Menopause and Healthy Aging

I'm really excited to be here to talk to you about our current understanding of where the science is in terms of menopause management. Now, I want to just be clear that I've been given 30 minutes to give that talk. I'm going to get through what I can get through, but we can have their multi-day conferences on this topic. I'm going to hit the highlights of really thinking about what people ask us. What are the key questions that I get asked, and hopefully, I can answer some of your questions before the Q&A;, which will happen right after my talk as well. These are my disclosures, and then these are the objectives. We're going to talk about how we define menopause. What are the hormonal changes? I'm really interested in physiology. I feel like if you can understand physiology, you can sometimes then understand what's happening in your body and then also how we manage it. We're going to talk about the symptoms associated with menopause and the various non-hormonal as well as hormonal treatments.

As I said, I got 30 minutes. We will try to get through as much of this as possible. I do talk fast, so we probably can get a little bit ahead here. First question people always ask is, what is menopause? I don't expect the lay audience to understand this, but you'll oftentimes hear people saying, Is it right after my period? Is it a year after? Is it when this hormone in my brain goes up? Is it when a hormone in my ovary goes down, or is it all of that? The truth is there's actually one very clear definition. The definition is that menopause is literally the day that somebody goes one year without a period. It is one day of your life, essentially. Everything leading up to that day is pre-menopause, and everything after that is menopause. Now, some people don't get their periods, and that's because they either had a surgery to remove their uterus, they had an ablation to remove the lining.

They're on a contraceptive or a hormonal method that suppresses their periods. In those cases, there are lab tests that we can do, but those lab tests require six months between them because sometimes you can see hormones fluctuating, and the hormone we're looking at is a follicle-stimulating hormone. FSH is what we call for short, and that is basically how hard is the brain working to tell the ovary to get an egg ready? And if there are no eggs left, the brain is working really hard, so you see high levels. Now, we don't test people for ovarian hormones to see when are you going to go through menopause? Are you in perimenopause, if they're over 40? Because if someone's having symptoms of perimenopause or menopause, it's pretty much a slam dunk. But when they're younger, sometimes people do go through an early menopause, and we always do want to try to diagnose that. Let's think about why testing sometimes isn't always the answer.

I'm just going to go over the menstrual cycle. The reason that I talk about the menstrual cycle is in a normal ovulating person, there is a hormone that comes from the brain, so that is the third row down. There's luteinizing hormone and follicle-stimulating hormone, and that hormone tells the ovary to get an egg ready. When it does that, there is a hormone called estradiol. We're familiar with estradiol that goes up. Estradiol stimulates the lining of the uterus and gets it ready for an egg to implant. After ovulation, that's the second half of the cycle so if you look at the bottom here, you'll see gluteal phase. The second half of the cycle is basically dominated by the hormone progesterone, and so you can see that just one below the bottom, that progesterone then becomes the dominant hormone, and this is important because progesterone's role in the uterus is to protect the lining and get it ready for an egg to implant.

Progesterone is really necessary to counteract the effects of estrogen in the uterus, and this comes into play when we talk about hormone therapy. But there also are progesterone receptors, just like there are estrogen receptors all over the body. That means that most of our tissues are sensitive to these hormones, not just the uterus. When we're looking for labs, basically, there's all these labs that people are oftentimes asking us for, and at the end of the day, the answer to this question is E. There is no hallmark lab finding in perimenopause. When somebody is still having irregular bleeding or irregular cycles, you're going to see wild fluctuations in both the hormones that the

pituitary are making and that the ovary are making. Why is that? This is the life cycle of hormones, and in pre-menopause. In the really what we call the reproductive years, when you're having a normal menstrual cycle, I showed you that you see this nice ebb and flow of estrogen.

Progesterone gets really high and then really low. You do not make progesterone unless you release an egg. Then in perimenopause is where you see that both estrogen and progesterone levels go all over the place and in post menopause, that's when all the hormones go down. It's very predictable what happens to our estrogen, progesterone, and I would say testosterone levels in post menopause. But in the years leading up to that final period, the hormones are all over the place, and testing them doesn't provide a lot of information except to say they're all over the place. When we talk about menopause, it's really important to think about what the symptoms are, and there is a difference between the estrogen withdrawal, those fluctuations, and then the lack of estrogen that's estrogen deficiency. The things that get better over time are the hot flashes, because that really is the fluctuating estrogen.

It's not just a lack of estrogen because otherwise, everybody would have them for the rest of their life. But most people have hot flashes for, can be months to years, and that can last for several years in some women, but it usually is only a few years, and then it does get better. Then estrogen deficiency is where you see this long-term effect of a lack of estrogen on the tissue that estrogen targets and so that includes the brain, the bone, the blood vessels, the skin, the joints, mucous membranes, which also includes the genitals, and so you see these long term chronic effects to a lack of estrogen. The things that we think about in terms of lifestyle, because I think it's really important, and we'll talk about longevity and healthy lifestyle, when people complain in menopause are the sleep changes, the mood changes, the trouble finding words, sexual changes. These are all going to be made better with healthy lifestyle and that really is, I think, about sleep hygiene, especially.

I think that the lack of sleep is contributing to so much of what we attribute menopausal changes to and it's because the sleep changes that happened in the 40s and 50s are timed very closely with perimenopause and menopause, and they are related in some way to the drop in estrogen levels, but they're also related to changes actually in melatonin and hormone secretion in the brain that helps people sleep. But exercise is going to help these dietary changes are going to help, but that's obviously not the only answer. I'm here to talk about the way we think about medical management of these symptoms. This is a busy graph, but the main thing is that this is a graph looking at cognitive behavioral therapy. These are strategies that are basically brain training. Across the board, the studies have shown that if you train your brain to respond to the symptoms of menopause, those symptoms will be reduced.

That is a benefit. Other non-hormonal options. This is, again, a lot of different things. The top of this graph basically is showing all the SSRIs. Those are the serotnergic drugs that many of them have been studied. The main one that's been studied is Paroxetine at low doses to treat menopausal symptoms. The SNRIs, the selective norepinephrine reuptake inhibitors like venlafaxine, have also been shown to be beneficial. Gabapentin has also been shown to be beneficial. Anticholinergic drugs like oxybutin that we oftentimes use for overactive bladder have also shown to be beneficial, but there is some concern about long-term cognitive changes from using that, so we don't oftentimes recommend it. The data on clonidine is mixed, but some people will use that as well. Then the biggest one are the newer players on the block, the neurokinin antagonists, and I'll jump into those a little bit because those are really the ones that are rivaling hormone therapy now in terms of managing the traditional symptoms we think about the vasomotor symptoms like hot flashes.

