So, what does the history sound like from you when you're taking from a patient who's reporting these symptoms to you?

Monica: It was really personal because what is really bothersome to one patient may be not so much to another patient. So, if somebody tells me that they have hot flashes, I don't know, three or four times a week, but those three or four times a week are extremely distressful to them, I'm not going to withhold treatment from them. Likewise, somebody may tell me, “Ah, they happen a couple of times a day, but it doesn't bother me that much. I just take my sweater off or I carry this cute little fan around with me and it strikes up conversation and they're smiling when they're telling you about it.” So, even though they're having them more frequently, it doesn't seem to be bothering them as much. So, I think that scales are good if you're doing research, especially if you're trying to quantify whether or not the treatment that you're studying or that you're prescribing has good efficacy, you're comparing it with something else and you're going to use that data later.

In a clinical practice, though, I think you can just talk to the patients and really say you can find out what their most bothersome symptoms are, what's really troubling to them. If they're telling you that they're having really bad vasomotor symptoms, I usually believe them. The one thing that I think is so frustrating to patients that I see is that they may be still having a regular menstrual cycle. Let's say, they're in their early to mid-40s and they're having bad hot flashes and night sweats. They're starting to have mood swings. It's impacting their personal and professional life. They feel that there's some cognitive fogginess. I feel like, I've just got this brain fog all the time. I'm not thinking as sharply, and I know it's got to be my hormones, but everybody keeps dismissing me because I'm still getting a regular period every month.

The reality is that we start having symptoms related to hormonal fluctuations up to seven, maybe even 10 years before you actually stop having menstrual cycles and fit the true definition of menopause. Oftentimes, it's in that perimenopause transition or time frame rather, that people are most symptomatic and so validating what they're experiencing and then talking about how to treat them and improve their quality of life is just as important as the person that fits the definition of menopause because they may even be more symptomatic.

Matt: Yeah, so you were just saying that because I was reading that on average, I think once women start with the menopausal symptoms, they tend to go for like seven years or

something like that. So, there's like a long span. Like, if it's starting that far before and then that long after menopause, that's a long time to be going through this.

Monica: It's variable though. So, everybody's symptoms are different. It's not terrible for everybody. I think that's the part that we can't put everybody in the same bag too or just assume that it's bad really because for some people it's mild symptoms and for other people it's really debilitating. I think patients start to compare themselves. They'll say, “My sisters or my friends don't have it as bad as I do,” Or they might be guilty, they might be the person that didn't have it as bad and they're telling the people around them, like, “Why are you so dramatic? It can't be that bad.” It's different. It's just like when you're at the start of the reproductive cycle, people start having menarche at various ages.

Some people are nine, some people are 16 and it's all normal. Some people are very fortunate. They get their periods. They come every 28 to 30 days. They only last three to five days. They're never really troublesome. Then one day they just stop and they just move on with their life. Then you have other people that from the moment they first get it, they hemorrhage every month, they're nauseated, they're throwing up, and it's just badness until they hit menopause and then you have everything in between. So that's I think the hard part about managing menopausal patients is that especially because menopause is getting its day in the sun right now, everybody's talking about it. I read an article recently that said that it's a 600-billion-dollar industry that patients are spending about $2,000 a year on menopausal treatments. So, everyone's trying to get in on it and it's making it as we move into our conversation about hormone therapy, it's making it seem like hormone therapy is the magic pill.

It's the antidote to aging and that we healthcare professionals have been withholding this really important treatment and give it to me. That New York Times article was-- I loved it, but it was like the bane of my existence. I was getting inundated with phone calls because I forget the title was, we have been misled right, "We have been misled about menopause." I don't think people are tricking anyone. So, there are some side effects that we need to talk to and everybody shouldn't be on hormone therapy. Unfortunately, I wish it was being a menopausal woman myself, I wish that it was the antidote to aging, but it's not.

Matt: Yeah, our first question was like, has the pendulum swung too far away from prescribing hormonal therapy? I was telling you beforehand when I went through med school pretty recently after the WHI so, like, that study had come out and scared a lot of people away from it from using any hormonal therapy. This New York Times article was just saying, like, “Why aren't doctors prescribing this more? It can be miraculous for people and it’s not-

Paul: One crazy trick about menopause your doctor's not telling you about, yeah, great.

Matt: -it's not as dangerous as everyone things and it's like, add this to the list of things that doctors are withholding from me that I should have access to. I do understand both sides of that argument of course. It sounds like you're not necessarily calculating a score. This happens a lot, Paul, when we talk to experts, they're so used to taking the history and they just have a gestalt about how severe symptoms are and you don't really need a formal score, it sounds like and also, you told us that first you try lifestyle, you talk to them about nonhormonal options, and then hormonal therapy is like maybe at a follow-up visit, you talk to them about that. Am I putting too many words in your mouth or is that the general approach?

