



Menopause and Cancer:
Supporting Women Through Every Transition
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Moderator:

Thank you for being here. We're very excited. We're very excited to have you with us this evening. We have a great topic tonight. This webinar, Menopause and Cancer: Supporting Women Through Every Transition is part of our annual summit, which brings together thousands of people virtually and in-person across the country and even beyond. And it's running from September 18th to October 23rd. The Sharsheret Summit is the source for the latest information on breast cancer and ovarian cancer, and we encourage you to visit the summit website and check out our virtual toolkit. There's a link in the chat box now that will link you to the summit page.

I'd like to take a moment to thank Sharsheret Summit sponsors, the Cooperative Agreement 24-0061 of the Centers for Disease Control and Prevention, AstraZeneca, Eisai, GSK, Lilly, Pfizer, Smart State, and the Weill Cornell Medicine Department of Genetics and Personalized Cancer Prevention. Additionally, thank you to our many summit program partners that you saw on the opening slides. Their partnership has helped to make our summit a success.

Today's webinar is being recorded and will be posted on Sharsheret's website along with the transcript. As always, participants' faces and names will not be in the recording. If you would like to remain private, you still have that option to turn off your video and rename yourself, or you can call in to the webinar. Instructions on how to do that are in the chat box now. Also, we now have closed captioning. To display live captions, on the bottom bar, click captions and then show captions. You may have noticed that you were muted upon entering the Zoom. Please stay muted during the call. If you have questions, please feel free to type them, your questions and comments into the chat box. We will have some time at the end of Dr. Emont's presentation to answer some of your questions.

And as we move into the webinar itself, I want to remind you that Sharsheret is a national not-for-profit cancer support and education organization and does not provide any medical advice. The information provided by Sharsheret and tonight's speakers is not a substitute for medical advice or treatment for specific medical conditions. You should not use this information to diagnose or treat a health problem. As always, be in touch with your doctor or qualified medical professional. Before we get to our medical expert this evening, I am so excited to welcome Sharsheret caller Shari from New Jersey, who's going to share some of her own experience with cancer and menopause. Shari, we'll have you... There we go. Welcome.

Shari:

Thank you, and thank you for inviting me to share my story. In April 2019, at age 52, I was diagnosed with stage one invasive ductal carcinoma. I was BRCA-negative, ER, PR-positive, and the Oncotype test showed that chemo would not be effective for my tumors. So I had a lumpectomy. They took one lymph node, they luckily cleared the margins, and then I had about 16 rounds of radiation and a year of tamoxifen. Then due to some side effects like severe cramping, I had a test that determined the lining of my uterus was thickening and tamoxifen can cause uterine cancer, and this thickening was a sign that it was not a safe option anymore for me. So at age 52, I was still not in menopause on my own, which was problematic, since my body was still producing estrogen and the estrogen suppressant tamoxifen was no longer an option.

So my doctor recommended to go into medical menopause using Lupron injections, and I was a little unsure about it. So I reached out to Sharsheret to be connected with two different women who had a similar journey. I wanted to hear their stories and just get a sense of what it was like. I wanted some reassurance that this was a decent path for me. One great piece of advice I got was if ultimately I didn't go with my doctor's recommendation of going into medical menopause, it would probably be time to find another doctor, and I thought that was a really good insight. At this point, I asked the doctor, what about a hysterectomy? It seemed like a good idea. I didn't need those organs anymore. But she felt strongly that statistics showed that in just a few years I was so close to probably being in menopause and it was major surgery, so she did not think that that was a good choice.

I ultimately chose to take the Lupron injections and be put into medical menopause. So I would go to the infusion lab every three months at my local hospital, and even though my body would be in medical menopause, it still would be producing a small amount of estrogen. So in addition to the Lupron injections, I also went on anastrozole. So when discussing all the side effects that come with menopause, I was really concerned and the doctor made a really good point saying, "Either I'm going to put you in menopause and you're going to have these side effects, or eventually you're going to go on it your own. So one way or the other, there's really no avoiding it." So it seemed like this was the time to do it. And after a few years of treatment, the hope was that my body would go into menopause on its own. I did come off in two and a half years, three years to see if my body was in menopause, it was not, so I continued on and I was on it for four years.

So what were my side effects? The hot flashes, vaginal dryness, tingling sensation in my body now and then, a terrible taste in my mouth, and I did have some radiation dermatitis. That wasn't really from the medical menopause, but just add to the fun. So some

suggestions of what I did to get myself through that, I had mouthwash at work and at home and in my pocketbook. I purchased tank tops to go under every single item of clothing I wore so that I was ready for those hot flashes. I had a WOOZOO fan, highly recommend, that has a remote control next to my bed, in my office, next to the couch, everywhere that I would hang out, and of course a portable fan in my bag at all times. That was key. And I shared with my work colleagues what was going on so I wasn't uncomfortable if I needed to strip in the middle of a meeting or in the middle of the winter when everyone else was freezing. And that's just kind of par for the course.

So after the four years, April 2024, a test was available to see if five years or 10 years of this treatment, which would provide the least risk of recurrence, and I was lucky to learn that staying on for 10 years only increased my chances of cancer recurrence by 3%. So my doctor said that wasn't enough to justify staying on, and so finally I was able to stop the treatment. All the side effects slowly went away except for the radiation dermatitis. Again, not related to the menopause, but just part of the fun. And I have a great steroid cream when that acts up, so it's really not such a big deal.

And then, really, I would just say, as luck would have it, my body seems to want to go in the Guinness Book of World Records. My period came back a year and a half after stopping the Lupron treatment, and I turned 60 this year and I'm still not completely in menopause. So not the thing that I wanted to be above average in, but that was the hand I was dealt. And so, that's really my journey. And I'm appreciative to Sharsheret who was very supportive during my journey and the excellent social worker that would check in, and I still hear from her now and again.