When we're starting with pharmacological treatments, you'll see that we start with really low doses. Oftentimes, we do the venlafaxine, the SSRIs, and then gabapentin. When we compare those medications to all the other things people do like exercise and the SSRIs and things like yoga and Omega 3s at the top there, you'll see that Omega 3s don't really have a lot of data for them. Exercise does have some data. Yoga even has data, but nothing works as well as the hormone

therapy in the long-term. When we talk about these new ones, these neurokins, and so this is, again, pretty detailed medical, but the way to understand this is that there is a thermoregulatory part of the brain, and to understand that in the brain, the cells talk to each other via neurotransmitters. Historically, we knew that estrogen must play a role because when you give estrogen or even you give these SSRIs, there's something that's happening that must be affecting the neurotransmitters.

Basic science research found the neurotransmitters, and it's basically this kisspeptin neurotransmitter, and it's affected by neurokinins, and so there are now these medications that target the specific neurotransmitters in that part of the brain that gives people hot flashes. There are two commercially available medications that are out there that really are rivaling standard hormone therapy in terms of managing these symptoms. These are the initial dosing studies. I'm going to just jump to say the longer-term data that you can see that the drug beats placebo in every way. But remember, the placebo effect is also quite strong. Now, when you look at hormones, the graphs that I'm showing you, the first one with the neurokinin medications, was looking at daily hot flashes. This is looking at weekly, but they're all about the same. When people are bothered by hot flashes, they're having about 10 hot flashes a day.

That is incredibly bothersome. What you want to see is these decreases that are sustained over time. This is a graph that shows that if you give people hormone therapy, you're going to see a sustained decrease, and it is dose-dependent. We oftentimes talk about the lowest doses of hormones, which can be very beneficial. But for many people, if their symptoms are quite bad, they will do better on higher doses. That's what's very nice. There's not just one treatment when it comes to hormone therapy. Higher doses of hormones will absolutely treat hot flashes better. When we talk about the hormone therapy data, this is where we need to get into the history of this, where historically we have really good basic science data that shows that estrogen was beneficial not just for the hot flashes, but actually to the heart, because we know that women have really low levels of heart disease until they go through menopause and at that point, their level of heart disease goes up to that of men and the big difference there is estrogen, and so there was always this idea that there's something going on in the menopausal transition.

Remember, the number 1 killer of women is not breast cancer, it's heart disease. If there's something we can do to mitigate that, it would be great. Historically, there was this idea that hormone therapy must be it. For years, many women, almost the majority, were on some hormone therapy, and that all then changed with the WHI. The WHI was a very big study that we hear about all the time, and I'm just going to review it because you probably are familiar with it, but I just want to go back to what it was. It was a very large study that was both an observational study. They were looking at dietary changes. They were looking at fractures and colorectal cancer, and then they had this group of women, almost 30,000 women, where they were actually, for the first time, randomized, where they took that, and they said, you're either going to take a placebo, a sugar pill, or you're going to take hormones.

This way, we can say, do the hormones prevent cardiovascular disease? And that was the entire point of the Women's Health Initiative. It wasn't to look at any other outcome like breast cancer or blood clots or any of the other things we hear reported. It was designed to answer this question of does hormone therapy truly reduce the risk of cardiovascular disease? If you randomize, you distribute the risk, so there'll be higher-risk women in both groups, and you can see an effect. They started recruiting in 1993. They started, and then they ended around in the late 1990s, and then they stopped after four years, basically. the reason they did that was there was an estrogen and progestin group. people that had a uterus, remember I told you that if you take estrogen alone, it will stimulate the lining of the uterus, and it puts people at risk of cancer so you have to take something to prevent the uterus.

either progesterone or in this case, it was a synthetic progestin, and that's important. Then there was an estrogen-only group for those that didn't have a uterus, and this is also really important because the estrogen-alone group gives us insight to what estrogen does, and it might be a little bit different than when you combine it with a progestin. In the WHI, they used conjugated equine

estrogen for the estrogen component, which is important. It's an oral form. It has many different estrogens. In the progestin arm, they used medroxyprogesterone acetate. They stopped this trial early because they saw significant increases in cardiovascular disease, venous thromboembolism, that's BTE, and BC, that's breast cancer. That's what we all had heard about, and that's what really put the black box warning on hormone therapy was this study that basically was a surprise to everybody. The first question I oftentimes get asked is, if you give somebody hormone therapy, does it cause breast cancer?

Because that's not the number one killer of women, but it is the most common cancer that we see. One in eight women will get breast cancer, and it's incredibly important to know, does hormone therapy play a role? The truth is, in my interpretation of the literature, it doesn't seem to be. Now, if you look at observational data, again, this is a lot of detail that I have here, you're going to see that if you look at large groups of women, you're going to see that those that took hormone therapy seem to have higher rates, but there are a lot of what we call confounders, meaning that there are other things that play a role in the breast cancer diagnosis. Namely, they had more screening oftentimes. If you're looking for more cancer, you're going to find more cancer, and that doesn't mean that it would be clinically significant. These are tumors that may never actually come to anything dangerous.

that's one of the big issues when we study anything is, like, how much are people looking for problems? You're going to be able to find them. That was the observational data. The randomized data in the WHI is really important because I told you that breast cancer was not the original goal of the study. It really should never have been reported on because they didn't organize the study in a way to look at this question truthfully, but they still reported on it, and they reported that there was a hazard ratio of 1.25, which comes out as a 25% increase. Now, that sounds like a very scary increase, but when they actually adjusted for risk factors, anybody that might have had a personal history, family history, That number did not meet significance. What that means is that any increased risk they saw was possibly due to chance, and that wasn't reported. The biggest reason for that is this is a graph that's showing you in the group on the right, the placebo group, this was the group of people who had taken hormone therapy before, and on the left, they had never taken hormone therapy.

What you see is that those that had never taken hormone therapy before, the hormone group and the placebo group, had very similar rates of breast cancer. That is not significant. We do not see that hormone therapy over years contributed to breast cancer. But in the group that had taken hormone therapy before on the right, what you can see is there was a very strange thing happening, the number of new breast cancers was actually the same as you can see on the other side. But the placebo group, the group that was taking a sugar pill, had an unusually low rate of breast cancer. It didn't make any sense. When you compare those two, it looks like there's a significant difference. But actually, there really wasn't overall. In the WHI, if you look at, does this combination cause breast cancer? It doesn't seem to, and this is, again, the estrogen and progestin. That reported 25%, even if it were true, that would come out to about eight per 10,000 women, which is a very low number.