Monica: Yeah, no, and I think that the patients are going to come in and they're going to tell you what-- many of them have already tried stuff before they came in or they're going to tell you if they're really miserable, you're going to see it. You know them and it's not our judgment really of how bad it is. It's really listening to them and seeing how much of a

disruption to their quality of life these symptoms are causing them, and certainly looking at do they have other medical comorbidities? So, your history is extremely important, just like for everything else. Are they hypertensive that are on antihypertensives that might be adding to it? Do they have fibromyalgia or some other chronic pain syndrome and they're on narcotic pain medications or muscle relaxants that also could be contributing to their perceived hot flashes and night sweats? So, do they have an underlying thyroid?

Maybe, everybody, all the women in their family have a thyroid disorder and she hasn't had her thyroid hormone checked. There's some underlying hypothyroidism that we haven't figured out. So, absolutely getting that history and physical history that you would get for everybody is going to be really important. But when it comes down to just asking what symptoms are you experiencing and capturing that, I think is very personal to the patient. They'll be able to tell you. They're going to tell you right away what's the thing that's most bothersome? “Yeah, doc, I'm having hot flashes, but it's this vaginal dryness that's killing me. I can't have intercourse. It's extremely painful and I can deal with that. I can't deal with this.” So, then you'll be able to talk to them about, well, these are the treatment options and this is what's going to be taken care of.

So, as we move into this hormone therapy conversation, I think that Women's Health Initiative trial was the thing that scared everybody. The trial was prematurely stopped because the people that were in the hormone therapy group had a higher risk of stroke and they had a higher associated risk of breast cancer. Everybody was terrified. The media picked up on it and doctors were afraid to prescribe it and patients were afraid to take it. We had just a lull. The reality was that one, that trial was not looking at whether or not hormone therapy actually helped hot flashes and night sweats or symptoms associated with vaginal atrophy. We already knew that it helped those things. That was not what was being evaluated. What was being looked at was whether or not being on hormone therapy minimized cardiovascular risk. Because what we saw was that after menopause, cardiovascular risk went up.

There were some small observational trials that looked like being on hormone therapy may actually be beneficial. So, they wanted to look at this on a large scale with our gold standard randomized control trial. So, half the people got hormone therapy, half the people didn't get it. But the average age of the women in the study was almost 64. It was like 63.5. So, these were people that were well past the onset of menopause. Many of them weren't even symptomatic anymore. They just took all-comers and so looking back on it, it's really not a surprise that the incidence of these other comorbidities went up. So, when people went back and looked and we said let's tease out, let's look at the younger people, let's look at the women that were under the age of 60, let's look at the people that were within 10 years of the onset of menopause and let's see if the risks were higher in them.

Then the reality was that those people, actually the benefits outweighed the risk. So, that's where this timing hypothesis comes in. So, most people will say if the patient is within 10 years of the onset of menopause, if they're under the age of 60, that without having any strong contraindications that the benefit in patients that are symptomatic, we'll talk about what those symptoms are for when hormone therapy is recommended, that the benefits outweigh the risk. So, the four indications are moderate-to-severe hot flashes and night sweats. Somebody that goes into premature menopause earlier than the age of 40 and we would put them on it to help until they would have reached the natural age of menopause, which is the early 50s. Then the other is prevention not treatment of, but prevention of osteoporosis and the genitourinary symptoms that can come after menopause from hypoestrogenism.

So, when patients are coming in saying, no, I don't really have hot flashes or night sweats, but I've gained weight or my skin is getting wrinkled or thinner, or my hair is thinner, or I just

don't have the same energy that I had before, I want to be on hormone therapy. That's not really the indication and actually it doesn't help with those things either.

Matt: Yeah, I like you had a tweet that was #HRT will not help you lose weight, prevent hair loss, stop wrinkles, or halt the aging process, don't kill the messenger. [laughs] I thought that was well said. So, with this we want to talk a little bit-- of course we want to talk about prescribing it. You mentioned comorbidities, you mentioned certain risk. What's your approach to that? We talked about this after one of the conferences we went to in the spring where the speakers were talking about how they assess cardiovascular risk and how they assess breast cancer risk and how that factors in. Do you have an algorithm that you use or like a standard line of questioning to assess for risk factors that would be a deal breaker for the patient?

Monica: Yeah, very similar to when you're counseling a patient about being on hormonal contraceptives. So, somebody that's had a history of a venous thromboembolism, whether it be DVT, PE, those are going to be people that I'm going to pause. I really am not going to put you on something that's hormones that are going to exacerbate the risk of recurrence. Now, there are some studies that did show that patients that are on full anticoagulation with vasomotor symptoms that putting them on hormone therapy didn't exacerbate their risk. So, there may be some role for that. But I think people have to understand that that's still controversial. Anybody that has an estrogen-derived cancer, whether it be ovarian cancer, endometrial cancer, or a breast cancer, are patients that are going to have strong contraindications to it as well. There are some nuances that we can talk about. But really for the general provider that's seeing these patients, the parting line is really probably those people should not be on hormone therapy, especially systemic doses of hormone therapy.