Moderator:

Shari, thank you so much for sharing your story. I know it resonated with me, and I'm quite sure it resonated with so many of the people on tonight's webinar, so congratulations on that world record. Thank you. We really appreciate it.

Okay, we are happy to have with us tonight Dr. Jordan Emont. Dr. Emont is a board-certified OB/GYN and certified menopause specialist with a deep commitment to helping women navigate menopause before and after cancer. He serves as an adjunct clinical faculty member at Stanford and is the founder of Meridian Medical, a telehealth practice specializing in complex menopause care. Dr. Emont brings an individualized evidence-based approach to care that cuts through fear and misinformation and puts each woman's values and goals at the center. You can see why we have him here tonight. He has a particular clinical focus on menopause in the context of cancer survivorship and previvorship and believes strongly that a breast cancer or gynecologic cancer diagnosis

should not mean having to suffer through menopause without support. He sees patients over multiple states and is a widely followed public voice on women's health through Instagram, TikTok, and Substack. He translates complex science into clear, empowering information for his patients everywhere. Dr. Emont, thank you so much for being with us this evening.

Dr. Jordan Emont:

Hi, everybody. Thank you. I'm so incredibly excited to be here today. We're going to have a lot to talk about. I have the very easy task of going through all of menopause and cancer in 30 minutes, so it's going to be a little bit of a whirlwind, but I'm hoping that we have a lot of time at the end for Q&A. There may be some things that I skip over a little bit just to make sure that we can get to that time to answer your questions. Also, in full transparency, I am at the airport right now, so if you do hear other sounds, that's where that's coming from. I think that hopefully the people who are sitting around me will enjoy the talk, and thankfully I have the chutzpah to talk about vaginal estrogen and vulvas in public, so hopefully it doesn't scare anybody away.

So let's get started. So I always start this talk by talking about a patient who I saw a while back, but she was in her 50s. She had had ER-positive breast cancer and was on tamoxifen. She had previously been on aromatase inhibitor and had not really been able to deal with the side effects of that, and so was switched to tamoxifen, but still was just struggling enormously. And she had hot flashes, which were making it very difficult to work as a physician associate. She had significant vaginal dryness that was making sex impossible with her partner. She had profound depression and anxiety associated with the mood changes that often come along with both menopause and endocrine therapies, and she was really struggling, and that's why she was seeing me, was to really discuss how we might be able to help her.

And so, I did what I do with all my patients. We went through her cancer history, we went through her values, we went through her past medical history, and we really came up with a plan together of how we were going to move forward. And at the end of the visit, she asked me a question that I get asked a lot, but it always makes me very sad, which was, "Do I have to tell my oncologist about this?" I know that there's a lot of cancer survivors or even previvors on the call today. I don't know how many of you have maybe been in this position, but unfortunately, I see so often that there is a little bit of this sense from oncologists, but even from people themselves that their suffering is almost the price to pay for surviving cancer. And there's almost sometimes even a guilt associated with that, that it's sort of just par for the course of how you're supposed to feel.

And I think that what it really comes down to is what is on this slide, which is there are so many things we're going to talk about today related to hormones, because I think there's an interesting discussion there, but at the same time, menopause is about so much more than just a discussion of hormones. And unfortunately, we've really reduced a lot of the ideas about how we manage menopause to just hormones. And then because of that, this idea that no hormones or hormones might be risky becomes no menopause conversation. And in my view, there is always something that we can do to help somebody feel better.

Now, we really need to figure this out fast, because we have almost 10 million women in the United States who have a history of all types of cancers. Almost half of these women have a history of breast cancer. Thankfully, survival from breast cancer is now, I think 94% is the most recent number that I heard, which is absolutely fantastic that we are doing such a good job with that with all of the advances. What that means also is that we have more and more people who are going through menopause as a consequence of their treatment, maybe being diagnosed earlier, which we know is on the rise, and then now having to understand what is the next 50 years of my life going to look like and how am I going to experience that from the perspective of my menopause? But unfortunately, this group of individuals is so incredibly excluded from this menopause revolution because of this idea that menopause is not something we can discuss because we can't talk about hormones.

We're going to cover a number of things today, talk about a little bit how menopause after cancer is different than natural menopause, some of the tools that we use, and then we're going to go through a couple of use cases of previvors after breast cancer and after ovarian cancer, and then talk about longevity more broadly. But honestly, what I really want everybody to walk away with today is more just the idea that we really need to prioritize this conversation. We need to think critically about the science here, and I want everybody to walk away with hopefully a little bit of an idea of how they might think about even their own story or maybe the story of a family member.

So this is a conventional diagram of natural menopause. So we have the reproductive years where there's this relative stability in estrogen, progesterone, and testosterone. We have post-menopause where, again, there's a stability, but at a much lower level where there's really no production of estradiol and progesterone. And then there's perimenopause where there is this massive fluctuation in those hormones, often with an overall decline, and this can happen over the course of 10 years.

But menopause after cancer is different. So first and foremost, for so many women, cancer treatments can put women into menopause. And so, we see overall for cancer survivors, about a third will actually go through menopause as a consequence of their treatment. But for some cancer types, especially certain gynecologic cancers where removal of the

ovaries or pelvic radiation is often a part of the treatment, this number can be as high as 90% of perimenopausal or premenopausal women who experience this.

As a consequence of some of those therapies, but also as a consequence of some of the endocrine therapies that come up afterwards, often the symptoms that come along with menopause are much more intense. So Sherry, your story about being on these treatments and experience that then got better when you stopped the treatment is a perfect example of that, that even if somebody was in natural menopause, they might have worsening of their symptoms as a consequence, for example, of being on an aromatase inhibitor.