Even if that were true, your risk of identity theft is higher than eight in 10,000. In the estrogen-alone group, for those that are familiar with statistics, multiple studies now have shown that in that group, that didn't take the progestin, they had lower rates of breast cancer. The estrogen-alone group, after even 18 years of follow-up, the estrogen group had less breast cancer, that estrogen type reduces the risk. I want to be clear that it was conjugated equine estrogen because a lot of people out there are saying, oh, all estrogen reduces breast cancer, and that's not true, the WHI showed that this particular pill did. This is the data, again, with the estrogen and progestin, and that it was all within the group that had used prior hormone therapy. Now, let's get into the heart disease risk. A lot of people get worried about this because, again, I said the WHI suggested that there was a heart disease increase in those that took the hormone therapy.

But the truth is basically all of that risk was in the older population. The average age of enrollment in the WHI was 63, and that was because to get 30,000 women, to have a number that you would be able to see a heart attack difference in within that group, you needed older women, and so they basically gave hormones to anybody that walked in the door, not even women who had symptoms, just to see, is it preventive? We're not doing this for vasomotor symptoms, we're doing this to prevent heart disease. In those that were over 60, they had a slightly higher risk, but in those that were under 60, they had a decreased risk, and especially a decreased risk in the estrogen-alone group, so there is a relationship between when you start hormone therapy and this benefit. There seems to be this idea of a timing hypothesis, and multiple studies have shown that. These are all the studies that have shown that if you start hormone therapy early, that could be either with estrogen-alone or an estrogen and a progestin, or progesterone, those groups all have lower rates of heart disease than if they took placebo, if they start closer to menopause.

The reason for that is, this is a graphic, that basically, if we think about the fact that hormone therapy probably, or that hormones in general are probably protecting the blood vessels for the years up until you go through menopause, once that estrogen is removed, the blood vessels are going to get damaged, and then if you put estrogen on top of that, it could worsen it. But if you have estrogen the whole time, you're going to get that prevention benefit. Then there's this question of how do we take the hormones? Because now you can take them orally, or you can take them through the skin, either transdermally or even transvaginally. This is just a graph showing that if you take it orally, you're going to see a significant change in many different things. You're going to see a change in your lipids, and in some ways, it's good, actually, your cholesterol goes down across the board, but you're going to see an increase in proteins made by the liver, so that's your sex hormone binding globulin, clotting factors go up, your insulin resistance actually can be affected by this as well.

Those things do not happen if you take it transdermally. It's really important to think about if we can, it's not always the option, some people don't absorb through the skin, you'll see that we recommend taking hormones through the skin because it's really mimicking what the ovary is doing, you're not introducing anything new to your body when you take it that way. But, again, I just showed you that the oral form in the WHI reduced the risk of breast cancer, reduces the risk of cardiovascular disease if you take it early, so a lot of people being scared of the oral forms is not well-founded in the literature, it's pretty safe, and especially oral estradiol, which is probably even safer for when it comes to something like blood clots. Then I'm just going to briefly mention the question about dementia because this is a super hot topic, and Dr. Bove is going to get into this, whether or not hormone therapy reduces dementia, and the answer is unclear.

So I want to be real clear about this. There's observational data that suggested that people who are on hormone therapy may have lower rates, but there are also observational data that suggests that being on hormone therapy gives you higher rates. Mechanistically, it makes sense. We know that there are estrogen receptors in the brain, and we know that there are changes that happen in the brain that predispose people to dementia at earlier ages. The problem is that if you give people hormone therapy, there's only been one randomized controlled trial that was part of the WHI, where women 65 and older took hormone therapy, and those that took this combination, this conjugated equine estrogen and medroxyprogesterone acetate, had more dementia, and that was the only time anyone was ever given a placebo versus a combined medication. Those in the estrogen-alone group had no benefit. Now, the question is, is there an age of initiation that would basically give us that benefit?

Because probably if you're giving it to people when they're older, they already have damage, it's like the timing hypothesis, if there's brain damage, adding estrogen is not going to make it better. Now, the question is, if you do it earlier, doesn't make it better? We have yet to answer that question. When it comes to hormone therapy and one condition that no matter what, it will improve, the WHI showed that there could be a benefit to colorectal cancer, but that's not across the board in every study, it's never been looked at primarily as an outcome. Endometrial cancer is uterine cancer that if you take estrogen without sufficient progesterone or progestin, you can get uterine cancer, and I

want to be really clear about that. I do not believe in giving people estrogen without something to protect the uterus if they have a uterus. Oral estrogens can be associated with blood clots, but all hormone therapy in the form of estrogen will reduce osteoporosis, so it reduces the risk, and there is data to show that it treats it as well.

That is across the board, there is no question that hormone therapy is quite beneficial when it comes to osteoporosis prevention, and I would argue treatment, even though it's not in the guidelines to treat, and that's mainly because older women are the ones that are getting osteoporosis, and there is concern about giving older women, over 65 is when we really start screening, we're concerned about giving them hormone therapy if they haven't been on it before for all the reasons I've already mentioned. Is there a recommendation for primary prevention? I just told you that the data suggests it prevents heart disease, we know that it prevents osteoporosis. Estrogen-alone does seem to prevent breast cancer, but all of the guidelines we have now do not say that we should be using this for primary prevention. Part of the reason is the way we prescribe now is a little different than the way that all these other studies were prescribing.

We don't have data on what we're giving, and most of the internal medicine and other providers who think about these primary prevention strategies do not feel confident to say that hormone therapy should be used to prevent illnesses, they really say it should be used to treat symptoms, hot flashes, night sweats, cognitive word finding difficulties, those kinds of things. The last thing I want to end on is this idea of bioidentical. Bio or body identical is does the hormone look like what the ovary makes? A lot of times people think that the only way to get this is to go to a compounding pharmacy where they specialize in basically getting the raw material, putting it into either a pill or a patch, a spray, something, a cream, and the truth is, when it comes to estrogen, especially, because that is the hormone that I know for a fact if you take it at not controlled doses and not with the proper amount of progestin or progesterone can cause uterine cancer.

This medication estrogen really should be gotten from an FDA-approved product, and all of the FDA-approved estradiols, the ones that are a patch, a gel, a spray, and the oral estradiol are body identical, they are bioidentical. Estestrol is also body identical, that is now being used in birth control, and it probably will come out in menopausal hormone therapy. That's just another form of estrogen that's made by female fetuses. Micronized progesterone is bioidentical. If you want to use a compounding pharmacy, it's only really if someone can't tolerate any of the other products, if there's something in the base or the gel, or the oral form they can't take, and the concentration can be very variable, so you really want to have a reliable pharmacy. There is one FDA-approved medication orally that has estrogen and natural progesterone in it, and so that can be really important. If people want bioidentical, which I think is reasonable, I encourage people to get the FDA-approved products.