Matt: We're cowards, right? Paul we wouldn't do that without involving an expert anyway. [Paul laughs]

Monica: You know, so thinking about those same contraindications, somebody that has extreme cardiovascular risk, those are people that are going to have a higher risk. So maybe using a transdermal option may not confer as much risk, but that's some serious counseling needs to go into it. I think that we should have exhausted every nonhormonal option and then had a real conversation because those people probably some of the medications are on and their underlying medical condition is probably contributing to way that they're feeling too and it's not all just hormonal. So, I think having those hard conversations with people too, because people want to feel better, but we also want to make sure that they understand that those potential risks could put them in a situation where they're far worse off.

Paul: So, we recount you're really thoughtful explanation of how to think about hormone replacement therapy. Ms. Jay is now less reticent than she was. Am I framing it the right way? She's more ready to consider it. Why don't we say it that way? So, she'd like to try hormone replacement therapy. Can you talk us through your approach to the menu of options? It seems like there's a bazillion different formulations which I think is maybe the other thing that intimidates people and might keep them from prescribing it. Do you have standard few choices that you start with or what's your general approach to choosing an initial therapy?

Monica: Yeah, so I like to explain to them that there're two categories. There's systemic dose hormone therapy and there's more low-dose local vaginal estrogen therapy. The low-dose vaginal estrogen therapy is going to be used for patients that really are only treating these genitourinary symptoms that are associated with menopause, your vaginal dryness, that could lead to pain with intercourse or bleeding with intercourse. Urinary symptoms are included in there too, frequency, urgency, recurrent urinary tract infections. So, one of the good things about the low-dose vaginal estrogen therapy is that there isn't

much systemic absorption. So, some of the risks that we are fearing with systemic dose therapy, we don't necessarily have to worry about. There's not a timeframe of how long someone can use it either. There're lots of options for vaginal estrogen therapy. There is a vaginal pill. There is a vaginal insert. There is a vaginal cream. It used to be that we would tell people to use it every day for two weeks and then drop down to twice a week. I think most of us now say that you could probably just start out using it twice a week.

I usually will explain to people that it takes about eight weeks for them to notice their maximum benefit, so don't quit after a week. Then there's a vaginal ring too. That's really nice because the ring you just put in and it stays in place for 90 days for three months. The patient shouldn't feel it, their partner shouldn't feel it. At the end of three months, you just put your finger in, pull it out, throw it away and put another one in. So, there're lots of options for vaginal estrogen that's efficacious and it works for those vaginal symptoms. For our patient, though, it's not probably it won't help for her hot flashes and her night sweats. So, we're talking systemic dose hormone therapy now and because our patient I'm going to assume nobody told me that she had a hysterectomy, so I'm assuming she still has her uterus in.

Matt: Let's say, she does.

Monica: Because she still has her uterus, then we are going to not only have to give her estrogen, but we need to give her progesterone to minimize the risk of hyperplasia and protect her endometrium. So, there are options, combination doses where the estrogen and the progesterone come together and sometimes that's much easier for patients to take and remember or we can split out, give them estrogen and then supplement them with a different type of progesterone. So, if we're looking at combination options for estrogen and progesterone, there is a pill option or a patch option. The pill options are many.

One of the things, though, with combination hormone therapy is that the doses are not as plentiful as if we're just giving estrogen alone. Sometimes that's where it comes in, where if somebody needs tweaking or we think they might need a little bit more estrogen because their hot flashes are better, but they're still having them. They're telling us, I can tell that this is working, but I need more. That's when we may have to start to talk to the patient about separating them out. In terms of I should go back too with there is an oral pill that's back on the market now, that’s a combination of estrogen and a SERM, a selective estrogen receptor modulator and the type of SERM that's in this pill with the estradiol is bazedoxifene. It works really well. Patients really liked it. It had been off the market for a little bit because of the packaging issue, but more recently has been put back on the market.

So, those are the combination pill options, like I said, there's a patch. For somebody that we feel like we need a different estrogen mode, we can do the estrogen separately and then we have the option of doing it either a pill, it could be a gel or an emulsion that they rub into their skin daily. We can do it as a transdermal patch that they either change twice a week or once a week. There are vaginal rings that are higher dose, not the low-dose ring that I talked about before. There are two higher dose rings that are systemic dosing, but they still work the same way. They're put in the vagina and they last for three months. At the end of three months, you take it out. Then when we're going to treat them with progesterone, we can either use a progestin IUD, which is like one of my favorite things to do because you just put it in, they can't mess it up [laughs] because it's there.