But I think that the worst part of menopause after cancer is the fear, that there's perhaps no other clinical scenario that inspires as much fear of management as a woman who has a history of cancer. And this is even true for women who don't have a history of a hormone-sensitive cancer. There's still just this overwhelming fear of doing anything that is in any way in conflict with that cancer, just maybe out of a fear of litigiousness or maybe just out of a fear that they don't really know what they're doing. And what I'll illustrate is that most cancers, actually HRT is a very safe and appropriate option, and yet we rarely discuss that.

So I'll skip over this briefly, but people who have been through cancer therapies will know that these different treatments like surgical removal of the ovaries, certain chemotherapy, pelvic radiation, the different endocrine therapies, all are going to affect the ovaries in different ways, and some of them will lead to a permanent surgical menopause and some of them will lead to a temporary menopause that may or may not lead ultimately to periods recovering and ovarian function later. But nearly everyone who goes through one of these treatments will have some form of ovarian dysfunction, experience symptoms associated with that.

And particularly these women who go through early menopause, this is not a neutral event. We have almost double the lifetime risk of heart disease for going through menopause before age 40. We have significant bone density losses, which we'll get to more in a second, higher risk of diabetes, consistent increase in dementia and cognitive decline. And I think that particularly it's important to think about some of these long-term consequences, because even among long-term survivors of cancer, even among long-term breast cancer survivors, the number one cause of death is heart disease. And so, we often are focusing all of our energy on the cancer, and of course that's a really important part of somebody's health history, but there's so much more to a person than just the cancer that they went through.

So I just want to illustrate the bone loss portion here. So we can see that for natural menopause, the rate of decline of bone density is usually about one to 2% per year. There's

a significant drop around perimenopause around the actual year that menopause happens, and then it stabilizes to about one to 2%. But you can see that for somebody who is on ovarian suppression, so that would be like the Lupron injections plus an aromatase inhibitor, they might have a 9% per year loss in bone density. So this is really a profound consequence of treatment.

I don't have to tell probably a lot of the people here the symptoms of menopause, but what I really want to illustrate is that menopause affects every single organ system in the body, and therefore leads to symptoms across the entire body. So hot flashes, night sweats being kind of the most obvious version of this, that's one of the most common symptoms, but we see vaginal dryness, we see changes in libido, we see sleep disturbances, mood disturbances, even heart palpitations, anxiety, all kinds of things, and 90% of breast cancer survivors will have menopause symptoms after treatment. So this is not an uncommon problem.

So I want to go through some of the tools that we use when we're thinking about this, and I'll admit that a lot of this talk is going to have a little bit of a bend towards discussing hormones, because I think that that is often the most controversial topic and the one that people have the most questions about, but we will go through some of the non-hormonal treatments as well, but I want to make sure definitely to review the data on that.

But when I'm having this conversation with cancer survivors, I have these four goals in mind. So number one, of course, is I want people to feel better and I want their quality of life to be better. What is the point of surviving cancer if you can't live some quality of life that you are enjoying afterwards? The second though is I want to be able to know that we're using the best available data to educate and to guide those decisions. So we shouldn't just be giving something out because we saw something on TikTok that some person said, right? We want to actually use the science to back up those decisions.

I want people to listen to their oncologist. This is maybe the most important thing. I think I see a lot of, especially social media content where people will say like, "Oh, your oncologist doesn't know what they're doing. You shouldn't be taking this treatment." But for me, I want you to stay on your therapy and I want to enable you to feel better so you can continue the aromatase inhibitors, you can continue the tamoxifen. Whatever your oncologist is recommending, I want to make sure that that is a part of the plan as well. But most importantly, I respect and I honor individual agency. That at the end of the day, cancer is something that happens to you, it doesn't define you. And at the end of the day, my job is to make sure that I'm prioritizing your cancer history, your symptoms, your values, your risk tolerance, to come to a plan together that prioritizes you as a human being and an individual.

So some of the classic non-hormonal treatments that we will use for particularly the hot flash part of menopause symptoms, the first one that I want to highlight here is fezolinetant, elinzanetant. So the brand names for these are Veozah and Lynkuet, if you've heard of them. These are the newest non-hormonal drugs that exist, particularly for hot flashes, but they also help with sleep, and they are targeting the neurons in the brain that actually cause hot flashes. So elinzanetant, which is Lynkuet, is my favorite of these two. It's the newer of the two, and it actually has very specifically been tested in breast cancer survivors who are taking endocrine therapy and been shown to be safe and effective. So I use this one all the time. It's a very common tool that I reach for.

The classic non-hormonal tools for hot flashes in menopause that are non-hormonal would be SSRIs and SNRIs. So these are antidepressant medications that can help with hot flashes, obviously are used for mood changes as well, like depression, anxiety, often can help with sleep for many people. They do often have a side effect of a lot of sexual consequences, which is already a big problem for people who have a cancer history, so we always have to keep that in mind, but this is very much an effective tool.

There are other tools in this category like gabapentin, oxybutynin that frankly I never use. They have a lot of side effects and may even be associated with a long-term risk of dementia, but they do exist on the list, and for the appropriate person, they may be the right choice. Cognitive behavioral therapy has been shown to improve hot flashes, also evidence for mood disorders. As you might imagine, this is therapy done in a very particular way, also can help with sleep.