The most important is that estrogen can be taken through the skin, but natural progesterone cannot. I see a lot of people taking progesterone creams, it does not absorb through the skin, it's too big of a molecule, and it dissolves right away. Micronized progesterone is body identical, and it's formulated in a way that will stay in the system so it will work. That's a really important thing to understand about getting your progesterone. This is how we prescribe, and there's no right answer for everybody. I'm just putting this out here because you're going to see that everyone's like, oh, I need to be on a certain amount and a certain dose, and I just say that there's many ways we can do it. I oftentimes will start with a transdermal patch, but people do gels, they do sprays, there's a vaginal ring. Oral is fine. I like natural progesterone, micronized progesterone, I give it nightly because it makes you fall asleep, but you want to take it either with food or a scoop of peanut butter, something to help it dissolve.

There are combination patches that have synthetic progestins, they work very well, and so that's one medication. A levonorgestrel IUD is an IUD, a lot of times, in perimenopause, people are using it or even beforehand for contraception. It can be used for up to five years for menopausal hormone therapy. There's lots of other ways we can do it. Now, people who have either a high risk of breast cancer or cannot tolerate a progestin, there actually is a commercially available medication that

doesn't have a progestin, it has a medication that blocks estrogen at the level of the uterus, that's called a selective estrogen receptor modulator. That's an oral medication, and I love using that because it's really good for people who have also abnormal bleeding, are concerned about progestins for whatever reason, and it seems like there's probably a benefit in terms of reduction of breast cancer, even more on top of just the estrogen-alone.

That was great, Dr. Rowan. Thank you so much. The first question is just a clarification of the nomenclature. Somebody asked that they were in menopause, so what is postmenopausal, when will they be in post-menopause? Great. It sounds crazy. We say in menopause, but the truth is that's just another way we say you're postmenopausal, is the way that I think about it. We just use those terms interchangeably. Once we say you're in menopause, it's the same as saying you're post-menopause, and that's anytime after that one year from your final menstrual period or all those other ways, And then when people are like, I just don't know when I went through it. I'm just telling you if you're a certain age and you've had the symptoms, you are probably post-menopausal or in menopause, either one interchangeable. Perfect. Thank you. Then there's a couple of questions that are about perimenopause and use of hormones.

One question is that since progesterone decreases first, does it make sense to start with hormone therapy with just progesterone when the sleep starts being lower quality, and only add estrogen later when hot flashes start? This is such a great question. There's no data on this, so there's no study that ever said, let's give progesterone for perimenopause. There is data that shows that progesterone alone will help with sleep and will help with hot flashes. My personal practice is absolutely that the first thing I oftentimes go to in perimenopause is progesterone because the first symptom that people are usually complaining about is the sleep, and progesterone does help people fall asleep. I also see people get mood changes, and I do think that those mood changes can be related to the lowering of progesterone. Now, if somebody has mood changes in their 20s and 30s, leading up to their period, oftentimes, they're a little more sensitive to progesterone, but if those mood changes started more in their 40s, I'm starting to think that they're sensitive to a lack of progesterone.

There is some biological explanation for how that is the case. I'm not going to jump into it here, but it is a good question, and that is oftentimes what I start with. Then, are there any risks or benefits to starting hormone therapy earlier, for example, starting at 46 in an individual who will eventually go into menopause at 52? Again, I think we have to just think about what our goals here are. If we're talking about prevention, I don't think there's any evidence that shows that if you start at 40, you're going to have a lower rate of cardiovascular disease more than what we already know the data confers. I wouldn't say that. If somebody is at higher risk of bone loss, if somebody is quite a low BMI, doesn't do weight-bearing exercise, for example, I think those are people who actually could benefit earlier on from estrogen, they're not making a lot of estrogen. People that use wheelchairs, for example, I see those are at much higher risk of getting fractures, so in that case.

But otherwise, I do encourage people, it's not the only way to prevent osteoporosis. Weight-bearing exercise is really good for you on multiple levels, and so you don't need it to do that, there's other ways you can do that. The question I have, and Dr. Bove can probably answer it better, my suspicion is that there could be a benefit in terms of cognitive changes or prevention of dementia, but I don't think, and Dr. Bove can answer this, that if we did a population-based study that we will actually see that clinical benefit. I think what the future is going to hold is that there is a group of people that are more prone to damage that puts them at risk of cognitive decline, and those are going to be the people that may benefit. I can't see Dr. Bove to see if she's agreeing or not. My suspicion is we'll find that from the cognitive change. But again, people who are like, I want to take hormone therapy to prevent dementia, we have no data to show that there is a benefit in that at this point.

So no, I think if people are having symptoms, they might benefit, but I think it's not necessary to start before that final period if you're asymptomatic. Yeah, I think that makes sense. As we know, there's about, I think the most recent statistic I heard from one of our OCD experts is there's one in

eight people that are on GLP medications, so there's also a question about GLP. If GLP-1 medication slow down stomach emptying, could that reduce absorption of oral progesterone leaving at the estrogen from the patch unopposed, which could theoretically increase endometrial cancer risk? This is a theoretical risk. We know that in oral contraceptives, that GLPs because they delay gastric emptying, we're seeing both a decrease in efficacy, but that's not the only reason we're seeing where people get pregnant on their GLPs, they're much more fertile when they lose the weight, and so it's not just that the oral contraceptives aren't working, people just get more fertile, and so they otherwise maybe had missed a pill or something.

It is a theoretical risk that it could delay the gastric emptying. I'm not convinced that would make a big clinical difference because, again, you want a slower absorption of the progesterone anyways, so it's different than the birth control where you really need to get that peak level of hormone at a specific time to suppress ovulation. It's different for the way that progesterone is working. You might not hit that peak level, but you may have a more steady state for a longer time, and that may be enough. I think it's a very good theoretical risk. I will also say that micronized progesterone isn't well absorbed in general, and so we oftentimes will see people need higher doses of micronized progesterone, even if they're on the doses we recommend, I'll see people will get bleeding or they'll get proliferation of the lining of the uterus, and so I think for those people, especially, I'd be more worried.

But right now, it's really a theoretical risk extrapolating from the birth control data, and I just told you why it's a little hard to extrapolate because they had different mechanisms of action. Then there's a question about the estradiol patch. Does the estradiol patch cause the body to reduce or stop its own natural estrogen production? That's a great question. Yeah. In other words, after you discontinue, how long does it take for it to resume? That's what would happen to people. A lot of people want thyroid supplementation now. They're coming in and that's all that that does. Your body's like, now I'm not going to make fibroid. It doesn't give you a lot of extra. Your estrogen is really all over the place. If you're taking an estrogen patch, it's not a whole lot, and so it's not going to be able to feedback on your natural estrogen. The way to think about the ovaries in perimenopause is they're basically like a sputtering gas tank that is spitting out hormone, and it is the spitting out that high and that low that's really leading to so many of the symptoms, and all the patch does is keep you from getting really low.