It's great for patients that are having wacky perimenopausal bleeding too, because you can put that IUD in. And for the vast majority of people, it'll stop their bleeding and they feel like they beat menopause a little bit. If somebody is not amenable to having an IUD put in, or there's some other reason why we don't think it would be efficacious for them, maybe they've got a bicornuate uterus or they've got fibroids or something that would make it more difficult to putting it in, then we would give them oral progesterone. So, there's an option for them

taking it just half the days of the month. If you do it half the days of the month, they're going to get a withdrawal bleed. My personal opinion, the best thing about menopause is that you're not getting a period anymore. So, in my wacky mind, there is absolutely no way that I would sign up for still having a period after I got the menopause prize. That's my favorite thing [laughs] personally about menopause and there're not many things to get excited about, but to me that's one of them.

Matt: It's like the only prize, right? [Paul laughs]

Monica: That's how I feel about it, so I'm not taking it. Otherwise, we would give them a progesterone pill that they would take every day and that does, for the vast majority of people, minimize that risk of breakthrough bleeding. Okay, lots of options.

Matt: Yeah. So, I want to summarize a little bit, then I want to get into some of the specifics, okay. So, if they have a uterus, we have to, of course, prescribe estrogen and progesterone. There are combinations of the two, which there're many different pill options or there's a patch option for the combination estrogen and progesterone. There's a combination estrogen and bazedoxifene, which is bazedoxifene is a SERM. Then that sounds expensive, by the way. [chuckles] Then estrogen comes in all forms if you want to have a little bit more control over the dose. So, you can do pills, there're gels, there're patches that are changed once or twice a week for estrogen or there're rings and these rings are a higher dose than what we would use for just genitourinary symptoms. Then for progesterone, we can just give an IUD if they're okay with that or we can give them pills.

If they take the pills for just the partial month, then they're going to have withdrawal bleeds. But if they take it continuously, then they should not have bleeding. I think that's where we're at because I do want to talk about dosing a little bit or types of estrogen. If I'm approaching this, I know there's going to be a million brands of estrogen, but when I'm going to just prescribe estrogen, there's like conjugated, there's estradiol and what else is there? Or what else do I need to know about that? And what's like a typical dose that we might prescribe? Hey, I just wanted to break in here really quick and mention that after the episode, Dr. Christmas shared with us some slides that she uses when she's teaching this topic. They have all the different formulations of estrogen and progesterone, the vaginal types, the transdermal, the oral, the rings, patches, what have you. So, that's all there in the show notes, so check that out so you can see the brand names, the generic names, the dosing range for all this. It was too much to get into on this episode, but it's a really nice supplement to the discussion that we're about to have here.

Monica: Yeah, so some of it is going to come down, unfortunately and this as you guys know this probably even better than me, that it's what's on your insurance formulary? And that's a bad answer. But the good part about that is most of them all still work and they're all efficacious, but sometimes it really is going to come down to what's covered under their insurance formulary. That SERM that you talked about, that you said it sounds expensive. Yeah, there's no generic of it. So, you were right. It is expensive. However, the company that makes it does offer a rebate program that actually works really well as long as a patient's not on Medicare, because you can't participate in those rebate programs. But when you bring that rebate card in or have it on your phone and they scan it at the pharmacy, it's good for a year.

So, I find that most people are able to access that option if they want it. There's only one dose of that one, though, so it makes it pretty easy. You don't have to stress out too much about that. Lots of people are very excited nowadays about bioidentical hormones. So, it just means that the molecular structure of the hormone is very similar to what your ovaries make. It's still not the same thing, but it's very similar. I think right now it's a marketing strategy or marketing ploy because you have a lot of compounding pharmacies, or people that are

making it sound like because it's a bioidentical, it is a lot safer and it confers the same risk. Many of these formulations that are compounded that are not FDA approved actually can be more dangerous because they don't have to undergo the stringent guidelines.

So, people are actually maybe getting more than what they need, and they have these super physiologic levels that increase their risk of blood clots or worse. But there are FDA-approved bioidentical options and estradiol is one. So, if patients want or feel very strongly about having a bioidentical option, there are FDA-approved options for that, that work equally as well, but still confer the same risk. Usually, if somebody is getting both estrogen and progesterone, the progesterone actually does give some benefit too. So, I don't go to the highest dose. I usually start somewhere in the middle, depending on how severe, how bothered they are by their symptoms. Because what I don't want to do is give them the lowest dose of something and then they get no benefit and think, “Oh, this is garbage.” I want them to feel better. But I usually will start in the middle.

That's usually for the vast majority of people, fine for them, they feel better. I personally try to do a transdermal option because you don't get that first pass liver effect, and so they don't get that bump in clotting factors. So, theoretically, it should confer a lower risk of venous thromboembolism and the associated risks that go with that, like stroke. [laughs] So, that would be our patches. It would be that transdermal cream or the ring. The patches are going to be extremely irritating to people if they have skin sensitivity to adhesive. So, if somebody already knows I don't do well with Band-Aids, my skin is really sensitive, they're not going to like the patch. It's going to cause itching, it's going to cause irritation, and it may even cause some skin discoloration that doesn't go away. So, if somebody already says that, “I'm going to tell them right away the patch is probably not the option for you.”