And then I put botanicals on here. The data is mixed, and there certainly are some where we might want to have some caution because they can actually trigger estrogen, but there are a lot of botanicals that can be very helpful for menopause symptoms in an individual person. And even if the data doesn't say that across the board it's the most helpful thing, I've had plenty of people who do amazing with black cohosh and they love it. So that, I'm never going to be the person to discontinue that or to recommend against it if it's helping somebody. But I do just want to illustrate that non-hormonal does not necessarily mean zero risk, that 81% of breast cancer survivors in one study reported side effects from non-hormonal options. I already discussed that there are some long-term health consequences associated with gabapentin and oxybutynin.

So let's get to the HRT conversation. So we have three main concerns with the use of HRT after cancer, the most obvious being hormone sensitivity, that things like ER-positive breast cancer or certain ovarian cancers can be hormone-sensitive and that the use of hormones may cause this to recur or to grow. Cancer treatment, both active treatment, maintenance treatment, even just having cancer can all increase clot risk. And so, there's a concern that

the use of estrogen can also increase clot risk. Now, what we'll get to is transdermal estradiol does not increase clot risk, but I can understand where the concern comes from. And then interference with therapy that, for example, aromatase inhibitors are the best example here, that the whole point of an aromatase inhibitor is to decrease the amount of estrogen in the body. And so, by giving estrogen back, you're basically completely invalidating the whole point of the drug, and so it's going to really interfere with that process.

A word on some language here, which I will run through, but this is very important. So estradiol is different than conjugated equine estrogens. These are different estrogen therapies that we use. Estradiol is the same as your body. Equine estrogens is an older formulation that comes from horse urine. Progesterone versus progestin. So progesterone is, again, the same body identical hormone as your body, whereas progestins are synthetic hormones that have actually been associated with a small increased risk in breast cancer. We'll get to that a little bit later, but most commonly we're using progesterone today for hormone therapy. We already discussed that oral estrogens are different from transdermal estrogens, with the main difference being that transdermal estradiol does not increase clot risk, whereas oral estrogens can. And then maybe most importantly is that throughout this whole discussion, I want to make it very clear that the use of vaginal low-dose estrogen is very different than the use of systemic estrogen for the rest of your body.

So with all of that in mind, when we ask the question, "Can I take hormones?" There's really multiple questions here. The first questions being, what hormone are we talking about? Are we talking about vaginal hormones? Are we talking about systemic therapy? Even within that category, what method of administration? Are we talking about oral estrogen, transdermal estrogen? Are we adding progesterone onto that list? And then we'll talk about testosterone a little bit later, but that's a whole other conversation, has a very different risk profile, and we're going to have a different answer of how that pertains to you specifically.

So vaginal estrogen is the easy part. This is basically low-dose, locally applied, so just to the vagina and the vulva. I call it skincare. This is like applying your morning lotion. It treats painful sex and vaginal dryness, and it decreases the risk of urinary tract infections by more than half, which is just insane. This is something you use twice a week forever, till death do you part. And I want to say something that might even sound a little bit controversial, because a lot of people hear opposite, but I'm going to make the phrase of saying that this is safe for everyone with a vagina and vulva to use.

And this is an unfortunate misinterpretation that there is a lot of confusion about this, which we'll get to a little bit later. I will acknowledge though that there are some areas where we don't have the most data. So certain advanced gynecologic cancers, we don't

really have a lot of data specifically in use in that. And we'll get to the aromatase inhibitor question, but even that I want to challenge and say that I am totally fine with somebody on an aromatase inhibitor taking vaginal estrogen. For me, this is the lowest hanging fruit in the treating menopause symptoms world.

Now, vaginal estrogen is not absorbed systemically. It all stays in the vagina and the vulva. But let's pretend that even it was absorbed. The dose is so low that we're talking about one to two milligrams total of estradiol in an entire year. That's basically one oral tablet that somebody would take in an entire year of therapy. So the modern systemic hormones that we use are transdermal estradiol, progesterone, 100% necessary if you have a uterus, but if you don't have a uterus, it's not mandatory. We often need to do higher doses for people who have early menopause, because we're really replacing estrogen in that situation. And then Duavee, I'll take some questions about it if it comes up, but it's a very unique choice where it's a combination of conjugated equine estrogens and bazedoxifene, which is kind of a cousin medication of tamoxifen and actually blocks estrogen at the breast and at the uterus.

The second part of it is which cancer are we talking about? So the ones here are the ones where there would be some caution with the use of hormone therapy, because these are estrogen-sensitive cancers. But even within the category of breast cancer, ER-positive is going to have a very different risk profile than ER-negative, and we'll get to some of this a little later. Again, most cancers are not on this list, so most cancers are not hormone-driven and there should be no concern with the use of hormone therapy. That should very much be an option. This includes cervical cancer, vaginal cancers, vulva cancers, things where a lot of women are often told that they can't ever take hormones. These are not hormone-driven cancers.

So let's talk about previvors, because this is another area of confusion. So I think people might be familiar with some of these numbers, but BRCA1, BRCA2 significantly increased the risk of breast and ovarian cancer, other cancers included on that list as well. And because there's no reliable screening method for ovarian cancer, surgical removal of the ovaries is usually the recommendation. For BRCA1, that would be age 35 to 40. And BRCA2, 40 to 45. And this significantly decreases the risk of ovarian cancer, breast cancer, and all-cause mortality.

Now, a common question that comes up is, "Can I use hormone therapy after I have my ovaries removed? Because I'm going through menopause when I'm 35 because I'm having my ovaries removed." And we have very good data here. There were just two big studies that came out just this year actually that showed no increase in breast cancer risk associated with a combination therapy of estrogen and progestogen. And in fact, in estrogen-only

therapy, there was found to be a 63% decreased risk of breast cancer. So not only is this safe, but in particular, estrogen-only therapy has been associated with the lower risk. And in fact, this is now recommended as the standard of care by the National Comprehensive Cancer Networks, which is kind of the guideline building organization for cancer treatment.