It's not going to keep it from spitting it out. It's still going to be sputtering out that estrogen. Could you talk about sleep disturbances separate from hot flashes during menopause? Sleep disturbances is very different than hot flashes. Hot flashes is really coming from the thermoregulatory part of the brain, the drenching sweat. The sleep disturbance is people have trouble falling asleep and then they have trouble staying asleep, so they get really early waking. Now, people can get hot flashes at night, which we call night sweats, and that can disrupt sleep, but that's different than what I'm talking about. What I'm talking about is that difficulty falling asleep, and that early wake, and being unable to fall asleep. That is going to be related to changes in melatonin levels, which are very clearly documented in the perimenopausal transition. We do think that progesterone it affects GABA receptors, and so those are like you're calming, that's the same receptor that alcohol targets, it's the same receptor that anxiolytic benzodiazepines, Valium target.

Progesterone targets those same things, so that is relaxing and calming, and that can help people sleep. Now, to stay asleep, it looks like estrogen plays more of a role, and so depending on where people are struggling, we're going to see which hormone we may want to add in. But I also want to stress, and I think there was a lecture in previous week about sleep hygiene, because hormones cannot fix everything, and you just cannot do what you did when you were in your 20s and think that you're going to be able to sleep. You have to get some sleep hygiene. You have to go to bed at the same time every night, you have to wake up at the same time every day, you have to lower the temperature in your room, you have to wear, maybe even if it's a heavy blanket, it has to be cotton. There's so many things that we need to do to protect sleep, and I wish hormones could, just like everything in your 40s and 50s, it can't hormone away all the things, and so we have to do some other things to help with it as well.

Wonderful. Two hot takes. Tell us again, dose of progesterone and should they ask to say, take it with food or peanut butter? Yes. Progesterone works twice as well if you take it with food. We tell everyone to take it at night because it makes you sleepy, but I will say take it after dinner. I want food in your stomach when you take it. If you go to bed at 10:00 or 11:00 P.M. and dinner is at 6:00, which is probably how it should be, then just take it with a scoop of peanut butter. Sounds crazy, but the progesterone is actually micronized in peanut oil, and like dissolves like, so if you take it with a scoop of peanut butter, it will dissolve it better, so it'll make it more bioavailable to you. Perfect. Well, thank you so much. There are many positive comments too, and asking if you take patients. Dr. Rowen's at UCSF, she's one of my wonderful colleagues and does take new patients. I don't take new patients for menopause management right now.

Oh, yes. If you want to see me for menopause, you would have to see one of my colleagues, and if it's a complex question, I would be more than happy to answer it. But if you're going to try to see me just for straight menopause, you're not going to be able to get in. We're seeing more complex and surgical consults. But we're happy to see you at UCSF for menopause in general. Yes. Wonderful. Well, thank you so much. It was great to hear your insight on this and sharing all of this wonderful information. Thank you, Dr. Rowen. I would also now like to introduce Dr. Riley Bove. Perfect. Hello. Dr. Bove is Rosenberg Ach, Family Endowed Professorship in Neuroimmunology, and the Founding Director for Sex and Gender Enriched Neurology Program at UCSF. She conducts research to understand how pregnancy, lactation, and menopause influence brain health and how to provide safe, effective, and compassionate clinical care to all women.

Thank you so much, Dr. Bove. We're very excited to hear from you too. Perfect. I really want to pick up Rowen left off. Dr. Rowen just did a tort for us through menopause itself, what is the physiology? What is the treatment for perimenopause? Where I'd like to go is to think about how do we plan for whole person wellness as we move through perimenopause and to the other side. Women spend a third, a half of their lives in the postmenopausal period, and we need to really plan for that. Just try to bring together some key tips and tricks for that. What if in the clinic, we had some women-centric care bundles? We have this for newborn visits, we have this for seven-year-old visits, well child visits, pregnancy visits, what if we had detailed care bundles where we could really look at the whole person through different phases of reproductive aging and really make sure that our care was optimized?

That's what I'm moving towards in some of my digital health work, and I think, really, as Dr. Rowen mentioned, there's an enormous push that she's leading at UCSF to do this also for menopausal management. First, let's just think about what wellness means head to toe as we go into menopause and beyond. Thinking head to toe, I want to think about cognition, sleep, mood, fatigue. We want to think about vision, hearing, and speech. I'm going to come back to these themes multiple times, really to make sure that we're anchoring them. Then we want to think about strength, muscles, joints, bladder, bowel, sexual function, walking, falls, things like that, really comprehensive assessment. We also want to center health within the multiple dimensions of wellness. Some key points that I'll bring up to really think about how do we plan for wellness in the big picture. From an intellectual standpoint, we want to think about meaningful engagement activities.

Air and water quality matter from an environmental standpoint, and I'll show you a little bit about that. We want to be thinking about financial, work, occupational, and big picture priorities, advanced care planning, things like that, making sure that the choices we make, the treatments we choose, are not going to put us in unmanageable debt. We want to hard-code time with friends and social engagement. Our former surgeon general put on the table that in the United States, there is an epidemic of social isolation of loneliness and that isolation, that epidemic is really a medical problem. It has immense health impact. If I can make one big key point, that is to establish a solid relationship with your primary care physician for your wellness, and then thinking about the pill, the purpose in life, what is that going to be, how is it working out, and how to plan to really deepen that pill?

I treat brain diseases, neurologic diseases, and I know there were a couple of questions about cognition. This is a study updated in 2024, this is a Lancet study where they looked at the preventable risk factors for dementia, and they found that there were 14 lifetime factors that if you address them, could reduce dementia by 45%. Almost half of dementia cases could be reduced later in life if these Lancet 14 were addressed. I'm going to go into them in a little bit of detail. In early life, educational attainment is a key protective factor. When we move into midlife, hearing loss is a major issue. High cholesterol, depression, traumatic brain injury, physical activity, diabetes, smoking, hypertension, obesity, and alcohol use. Even later in life, there are still factors that occur that influence risk of dementia and that can be addressed. I mentioned social isolation, air pollution, and visual loss.

Those are all really targetable things. What is not in the Lancet 14 is menopause and female reproductive health. They seem to have forgotten about that concept, so I'm going to do a little U-turn and talk about that for a moment as it relates to later life well being. As Dr. Rowen expertly showed, we are talking about the final menstrual period or FMP, and in the years just before the FMP and the early years after, that's perimenopause, and that is where the cardinal symptoms of menopause arise, hot flashes or vasomotor symptoms, and then changes in sleep, mood, libido, energy, cognition, bowel bladder, and pain. Then move into the later postmenopausal years, and that can be a third, a half of the remaining lifespan, and that is where when we think about the menopause trace, we see the genitourinary syndrome of menopause, musculoskeletal syndrome of menopause, and cognitive concerns, which is one of my big areas of research.