Even though they're meant to stick on really well, and they do stick on very well for people that are swimming a lot, exercise really isn't a big problem because it still sticks on. But for people that feel like it's not going to stay on, “I'm in my hot tub all the time,” or that adhesive may not be good for them, but they might do well with the transdermal, the gel or the emulsion that you rub in the skin it's daily. I do tell people, though, and I see your cat in the background, Paul, but if you have small pets that are maybe holding or even small children, you want to let that estrogen gel dry on your skin because there is evidence that it can transfer from you to the pet or the small child.

Even some people, this isn't as severe, but people will tell me, “Dr. Christmas, it just takes forever for it to dry. I feel like I stain my clothes if I put it on in the morning and then I get dressed and it is daily.” So, those are small things, but they are considerations that you want to tell people when you put it on, let your skin dry or have long pants on or something so that it's not being transferred. I don't know if that specifically answered. It's really hard to say. I start with this one thing. I usually will say,” Okay, these are your options”. The patient says, you know what? “I take pills for other things every day. It is not going to be cumbersome for me to take a pill. I'll just take it with my other ones.” Then I'm like, “Great, we're going to find you a pill.”

For people that say, “No skin sensitivity, I never had any issues with Band-Aids. I like that transdermal option because depending on which one their insurance covers, it's either changed once a week or twice a week. That sounds perfect for me. They've got one that has estrogen and progesterone in it. That's what I want to do. So, then we go with that option. For patients that love the ring and the IUD, then that's where we go.

Matt: It looked like a low dose for conjugated estrogen, I saw like 0.3 mg per day, and then the high dose is 0.625 mg per day for estradiol, 0.5 mg per day as a low dose and a milligram per day as a high dose. Then the patches have like a different scale. So, to me that seemed a little confusing. But I guess if we're prescribing it, we can just look at the range of

doses for the specific agent we're trying to prescribe and then decide if we want to go low dose, high dose, or medium dose if they have one available.

Monica: Yeah, what I didn't say is for people that don't have a uterus that you're not having to supplement the progesterone for, especially if it's a surgical menopause, those patients tend to need a higher dose of estrogen. So, then I don't start them out. So, if I have somebody that recently had, I did their hysterectomy, their ovaries, and they came out with the uterus and I put them into surgical menopause, I'm going to start them out at that 0.1 mg dose. Whether it's a transdermal patch at the highest. The gel has lots of options for dosing. So that's always a nice way because you can tweak it up or down. But I'm going to start a little bit higher for them because they don't have that synergy with the progestin and the estrogen. For people that still have a uterus, you're getting some benefit from both and for those patients, they often don't have to be at the highest dose.

Matt: Oh, interesting. Okay. You mentioned this, this is a case variation that we did want to talk about a little bit was how do the doses differ? Because if someone's prescribing oral contraceptive pills, how does that differ from hormone therapy based on the dose or the potency of what we're giving?

Monica: Yeah. So, when you're giving somebody birth control dosing, you are trying to block ovulation because it's preventing pregnancy. When we're giving hormone therapy options, we don't need that high of a dose, we're not blocking ovulation, we're just trying to get them back up to a physiologic level so that their symptoms are abated. So, it's really different. So even for people that tell me, “I could never take pills, it made me crazy or it made me nauseous,” it's completely different not the same dosing and just because somebody didn't tolerate hormonal birth control does not mean that they won't be able tolerate hormone therapy dosing.

Matt: Okay, this is a totally different pool of estrogen and progesterone pills and therapies for the most part, I mean, you said the IUD, I guess the IUD would be the same for either indication, is that correct?

Monica: Right. So, the reason I brought up the progestin IUD was because the progesterone and the IUD is keeping that lining suppressed and thin. So, we're using that for endometrial suppression and then if somebody were still to have hot flashes or night sweats, then we could add estrogen to that, adding a transdermal estrogen, and now we've got endometrial protection, but we're also stabilizing or giving them the estrogen so that in particular, their vasomotor symptoms are improved.

Matt: So, Dr. Molly Heublein, host of our Curbsiders Teach and occasional cohost on this program, she had sent a question about, “What if a woman was-- let's say you had a 48-year-old woman who's on combined oral contraceptives, and she's 52 years old, she doesn't want to get pregnant, and she's not sure if she went through menopause.” How do you handle that patient who has been on OCPs and probably went through the transition, but we're not sure and would also maybe like to avoid the symptoms.