Now, despite this, only 50 to 60% of women who have their ovaries removed premenopausally ever take HRT. And this is largely because there's so much confusion about this, there's so much misinformation, but I want to be very clear today that this is very much something that is a safe option for you, and like we talked about, can help decrease that risk of bone loss, the risk of cardiovascular disease, the risk of diabetes. So you should be having these discussions before the ovaries are removed. You should know whether or not you're going to start hormone therapy and have that discussion. You should decide whether or not you're going to keep your uterus, which I'm happy to get into in the Q&A.

Most importantly, like I said, menopause is not just about the symptoms. This is also about your body changing. So you should be getting a baseline cardiometabolic panel checking for things like insulin resistance in your lipids. You should be getting early DEXA scan because of that bone loss component. And then make sure that you have a team behind you, that this isn't just your oncologist, this is also a menopause clinician. This is a mental health professional. This is a pelvic floor PT.

Okay, breast cancer. So the first just really important topic here is that breast cancer is not one disease. We conventionally have this idea saying breast cancer means that you can never take hormone therapy. But I want to illustrate here that really breast cancer is multiple different diseases. This isn't even a comprehensive list. But first of all, I want to illustrate again, vaginal estrogen, totally safe across the board. We have very good data on that. But kind of moving from top to bottom, you can think about it as a little bit of a risk stratification where ER-negative, triple-negative breast cancer, this is probably the case where the risk is the lowest. And in fact, there was this large analysis of all of the data that has been studied about the use of hormone therapy, and they actually said that for ER-negative folks, the benefit of hormone therapy usually outweighs the risks. So very much I think a good use case for that.

DCIS has never been studied, at least in terms of the use of hormone therapy, but because it has a very favorable long-term risk profile, we generally think about this as being kind of a lower risk scenario, very much a shared decision. The Duavee may be a good consideration, because again, it has that component that is kind of like tamoxifen. And there was actually one study that was presented at a cancer conference last year where they found that people with DCIS who took Duavee for a month before their surgery

actually had a lower Ki-67, which is the marker of cell turnover, meaning that maybe those cells were not reproducing as fast.

And then ER-positive, obviously this is going to be much more of a nuanced conversation and may not be the right choice for everyone. But the main thing I want to illustrate on this slide is that it is an appropriate thing to do medically to be on estrogen at the same time that you're on tamoxifen, but it is not appropriate to be on estrogen while you're on an aromatase inhibitor, because like I said, it really invalidates the whole point of the drug.

And then metastatic, obviously we think about this as being the highest risk scenario, but I do just want to illustrate that if somebody has metastatic disease, if we are actually moving in to direct more of comfort care, this may actually be one of the best scenarios of thinking about the use of hormone therapy, because we are really prioritizing a quality of life at that point and not quantity of life.

So let's get back into the vaginal estrogen conversation, because again, this is the lowest hanging fruit. I wanted to get into the data a little bit more. So the largest study of this was almost 50,000 breast cancer survivors followed for up to 20 years. They had no increase in recurrence risk, no increase of breast cancer death. And this has been reproduced in multiple study after study after study, including these large meta-analyses where they put all of the data together. And in fact, the coolest part of this largest study with 50,000 people is they actually looked at women who had active breast cancer, actively being treated for breast cancer, and the women who were taking vaginal estrogen actually had a lower risk of death from breast cancer. Unbelievable. This is for me probably because those women were probably staying on their endocrine therapy longer than the other people who discontinued it.

Now, many people have probably heard about this and maybe even have been told this by their oncologist where they'll say, "Oh, well, we're not really sure about women on aromatase inhibitors." So I wanted to just get into the data on that. So there's really just one study that has said this. It was this observational study where they basically just looked at a whole population of people who had breast cancer and they looked at what they were taking, whether or not they got a vaginal estrogen prescription, and they found that there was no increase of recurrence across the board and there was no increase in breast cancer death. But there was one subgroup, which is the women who are on aromatase inhibitors, where there was barely this association statistically with an increased risk of recurrence, but no increased risk of death. It's important just to say that this is an observational study, meaning that sometimes just statistical things will come out that aren't really real findings, because we've never really tested it with a formal randomized trial.

And importantly, in all of those other studies that I mentioned, including women who are on aromatase inhibitors, they've never seen this finding ever in the past. So no increase of recurrence in any of the other studies about this. And then also, even just methodologically, there may be some challenges in how the groups were put together in this study. So I think, sure, you could take it with a grain of salt. I don't want to say that there's a nothing finding there, but I also think that when we look at the conglomeration of all of the data about this, this is probably much more a study design issue than an actual real recommendation. And I have no qualms with recommending vaginal estrogen for all of my patients.

When we look at systemic, this is a very different story. So there's really three randomized trials that have been done about this, the HABITS trial, the Stockholm trial, and LIBERATE. I'm going to ignore LIBERATE a little bit because of the main problem that it tested a hormone therapy that doesn't even exist in the United States called tibolone. This LIBERATE trial did find an increased risk of metastatic recurrence, but again, it's kind of the least relevant because it doesn't use hormones that we actually have available to us in the US, and it's a really uncommon therapy in general.

HABITS found an increase in local recurrence risk. Stockholm trial was followed for longer and did not find that. There's maybe some methodologic differences between the two group, but the main thing that I want to illustrate is that the HABITS trial is really the only study that has ever shown an increase in recurrence risk, and both of these studies actually had no increase in death from breast cancer. Also, the HABITS trial did not have any requirement for a baseline mammogram coming into the study. So it starts to beg the question of whether or not some of these women already had a breast cancer recurrence coming into the study, and maybe that was fueled by the use of estrogen. The problem is all of these studies tested regimens that are different than what we use today. They were all done 20 years ago. And so, I always say the craziest part about this is that the last time that we collected data on this question was when the first iPhone came out.