During perimenopause, I saw some of the comments in the chat already about this, what I hear as an MS doctor as someone who treats women who already have pre-existing conditions moving into perimenopause, there's really a lot of confusion around what is perimenopause, what is their underlying condition, and how do those intersect, and also, who's going to take care of you in that situation? Collaborative care is really the key here. Another thing I hear commonly from my patients is they want to know, am I developing dementia because of the cognitive changes? What should one expect during perimenopause about cognitive changes? One should expect some word finding difficulty, some tip of the tongue, some going into the room and losing track of why you were there, difficulty with working memory, so harder to keep everything in your head while you're processing information. Those would be the things that would be commonly expected during perimenopause.

I can tell you that almost all of my patients during perimenopause tells me about these symptoms and many of my colleagues going through this as well. That would be expected. What might be different is someone who has marked personality changes, not somebody who becomes more irritable, depressed, or anxious, but someone whose personality really changes dramatically, or things like truly getting lost or leaving the stove on catching fire, things like that. Many people are concerned, and these cognitive changes that occur during perimenopause, they tend to get better. But one of the areas of ongoing research is whether that wobble, I call it the cognitive wobble, really is related to later life changes, and we don't really know that for sure. What we do know is people often can develop strategies around it. You don't have to be embarrassed every time you can't find the word. You can come up with a strategy to just like, while that word is coming back to me, let's focus on this other thing.

We can come up with tips and tricks, especially for people in the workforce to mask and move on. Because the first few times that happens, you're very shocked that your mind is doing this to you. But it's very common and often improves a lot. Then there's another thing that I hear often, and that is the sensation of overwhelm and something has to give, and it really is overwhelming to be going through perimenopause when they're also children who may be adolescents, young adults, empty nest syndrome, a lot of pressures, and things like that. These are just really common experiences. This is my cheat sheet for perimenopause management, and again, I wanted to show you early on that we really go head to toe and think about all of the different things. Dr. Rowen really lasered in on the vasomotor symptoms, but there are many other symptoms that people experience and that we really want to treat during perimenopause.

She did touch on several of these, so sleep, and really thinking about how to mood, bladder function, spasticity, pain, influence sleep. Fatigue, ruling out metabolic disorders, thyroid, vitamin D, B12, things like that. Thinking about bladder, frequent urination, vaginal dryness, those are symptoms that actually can improve a lot just with vaginal estrogen, not systemic, not oral transdermal, but just tablets or cream or other formulations that are inserted vaginally. Then finally, joint pain and stiffness occur commonly, and stretching, ibuprofen, things like yoga, things like that can be very helpful. Connecting perimenopause to later-life brain health. This is a big area of my research and many others. What we see is when women undergo menopause early or surgically, having both of their ovaries out early, that is linked to later-life cognitive changes. Whether that's Alzheimer's disease, mild cognitive impairment, Parkinson's disease, risk of strokes, there is a connection between the ovaries coming out early and later-life brain health.

Why is that? What is this link? Of course, one hypothesis is the estrogen and changes in estrogen and other hormones can influence, if these are protective, the loss of these hormones then exposes the brain to increased vulnerability. But there's many other pieces to this puzzle, because as Dr. Rowen went over, loss of estrogen is related to all other things: musculoskeletal conditions, cardiovascular conditions, diabetes, obesity, things like that, that also influence brain health. It's hard to say whether really the menopausal changes in brain health are directly connected or indirectly connected through these different things. We also know that many earlier life exposures can influence both the menopausal age and transition, as well as these other medical conditions as well. Finally, when we're thinking about reproductive aging, we're also thinking about just what is general aging and what is the loss of ovarian hormones.

It really is quite a complex picture that many people are trying to tease out so we can find the things that we can do something about. Moving on a little bit. I talked a little bit about how I like to think about perimenopause, counsel patients from head to toe, and really set them up a little bit for the future. Let's move on. What would a care bundle look like in someone who is 65? I showed you some of that general glance at 14 protective factors. But how do we really think about wellness, how to set people up for thriving? Again, taking this holistic picture around age 65, thinking again about meaningful engagement and starting to think more about advanced care planning, financial planning, social engagement, etc. What are the functional things? What are the tests that you need to do for your body and your mind that would indicate that something is awry, something needs treatment or optimization?

Taking that head-to-toe approach again, that sleep screening is key. At your annual visits, you should go over sleep and think about what are the factors that are preventing you from getting a good night's sleep. We know that with aging, there's some fragmentation of the sleep architecture, meaning the normal pattern of falling asleep, staying asleep, waking up can change a little bit, and we know that. We're looking for things that are really consistently a problem and that are leading you to wake up the next day fatigued. Is there a sleep apnea, so that we know that after menopause, rates of sleep apnea in women, which are a little lower than in men before menopause, catch up with men. Is there sleep apnea? Is there truly fragmented sleep? Is there snoring, etc? What is the bladder doing? Going to the bathroom more than one time during the night is not optimal and can be managed. Is there anxiety?

Is there worries? Is your mind racing that's keeping you up at night, preventing you from falling asleep or waking up early with depression? I do recommend cognitive assessments, and so primary care doctors have a lot of general cognitive checklists that they have to screen for cognitive difficulties. If there are problems on the routine screeners, which are really quite good at picking up cognitive problems, if there are difficulties, then referring for evaluation. Vision testing and hearing testing should be really part of your general health and well-being. Vision testing in its own right and also because it is associated with fall risk. Hearing testing, because it is associated with cognitive impairment, as I showed you, but also social isolation and increasing mental health disorders as well. Bladder function. Pelvic floor, PT, is a great first-line treatment, so is vaginal estrogen.

Bone health. The US Preventive Task Force recommends a DEXA scan, a bone density screening at age 65. I'm going to show you. Let me just skip to the slide. They recommend screening in women 65 years or older. Or women who are younger than 65, but postmenopausal and who have one or more risk factors for osteoporosis. What are the risk factors? These can include lower body weight, family history of osteoporosis or fractures, early menopause, certain medical conditions, and use of certain medications. Certainly by age 65, everybody should have a bone density screen. But often, I start my patients because they have medical conditions at the time of menopause, and we often pick up osteopenia, so bone thinning, and the goal is to implement prevention prior to the bone true frailty or osteoporosis. Then fall risk assessment is a really good idea even before people fall to think about what could cause you to fall?