Monica: So, somebody at 48, I would say that the median age of menopause is about 51 and a half, 52. But the range that 90% of people will fall into is going through menopause between 45 and 55. I guess a better way to say that is by 55, 90% of women will have met the definition of menopause. So, at 48, if she's not having any issues, I might try to see if she'd be willing to switch over to a progestin IUD just because being at that higher birth control dose of estrogen could increase their risk of stroke. But if she's not a smoker, doesn't have poorly controlled high blood pressure, diabetes, is of a normal or average weight and is like, “No, I've been on this, I feel fine on it.” Then I typically will say, “Well, we'll leave you on it until you're 55 and then we can take you off at 55.”

If you are experiencing troublesome menopausal symptoms at that time, then we can talk about hormone therapy. Some people want to just go straight to hormone therapy so that we just transition them from the birth control straight to the hormone therapy. So, I think that would be the way to think about that in somebody that doesn't have any contraindications and it's something that I reevaluate on an annual basis. So, they have to come in to get their prescription. I have to see their blood pressure. I need to see that they've gotten their mammogram. We talk about an updated family history. [laughs] Nothing crazy has happened in the family in a year that might give me pause for this 50-year-old to still be on combination birth control. I would ask them again about maybe being on an IUD, if they would be willing to do that. Of course, I think for these patients that are perimenopause or in that age range, having them on the lowest dose, so that's where those lowest dose birth control pills would be a better option than them being on something that's higher dosed.

Matt: Are those still higher than the typical hormone replacement therapy for vasomotor symptoms they are-- [crosstalk]

Monica: They are still different, yeah, because again, it's still considered birth control and you're trying to block ovulation so the person doesn't get pregnant. With hormone therapy, we don't need to block ovulation anymore. So, we're not trying to block ovulation, we just want to get them at a physiologic level and so that's a little thing.

Matt: Yeah, yeah and what about the woman that let's say you have a 32-year-old who has primary or premature ovarian insufficiency? What about the dosing there? And how long would you continue hormone replacement therapy? I know it's a different situation than using it for vasomotor symptoms, but how would the approach differ?

Monica: Yeah, I guess the difference we'll say if you're premature menopause, then they're definitely in menopause. They're hitting the definition of menopause. They're not having menstrual cycles anymore. The ovaries are not producing any hormone. So, for those patients that are under the age of 40 and that's the definition of premature menopause, unless there is a strong contraindication, those patients absolutely should be on hormone therapy. They should be on hormone therapy up until the point that they would have reached natural menopause. So, about age 52, they should be on a higher dose of estrogen to help. The purpose for putting them on is because we want to minimize their risk of developing osteoporosis in the future. We want to minimize their cardiovascular risk and we also want to minimize the risk of cognitive decline and so they should be on at least 0.1 mg of estradiol.

Now, people get confused, though, because they'll say, “We'll, wait a minute, everybody should be on it if it's going to minimize those risks, if it's minimizing cardiovascular disease, if it's minimizing osteoporosis, if it's going to help me not get dementia in the future.” The problem is that it hasn't been shown in older patients to actually minimize those risk. So, it isn't even a cumulative effect, like, “Oh, we should all just be on this. There actually is evidence that for patients over the age of 60, that the associated risk of dementia and cognitive decline are higher on hormone therapy. As we know from the WHI trial that we talked about earlier, we are not using hormone therapy to minimize cardiovascular risk. This is only in women that are under the age of 40 that go through menopause.

Primary ovarian insufficiency means that ovarian function is waxing and waning. So, for those individuals, they still might get periods and they still might, albeit not every month, synchronize. They might still ovulate. So, somebody that has POI or primary ovarian insufficiency, one, we want to make sure do they want, if they don't want or desire pregnancy, then they should actually be on birth control because it's not unheard of or unusual that they could get pregnant. So, we wouldn't put them on hormone therapy yet. Now, usually what happens is at some time point they move from being an ovarian

insufficiency to going into menopause. So, then hormone therapy would be beneficial then. But if it's POI, its usually patients are being put on birth control.

Matt: I was not realizing there was a distinction. I was thinking it was just like a woman under 40 just stops having periods and you test and her LH and FSH are through the roof and you're just like, “Oh, I guess you're in menopause for whatever reason.” You're saying there's a difference between the woman who just has amenorrhea at a young age.” How do you clinically differentiate? I'm not sure if I'm following.

Monica: Yeah, so premature menopause would either be that they had not had a period for a full year, or they have labs six months apart that put them in a menopause range. Usually, the way you can tell the difference with primary ovarian insufficiency is that the periods are changing, they're spacing out, they're regular. So, you may check an FSH in particular or a follicular stimulating hormone level in estradiol. Sometimes what you may see is that FSH level is borderline or it's high, it's in the menopausal range. They might still have estrogen, though. It's weird. You're like, “Wait a minute, the estrogen is not less than 10, why do they have a higher estrogen but their FSH and their periods are irregular?” and so it's waxing and waning. It's coming and going, and they're still having periods although they may be irregular, so they haven't met that definition of not having a period for a full year.

Matt: I see.