When we put all the numbers together, a number that you'll frequently hear is, okay, when we put all the numbers together, the risk of recurrence is 46% higher. But the problem is that a lot of those studies include LIBERATE, which again is the least applicable to this data here, tested a completely different hormone therapy. And when we remove LIBERATE from those analyses, we actually see no significant increase in recurrence across the board. I do want to highlight though that in that study that said the 46% higher with full recurrence, there is a clear difference in ER-positive versus ER-negative. So 80% higher risk in ER-positive versus no significant increase in ER-negative.

So ultimately here, there's a lot of factors that go into this. So there's your baseline recurrence risk, there's your ER positivity. I'm particularly excited about a lot of these new genetic tests that exist like Oncotype and BCI and circulating tumor DNA and how that may be used to risk stratify. But also, like I said, individual goals and risk tolerance and value are going to come into this question as well, as well as other therapies that somebody may have tried.

Now, what about testosterone? This is one of the most common questions that I get. So I think testosterone is also a very low-hanging fruit in the world of hormones after breast cancer. So in ER-positive breast cancer, we actually see that testosterone may even be associated in the lab with regression of those cell growth. So it's early data on that. We have really just one study that has followed breast cancer survivors over about 15 years using testosterone, and they've had no increased risk of recurrence in that population, but definitely needs to be studied more. But I think one key thing is that we see that this improves symptoms beyond sexual function, which is what we often associate with testosterone. And most importantly, at the physiologic doses that we normally replace testosterone, we see no increase in estradiol levels in the blood.

So mostly we're left with more questions than answers, but that's why when we're having these discussions, we need to have a very informed, individualized conversations, because you can see that the data is not so clear cut in my view as saying hormones are dangerous after breast cancer. There may be a lot of situations where that may be a very appropriate conversation to have depending on an individual person's history.

Let's talk about ovarian cancer, because I know that that's another important topic for the Sharsheret community. So again, we see that ovarian cancer is multiple different diseases. So the most common type of ovarian cancer is high-grade serous, which is very strongly linked to BRCA. This is not always estrogen-sensitive. And in fact, for most high-grade serous ovarian cancers, we don't necessarily put somebody on endocrine therapy like estrogen blocker medications. So it's very much a discussion. We'll get to some guidance on that in a second.

Low-grade serous is very estrogen-sensitive and is very difficult to treat. So I often feel pretty uncomfortable with the idea of hormones for these folks, because this could be a very difficult cancer to treat, particularly when it's more advanced. Similarly, endometrioid, probably reassuring at earlier stages, but later stages definitely can be estrogen-driven. But importantly, clear cell, mucinous, these are not hormone-driven. So I had a patient just recently actually who had had her ovaries removed from mucinous cancer when she was 20 years old, and nobody had ever discussed hormones with her. And this is just a perfect example of somebody just slipping through the cracks because they said, "Oh, you had

ovarian cancer. You can never think about hormones." And unfortunately now she's in her late 40s and we're just having this discussion for the first time. Granulosa cell, definitely estrogen-driven. And then most germ cell ovarian cancers are not estrogen-driven.

So this is my favorite guide on this. So this is the British Menopause Society and British Gynecologic Cancer Society joint guidelines. You can find this online if you want to read it. It's available for free. But they created this really nifty table where they go through sort of this green, yellow, and red, where green is absolutely no concern, yellow is sort of discussed risk benefit, and red is that the risk may outweigh the benefits. But what I want to illustrate here is, again, vaginal estrogen, really safe across the board. They say this low-grade serous stage two plus just because we don't have a lot of data on that. But even the systemic therapy, there's really only two red categories. Everything else is green or at least a discussion.

So just to close things out, it's really not all about HRT, that I think a lot of women with cancer who, particularly if they have hormone-sensitive cancers, they sort of leave social media or they leave this world feeling like they're missing out and they're like, "I'm worried about my heart. I'm worried about my bones. What about me? I can't take this or I don't want to take it." And what I want to say is that it's not all about HRT. There are plenty of people who are taking HRT, but are still not exercising, not eating a healthful diet, drinking alcohol all the time, smoking. All of these things are going to make a much bigger difference in your long-term health than any effect that would come from HRT.

So when people ask me about it, I always say, "Well, what is your cholesterol like? What are you doing to control your cholesterol? Are you doing regular exercise? Are you strength training?" All of these things are going to make a much bigger difference. And then importantly also, all of these things that also benefit your long-term health also help with the symptoms of menopause. So we see consistent improvements in mood, hot flashes, joint pains with regular exercise regimens and healthful diet and avoiding alcohol.

So this is a little bit of a guide, so thinking just section by section. So if you are concerned about your bones, if you have gone through early menopause, if you have gone through cancer treatment, you are very much eligible for an early DEXA scan. We normally do DEXA scans at 65, but this is the scan where we are looking to see what your bone density is. Do not wait until you're 65. Ask your doctor for this now.

Strength training, one of the best things you can do both for bone health, but also for cardiovascular health. And most importantly, it also helps with your aging process, that it's not just about losing bone, it's also about are you able to catch yourself when you fall? Do you have the stability and the strength to do that?

For your heart, check all of your other risk factors. So what is your cholesterol like? What is your risk of insulin resistance? What's your blood pressure like? Consider a coronary calcium scan, which would help evaluate how significant your cardiovascular risk might be. And then again, those daily habits of regular exercise and healthful diet being so important.

So if you're kind of thinking about this, I think that we focus a lot on hormone-sensitive cancers, but I think that I really want everybody to go through these and maybe even go through these with your oncologist or your menopause specialist, whoever is managing this for you. But first of all, just think, was my cancer hormone-sensitive? And if it was, then what were the characteristics of that? Because a very advanced stage might be a very different conversation than an early stage, which we can definitely see in the gynecologic data.