What are the potential hazards in your home? Do you have rugs that are unsecured? Often, my patients have thought about things like rugs, but then they have their cat who sleeps on the stairs, or they wake up in the middle of the night rushing to go to the bathroom and trip and fall. Thinking about how could you set your home up and also what is your balance like? How resilient are you to being knocked off kilter on the street, on an uneven sidewalk or pavement, things like that? Thinking about this because these are really important preventive aspects when we're thinking about supporting longevity. Then prevention. I talked about that. We want to think about cancer prevention. We wanted to think about heart health, and we want to think about infection prevention. There are guidelines for each of these different cancers that start at different ages. In someone who's aged 65, they would be screened at least every two years.

Others may even recommend every year, up until around age 75. Colonoscopies used to start at age 50. They're starting now at age 45 or even younger in some at-risk groups. A fecal occult test every year as well. Cervical cancer screening, really depends, and it's great to ask our gynecology colleagues because it really depends on whether the person has had HPV or HPV vaccination or abnormal paps in the past. Then lung cancer for smokers. In terms of heart health, so as Dr. Rowen mentioned, heart disease is killer in women. What do we do? We want blood pressure checked at least annually. Cholesterol every four or six years and perhaps even much more frequently if there's risk factors. Diabetes, checking hemoglobin A1c every three years or more frequently, and then thinking about whether the person would be eligible for statin therapy. Then all the vaccines. There are many vaccines that prevent age-related morbidity mortality.

One that has gotten recent interest in the news is whether the shingles, the zoster vaccine, actually can play a role in preventing dementia? I think there's going to be a lot more coming down the pipes in terms of that research and approach, but definitely, making sure that we're not having unnecessary morbidity mortality from vaccine-preventable illnesses. What if we moved along now and thought about what would longevity, comprehensive health look like in someone who's 85? I gave a talk on menopause and brain health a few weeks ago, and somebody who was, I think, 92 came up to me and said, you shouldn't just talk about menopause. You should talk about healthy person care at age 80, 90, 100, etc. Then she was absolutely right. We want longevity. We really need to think about what is the best care in each decade? As we move beyond age 75 and 85, the cancer screening and the heart screening, actually, that's like a bit of a good news.

You don't have to do as much of that. We really have to be mindful of polypharmacy, all the different medications. I often recommend that people set up care, I mentioned with a primary care doctor with someone who has expertise in geriatric medicine. It sounds bad. But really these are doctors who think very comprehensively about quality of life and healthy aging in as comprehensive a way as possible. We also want to think about comfort, pain, again, sleep, skin frailty, things like that, fall risk reduction, and then really planning advanced directives, things like that. Let's go into some of those. The big medical goals are going to be quality of life, comfort, independence, thinking on the physical realm about what are the home health requirements, PT/OT needs? There may be none, there may be some. Also thinking about, are there caregivers involved if the person has medical conditions or functional limitations, and are the caregivers well supported?

Thinking about who is your healthcare proxy to make decisions, so as to limit the potential for family stress, family squabbles, and medical care that's not aligned with goals? Then maxing out on that purpose in life, that well deserved well-being, quality of life. Here, what would be things that would be a part of a well person exam and thinking about maximizing, again, well being. Sleep screening, huge, depression screening, anxiety, cognitive assessment, those should be quite regular because there's a lot of aspects of cognition that can be managed. As the brain becomes a little older, a little more frail, people are at increased risk of delirium. Delirium is not dementia. Delirium is not loss of memory, loss of cognitive faculties. What it is is when the person is stressed from often UTI or from being in the hospital, being in pain, different medications, the person can basically become confused.

Transiently, for a day, hours, days, sometimes longer, they can be confused, and they can then recover some or all of that once the stressor, the infection or whatever has been addressed. People as they age, become more vulnerable to delirium. I recently had my aunt who lives alone and is about 87, and she had a bladder infection and became delirious and everything cleared right up with antibiotics. Thinking about appetite, nutrition, food access, of course, with the Osher Center, we're really thinking really holistically about nutrition, continuing to do vision testing and hearing testing. Then bladder function, we really don't want people to have UTIs. We really don't want them to wake up at night, rushing to the bathroom. Constipation becomes more common with aging, and thinking about having really good bowel regimens and really consistent bowels, whether that's every day or every few days, but consistently and not uncomfortable.

Then thinking about home safety evaluation. Again, do we need assistive devices? What is the gait, balance, etc? As I had mentioned, moving on to 85, there aren't really good guidelines about cancer screening or heart health screening. Too often, a lot of people start really requiring that, but really we want to think more about medications, not going overboard with medications. What are the ones that we can peel away? Not chasing our tail, giving a a medication to help people sleep and then having to give them a medication to make them more awake during the day, that thing. We really want to think comprehensively. We don't want the medications to be a setup for confusion, fall risk, etc. Then continuing the vaccines because with what we call immunosenescence, the immune system ages, and the risk of infections can increase. Okay, so that is the end of my sort of structured talk, but really look forward to the questions, and thank you for your attention so far.

Thank you so much for such a great lecture. We have a few questions that have come up. One is a question about word finding and sometimes they can start even before pair menopause or menopause or post menopause. And how do we know if the word finding is normal brain fog or something bigger to worry about? Yeah, that's a great question. So just to put out there, this is going to be my feminist little hat for a moment on this topic. I think as women's lib started, as women started entering the workforce, as women started saying that they had the cognitive abilities, etc., as men as everybody else. I think there was a bit of a bias against talking about the ways in which pregnancy, menopause, etc., might influence brains because people could truly be discriminated against even today sort of, oh, you're going to go out on maternity leave and leave the company, etc.. And so women wanted to show that they could maintain good cognition in the workforce.

And I think one of the things that happened is there was a bit of a bias against examining the very real effects of pregnancy of menopause on women's brains. And so now that we have women in science, women in medicine, women in decision makers, and women who are savvy patients who are going through this and saying, hey, what is going on? I think we're going to see a lot more science and understanding. And so to your question, there is word finding that happens during pregnancy. I remember I was a resident with my first pregnancy and I absolutely lost my math. I could no longer remember math. I could not find words. I gained olfaction. It was like, no, thank you. I don't want to smell everything in the hospital. I want to be able to do my job. There is not a lot of data at all. And I think there are some really beautiful studies now that are happening where we're imaging women across their pregnancy, imaging them across menopause, and really trying to dig deep into what's happening.

From my understanding as a clinician and as a reader of this literature, there is brain fog in general where people feel a little less sharp, more dull, more fatigued, that thoughts don't come as efficiently, etc.. There's also these specific things like word finding difficulties, and I do think that that is when the cognition is stressed. I do think that that is a very real deficit. We don't know at all whether that actually tracks at all with any later life risk or whether these are just wobbles that happen when the hormones change, and that's it. We do know that after pregnancy, the word finding gets better. We do know that after perimenopause, the word finding gets better, and it'll just be really interesting to see what happens later. In terms of what to do, I think a couple of things you want to absolutely be sleeping well, You want to feel supported and not stressed in your home environment or your work environment.