Monica: Their labs may be suspicious, elevated or borderline FSH, or we're starting to say something's not quite right here, but their ovarian function again isn't stopped. They're not depleted. They still have some follicular reserve there. With premature menopause, it's nothing. Their FSH is high, their estradiol is zero, they haven't had a period, and there's no thought that this person could get pregnant. So, we're not putting them on birth control. We're putting them on hormone therapy.

Matt: Hormone therapy. Okay. Got it. Thank you.

Paul: So, Monica, let's circle back to Ms. Jay. [laughs] She's now 55 years old. Just to remind you that's I think seven years after we initially started treating her and she's been doing much better on hormone therapy, but she still has a few hot flashes few times weekly that are quite bothersome. As a result, she'd like to continue therapy because she does think it's helping, but she wants to know if it's still safe. So, Ms. Jay's question and I think our question for you is, how long can we use hormone therapy for in this type of patients? For the patient who does not have primary ovarian insufficiency or early menopause, that we've started it for these vasomotor symptoms, how long do we treat them for and how long it’s safe?

Monica: So, it used to be that we told people that they could be on it for five years and then we just yanked it away, and most of us are not doing it anymore. So why-- it was five years just random? Where did five years come from?" [laughs] Did you just-

Paul: It is just half a decade, I mean, it does make sense.

Monica: -pull that out? so the five years came from, really, that the symptoms are typically the most severe. This comes from the SWAN data Study of Women's Health Across the Nation, some other the bigger trials too. But it comes from longitudinal study trials that show that the symptoms are typically most severe, most bothersome around the initial five years after the final menstrual period. That for even people that don't go on treatment, that the symptoms tend to get better on their own. For the vast majority of people, they go away.

There's a small percentage of people. My mom happens to be one of them that I call chronic flashers. She's continued to have them. I'm not going to say her age because she would disown me. [laughs] Now, we don't yank it away at five years, but the pause comes in. If you are over the age of 60 and you are more than 10 years from the onset of menopause, the risks start to outweigh the benefit. That's when we're really having a serious conversation with people, because as I shared, the associated risk of breast cancer goes up, the risk of cognitive decline and dementia may be more of a factor at that time that's not as a consideration in younger people. So, do I have to take it away from them? Is there something magic?

You turn 60, you can't have this prescription anymore. I don't do that because there's some people that tell me, “Hey doc, I got to die from something and if I'm going to die from my hormone therapy, so be it.” "I feel like I'm much more energetic and I think that I look younger than my contemporaries." It's not the hormone therapy. Most of those people are also avid tennis players and they are meticulous about what they choose to fuel their body with. So, yeah, they look great, but it's not necessarily a hormone therapy that's doing it for them. But I will then tell them, “Well, I want you on the lowest dose and I would prefer you be on a transdermal if they're not on a transdermal option.” Then we do talk about it, sometimes I'm able to get people to just stop the systemic hormone therapy and go down to a vaginal option so that they don't have the pesky vaginal symptoms. Because remember, we don't have to have a time constraint on that and there's going to be a recurrence of the hot flashes for a minute or two or three after they stop the [chuckles] hormone therapy.

It usually subsides, but if it's really bothersome, we can talk to them about some of the nonhormone options and if they really feel like, “No, I want to be on hormone therapy, they're coming in annually, we're doing their annual mammograms. They don't have any other strong risk factors.” I usually will leave them on it. I'm not saying that's the right answer, but I think that there is some autonomy in this and I think it's individual. The vast majority of people, the risks scare them, especially when people will say, “Oh well, it's no higher than drinking a glass of wine or it's no higher than being obese.” Well, what if you have somebody though that's a little bit overweight and they do like a glass of wine with dinner and they're on hormone therapy? Well, what do we do with that risk? Is it compounded?”

So, I do think that people are really mindful of that and they understand it. They want to feel better but they do understand that hormone therapy isn't the magic pill. I think it's important when we're putting somebody on it to tell them this is not forever. I'm giving it to you now, but eventually we're going to talk about when we come off of this and most people are pretty reasonable about and say, “Yeah, I understand that, thanks for letting me know that.”

Matt: It sounds like there are patients out there that would want to at least have that conversation and especially if people are going moving back more towards starting it, I think this conversation is going to be more common than it probably is right now.

Monica: It's documenting all of it. Every year she's came in, we talked about it, I've documented these risks, because I think what I don't want to happen is, I have somebody on hormone therapy that is well past the time, we'll say that should have been and now all of a sudden, because the risk of breast cancer goes up just with age in general. So, it may not have anything to do with the hormone therapy, but they now have a breast cancer because the first thing the oncologist is going to say is, “Oh, my gosh, who is this Dr. Christmas that's been prescribing you estrogen at 0.3 mg all this time. You're 75 years old. What is she doing?” The oncologist, it's fair they can say that because that's true. But what I want the next thing to happen is the patient to say, “No. Dr. Christmas has counseled me. She's been trying to take this away from me for the last 10 years. I did understand the risk, and that's something that I knew, and I understand that.” Because I think that's that humbleness of medicine and the imperfection and people get to be the boss of themselves for certain things

now. Once they have the breast cancer, you're not getting the prescription from me anymore [laughs] you know.