If it's not hormone-sensitive, then can this be a part of my conversation? Similarly, what does my recurrence risk look like and how is that going to inform the conversations around HRT? Is this an option? But also, again, can I consider vaginal estrogen? And I would say the answer is always yes. That even though you may have been told this, if you are being told that vaginal estrogen is not an option, ask your doctor to show you the data that they're relying on, because I can guarantee you the data does not exist.

Now, that being said, what is your comfort level? So some people, they are like, "I don't want to think about anything that might increase my risk of recurrence that is not even remotely a part of the conversation." And other people might say, "I'm willing to accept this because I'm suffering so much and I've tried everything else, and I understand that this is going to be a nuanced scenario." Before surgery, figure out your plan and your team, and then make sure that that team is all communicating with each other.

So I always just close with this, because I think that this is really the key message, is that so much of going through cancer is having choices taken away from you. There is just this endless process of going to doctor and to treatment and to just one thing after another, and all of a sudden you don't even recognize who you are on the other end. And so, I really want to make sure that when we are having these conversations, we're restoring that choice, because the whole point of surviving cancer is to live the life that you want to live. We want to make sure that you are able to do the things you want to do with the people that you want to do it with and make sure that we are honoring that agency, that individuality, and your values.

So here's just some additional resources. One thing I do want to just highlight on here is if you are looking for a menopause specialist who can have these discussions with you, it is very hard to find these people. A lot of people will go to Menopause Society certified

practitioners. I'm going to say something a little bit controversial, which is that unfortunately, the vast majority of people who have Menopause Society certification really don't know how to have this conversation, some of whom don't even really know how to have a hormone conversation generally. So I really trust this organization, International Society for the Study of Women's Sexual Health. They are incredible and every single person who's a part of this organization cares so much. And if they don't know somebody, it's a small org, I guarantee you that they can find somebody who does. So thank you so much. I wanted to get through this as quickly as possible to enable Q&A. I know it's an enormous topic and I'm sure there's a lot of questions, but I'm happy to talk about anything that has come up.

Moderator:

Wow. Thank you so much. And kudos, I did not think you could get through it all in that amount of time, and you did. And I know that for this webinar in particular, even the people who are here tonight are going to be going back and watching the recording.

Dr. Jordan Emont:

Please do. Definitely. Yes.

Moderator:

So okay, the challenging news is this webinar brought in more questions before we even began than any other webinar I've been involved with. The really comforting news is you answered a lot of those questions during the presentation. But let me start, because we have some. So I just want to confirm that we're right, I think I know the answer to this, but a couple of people asked again, vaginal estrogen is absolutely acceptable even when someone has a hormone receptor-positive cancer? I just want to confirm that and make you say it clearly.

Dr. Jordan Emont:

Yes, 100%. So with breast cancer, so across the board, I can answer that question as yes. But I'll give the one little caveat that there are some areas where we haven't really studied the question. And so, those would be advanced endometrial cancer, leiomyosarcoma, which is another rare type of uterine cancer. And I will say that these are very estrogen-sensitive cancers that tend to recur at the vaginal cuff, so where the uterus is removed from. So I can understand a little bit of the hesitation that somebody might have in that specific situation, but I would make the argument that even for those people, at the very least, applying a small amount of vaginal estrogen at the vulva, at the introitus, the opening of the vagina can help enormously. Because often when people have pain associated with

sex, it is typically right at the entrance there and applying that very small amount can make a big difference very far away from the cuff.

And if you are at all concerned about systemic absorption of that estrogen, again, it's minimal, if any at all. But theoretically, the higher up in the vagina, there is more systemic absorption. So if you're still nervous about this, if it still makes you scared, if you don't trust what I'm saying, then at least just feel comfortable applying the smallest amount at the vulva, because that is typically the place where it makes the biggest difference.

Moderator:

Thank you. And I just want to clarify, because a couple of questions came in about this too. If we're talking about vaginal versus systemic estrogen, using vaginal estrogen is only going to help, you mentioned with UTIs and with sexual function. It's not going to get rid of brain fog or hair thinning or other menopausal symptoms, correct?

Dr. Jordan Emont:

Exactly. Yeah. So again, this is skincare for the vagina and the vulva. So often when people are on hormone therapy, they typically will take both, because the systemic therapy doesn't really help with the vaginal symptoms very much and vice versa. I will say that every now and then I have somebody who is using just vaginal estrogen and they feel systemic effects. So I don't want to totally neglect. I don't know if it's a placebo effect or if there's actually a tiny microscopic amount of estradiol that's getting into their bloodstream that is helping with that. But for the most part, we would say that these are completely separate things.

Moderator:

Okay. A couple of people, including one just right in the chat box now, asked about MonaLisa. What do you think about that? And could you explain in one sentence what it is?

Dr. Jordan Emont:

Yeah, sure. It's not something that I do, so I don't have a lot of practical information to give you about it, but there's a lot of these energy-based devices. So some of them are red lights, some of them are laser. I believe the MonaLisa is a laser procedure. The evidence is very mixed right now, so I would personally never say that that is going to be better than vaginal estrogen. It also can be expensive and you usually have to pay out of pocket and vaginal estrogen is often covered by insurance, or if it's not, you can get it on Cost Plus Drugs for \$14 for a tube. So I would personally never recommend that somebody do that as a first-line treatment, because we know the vaginal estrogen is so safe, but we're not quite there yet with the data in my view to say that this is definitively something that we can recommend across the board.

Moderator:

Okay. Just a yes or no answer. Somebody just asked about lichen sclerosis and does vaginal estrogen help with that too?