You want to address any of the real mental health things, depression, irritability, anxiety, etc., and then you want to give yourself grace. It's really reassuring to go and talk to friends, to go online and see what other people are saying because it's really you feel a lot better when you realize that your symptoms are so common, and you want to come up with strategies, again, to talk around the deficit, and you have to have faith that you will get a little better. With regards to supplements, which ones would you recommend and which ones would you not recommend over the course of period to post menopause? Yeah, I think there's just to lay on the table the idea that we absolutely don't know enough here. We want to be able to recommend the healthiest diet. We want to be able to recommend the best supplements. And then there's just this big gap between the promise, the hype, and then the data.

So from my perspective, I do like my patients to have a probiotic. Just the idea of being like extra colonies in the gut, maybe doing good things for gut health, brain health, and all the health. I do like patients to have a probiotic and I typically recommend like whatever you can afford, whatever you can tolerate, and whatever has as many bugs as possible, as many types of bugs, diverse. I do recommend vitamin D, vitamin B12, up to high normal levels, not beyond. I think the Omega-3, I think the CoQ10, those are supplements that are intriguing, interesting, perhaps. Currently, my patients have there's a big peptide push, a big push on the peptides. This seems to have arisen very quickly. I think there are maybe some peptides relating to collagen that may be interesting. The rest of those, they're really not proven in human people. They may have some evident insulin rodents, there may be some hype, but I really don't know enough, and they're not well regulated, and there may be risks taking them, and everything's expensive.

So I like to think about what are the ones that have maybe not great data, but are somewhat regulated and have some data. Perfect. Thank you. Then there's another question about GLPs. What are your thoughts on GLPs and longevity? Oh, I'm so excited to see. We don't know. We don't know because they've been around so quickly, so definitely if you can curb people's diabetes risk, their cholesterol, if you can get people feeling better, feeling better about themselves, getting out and about, those are all going to be good things. What we also know is rapid weight loss, you lose bone and you lose muscle. And we know that people need healthy bones and healthy muscle for healthy aging. And so if people are losing weight on GLP-1s, we want them to be maintaining bone and maintaining muscle through weight training and the protein and things like that. We- I like the good that comes with the GLPs. And then, of course, there's specific risks pancreatic, liver some vision changes, things like that.

There's specific risks. Then I don't want people to lose their bone and muscle. Another question about longevity. What are your thoughts on fasting? Of course, love the concept. I love the idea that we paleo and we're not supposed to eat all of our square meals right predictably on time every day, etc.. I think, I'm curious. I'm curious like many people are. I don't know that again, we've seen the long, long term data. I definitely don't want people to fast to the point where they may be starving, dehydrated, or falling. But otherwise, I think there are some intriguing studies that suggest some effects on metabolic regulation, immune, things like that. I would say I'm following enthusiastically. Beautiful. There's a question about sleep hygiene. I know it's come up a lot. One of the questions is about why we recommend sleeping with cotton sheets, and then other thoughts that you might add

to the overall sleep hygiene recommendation.

Yeah. First, I know it's our medical term, and we have to own it, sleep hygiene, but I feel like it has this pejorative intonation, like, oh, you're not hygienic if you can't sleep. definitely, I would say healthy sleep behaviors. What might those be? So, certainly, one guidance is using the bed for intimacy or sleep and everything else, not in the bed because people who have difficulty falling asleep, if they're lying in bed worried about not being able to fall asleep, that can become its own monster. In terms of the cotton sheets, I believe Dr. Rowan said that, and my understanding is really that can help with some of the night just like feeling hot, hot flashes, and night sweats and things like that, and just more breathable material. So I believe that's why she said that. Oftentimes, people in the US are very hydrated. There's this big emphasis on hydration, and oftentimes what that means is then you fall asleep, you lie down, and then all the blood that was in your feet and your legs then comes back toward the center of the body and gets taken out by the bladder and you've got to go to the bathroom.

I tend to tell people who wake up several times a night to go to the bathroom, try to get your hydration early in the day. Then by three o'clock, five o'clock, just only drink if it's because you're thirsty or because you're having a glass of wine with your meal or whatever. And I think that is another big component, bladder health. Definitely, the caffeine during peri, people start just noticing that a glass of wine, you can't sleep. Caffeine, you can't sleep, and that's of some of the sad changes with aging, but just really making sure you may think that a glass of wine is going to put you to bed, but it'll wake you up at 3:00 AM. Those are some other behaviors. And then one question that bridges Dr. Rowan's talk in your talk is what are your thoughts on hormone therapy and perimenopause for the brain? Yeah, I think we're still missing a big part of the puzzle. When you look at observational studies, and so this is some of my work.

We look at women who have been like, super well followed, and we see that the early surgical menopause, they have more dementia. You see that they get menopausal hormone therapy that is protective to some extent. The observational studies, when you follow women, you see a clear effect of menopause hormone therapy and brain protection. As Dr. Rowan said, the Women's Health Initiative, we did not see that. And there was a more recent trial called the KEEPS. Kronos, something something. The KEEPS gave menopausal hormone therapy in the way that we do today, certain doses within five years of the final menstrual period and the right patients not giving it to 65 year olds, but to giving it to 50 year olds, etc,. The KEEPS, they've followed women now for, I think seven years, moving to 10 years. We do not see that menopausal hormone therapy in a properly done randomized controlled trial does anything to cognition.

I think it's still too early. Before really saying, no, I want to see 10, 15, 20 year data, because we really need to see longer term whether that menopausal hormone therapy is protective. I think if it's going to help with sleep, if it's going to help with quality of life, if it's going to help with heart, diabetes, cancer, etc., you have to think that by working on some of those other things, it would be good for brain health, but we just don't see it yet. Just the last thought on how to connect the integrative medicine practices with the medical practices and neurology when thinking about longevity. Any last recommendations from that standpoint? I think everybody's quality of life, everybody's wellness is really individualized and personalized, and so I think that for some people implementing a really healthy lifestyle, really setting up a really great mind body dialogue can be instrumental to longevity and to healthy aging.

I think sometimes there are very specific medical conditions and specific blood levels and things that require specific pharmacological or other interventions. I think that people who have access to the Osher Center have access to all this really beautiful resources and also access to people who have access to very specific pharmacological interventions or medical interventions if needed. I think personalization is everything. I have patients who I'll go through their exercise, their sleep, their nutrition, treat their bladder symptoms. Then I realized, oh, she's really unhappy in her marriage, that was missed by everything else, and other people were just putting into practice some self care every day is everything. So I think it just really depends. Yeah. Well, thank you so much.

You did such a beautiful job, describe me through each of the different age ranges and thinking through the important things to cover and be thoughtful about.

Thank you so much for that lecture. Your pleasure. [Music]