Matt: All right, well, I think we definitely should go to take-home points. I'm sure we could keep you for another hour, but we shouldn't. This has been fantastic. So, a couple of take-home points that you want the audience to remember about this topic.

Monica: One, menopause is ubiquitous. If you live long enough and you were born with ovaries, I should say, [laughs] you're going to go through menopause. You can't out pay it. It doesn't matter what race, ethnicity you are, how rich or poor you are, 50% of the population goes through menopause. It's a natural process and it is inextricably tied to the aging process. So, I have to remind myself of that because it's very easy to want to compare your 55-year-old self to your 25-year-old self, and that's never going to be a fair comparison. We're not going to ever be 25 again and I don't have any pill that's going to make somebody feel that way again. So, that's really how I like to start, that this isn't good or bad, it just is. What we were able to get away with when were on the underside of 50 isn't what we're able to get away with on the upper side of 50. [laughs] So, diet matters, exercise matters, our self-care matters, just overall mental wellbeing. That's a bigger part of managing this menopause transition than even the medicines that we may be able to give people.

Matt: Yeah, I think that's a great point. I love how, as somebody who is also a surgeon, that you are also so like talking to patients about primary care, this is like a lot of primary care stuff that you're doing, which is fantastic, and I'm sure our audience will appreciate that part of how you approach the care of your patients. Anything that you would like to plug? I know you do a lot of different things. Your Twitter is great, so people should follow you on there. I'll give that one, but anything else you'd like to plug?

Monica: One last shameless plug. I'm working on an international project that was started by Professor Martha Hickey out of Australia. But we are doing a Menopause Priority Setting Partnership. I don't know if you've heard of these PSPs before. They have them for over a hundred other medical conditions, but it is where we go to the people that have the lived experience and in this case it's menopause, and we're asking the people, the professionals that treat the patients with menopause, and we're asking them what their priority questions are, what they want research to answer, as a practitioner what are you seeing on a daily basis about menopause or this menopause transition that you can't answer, or we don't have a fix to? So, we're surveying them, and this is going to come out soon. It's called MAPS, Menopause Priority Setting Partnership. We are internationally, globally, trying to survey as many people as we can.

If there is a question or answer that's already been answered, let's say it's about, does hormone therapy help vasomotor symptoms? Well, those questions are thrown out. We only want the questions that truly haven't been answered. Then, we have this consortium meeting involving people with the lived experience, healthcare providers, researchers, and we come up with a top 10 priority list that then fuels the research priority forthcoming. I think that this is so exciting. Like I said, it's never been done for menopause before, but there're so many things that we don't know, especially with transgender individuals. How is hormone therapy in that patient population? How does it impact the menopause? Does it increase their risk for other things later in life that maybe we don't know about? Do they have a different trajectory than not? I don't even want to put questions out there because I want people to come up with their own questions. But we will be blasting it on social media. Lots of different partners and other major menopause organizations globally are supporters, and we'll be distributing the access link to people, that members are in their community. So that's my plug about MAPS.

[music]

Matt: Fantastic. That sounds like a great idea way to get research questions. That's a really smart idea. All right, well, we will let you go. Thank you again so much for all your time in teaching. We'll have to think of a reason to have you back for a third time in the future.

Monica: [laughs] All right, take care. Good night.

Paul: This has been another episode of The Curbsiders bringing you a little knowledge food for your brain hole.

Matt: Yes, it has, Paul. [laughs]

Paul: Hoist by my own petard. Still hungry for more? Join our Patreon and get all of our episodes, ad free, plus twice monthly bonus *episodes@patreon.com*/*curbsiders*. You can find our show notes at the *thecurbsiders.com* and while you're there, sign up for our mailing list to get our weekly show notes in your inbox, which includes our Curbsiders Digest, which recaps the latest practice-changing articles, guidelines, and news in internal medicine.

Matt: We're committed to high value practice-changing knowledge. And to do that, we need your feedback. So, you can email us at *askcurbsiders@gmail.com*. We also want you to subscribe, rate, and review the show on Spotify, Apple Podcasts, YouTube, wherever you get your podcasts really, that does help. Reminder that this and most episodes are available through VCU Health at *curbsiders.vcuhealth.org*. You can claim your CME there. A special thanks to our whole team who helps us write and produce the show. Our technical production is done by Pod Paste. Elizabeth Proto runs our social media, Chris "The Chiu Man" Chiu is the moderator on our Discord, and Stuart Brigham composed our theme music. And with all that, until next time, I've been Dr. Matthew Frank Watto.

Paul And as always, I'm Dr. Paul Nelson Williams. Thank you and goodbye.