Dr. Jordan Emont:

Yes, it does, but you still should take the steroid treatment.

Moderator:

Okay. Let's shift gears for a second. How does someone who carries a hereditary cancer mutation, how does that impact the decision as to whether or not somebody should take any kind of hormone treatment?

Dr. Jordan Emont:

Do you mean somebody who has had cancer or somebody who doesn't have cancer?

Moderator:

Either.

Dr. Jordan Emont:

Okay. So for somebody who doesn't have cancer, I think that the data mostly comes from the BRCA population. So I can't give you the same data that would exist for a PALB2 or CHEK2 or something else, because we just haven't really studied it. But for BRCA carriers, we have very good data that says that the use of hormone therapy does not increase the risk of breast cancer in its modern form. And in fact, again, estrogen-only therapy actually decreases the risk.

This is part of why... I didn't get into it, but I figured it would come up in the Q&A. This is actually part of why you should be having a discussion about having your uterus removed or not at the time of ovarian removal if you are undergoing a risk-reducing oophorectomy. For one, people who carry BRCA1 have an increased risk of serous endometrial cancer, so that is often a part of the recommendation just because of decreasing that risk. But for BRCA2 carriers, you don't have that risk, but I still will see a lot of BRCA carriers get their uterus removed purely so they have the option to use just estrogen therapy, which has been associated with a decreased risk of breast cancer.

Actually, across the board, high risk or not, estrogen-only therapy is associated with a decreased risk of breast cancer. So it's important to say that estrogen does not cause breast cancer. And I think that that really informs the rest of that discussion, which is that if somebody hasn't had cancer, I can tell them pretty definitively that the use of estrogen-only

therapy is probably going to lower their risk of breast cancer, and the use of combination with the body identical estradiol and progesterone is going to have a neutral effect and not increase the risk of breast cancer. So I don't think there's anything to be concerned about.

Now, if you've already had cancer and you have some sort of genetic predisposition, I think it basically falls into the same category as everything else we discussed. It's a very individualized discussion. A lot of people may have had a double mastectomy if they have BRCA and they get breast cancer. So to be honest, that actually really does inform that conversation, because that baseline risk of recurrence or a new cancer is already so much lower after having a mastectomy. So sometimes people actually feel a little bit more comfortable with that discussion if they've had that procedure.

Moderator:

Okay. Next question would be, if someone is not comfortable or has been advised against taking systemic estrogen, what are some treatments that might help the non-sexual function side effects of menopause, including hair loss, brain fog? Brain fog came up a lot. Are there medical ones, natural ones?

Dr. Jordan Emont, MD:

It's a great question, and it really does depend a little bit on what symptom we are talking about. So as far as medications, really the main one that I would typically focus on is going to really be more addressing the hot flashes, the night sweats, and the sleep, which would be those neurokinin inhibitors, so the Lynkuet, the Veozah, they're definitely effective. And sometimes they do help brain fog, because if people are not sleeping, they usually can't really think very clearly either. So if we're improving people's sleep, then it typically does get better.

Outside of that, there aren't really clear pharmaceuticals that can improve brain fog, for example. So it is really challenging. I will say, and sometimes this can be a little bit of a controversial discussion as well, but I often recommend creatine for a lot of patients with brain fog. It can actually be very helpful even at higher doses. I think that there can be a little bit of this concern that sometimes creatine can fuel cancer cells. I don't really think that the data is actually very secure on that, so I usually feel comfortable with that, but I've definitely seen people who take higher doses of creatine can have improvements in their brain fog, but it is challenging. I don't know if I have a go-to that works for everyone. Everyone is going to have to sort of find an individual thing that works for them.

Moderator:

Okay. Last question. I wish we had more time, but-

Dr. Jordan Emont:

I'm happy to stay as long as possible. My flight is not for another two hours, so...

Moderator:

Okay. Well, then maybe not last question. For people who are put into medical menopause, it's sudden, whether through the removal of their ovaries, an oophorectomy, or whatever cancer treatments they're put on. Is it actually true that the symptoms are worse? Are they physically worse or is it just a psychological thing because perimenopause wasn't a part of the experience?

Dr. Jordan Emont:

So it is very much true, and we have actually very good data using validated symptom scores that shows that symptoms across the board are more severe when people are put into menopause because of treatment or surgery. And I do think that probably the abruptness is a little bit a part of it, but even for people who that is a more gradual process, they still have more severe symptoms across the board.

Just to go back to your last question, one thing I thought about, because you mentioned hair loss, I realized it didn't address that. The red light can definitely actually help. So red light therapy can be very helpful. So there's those red light caps, they really can be helpful. I mean, hair loss is one of those things that it takes a long time to come back. Also, minoxidil, definitely helpful. So you can apply minoxidil topically, but you can also take a really, basically microdose of it orally, and it can be very helpful as well. Because you mentioned that, I just wanted to go back to that one.

Moderator:

Yeah. Okay, let me throw a couple more at you... One question was, when you enter menopause, and I think this question was just in general, not even related to cancer, because of the changes in the body, at that time, does a woman's risk, is that the cause of a woman's risk increase for a cancer diagnosis?

Dr. Jordan Emont:

I don't know if anybody can definitively answer that question, but I will tell you that there are a number of risk factors that happen around the menopause transition that could potentially increase that risk. So when we think about risk factors for cancer in general across the body, this is not any specific thing, but just broad categories of things. So first of all, just getting older, you're more prone to genetic mutations in cells. So cells just become a little bit less efficient in their reproduction, and so it introduces the possibility that these

genetic changes can happen, and that's really what cancer is. We have genetic changes in cells that lead to cells going out of control. So that's just one thing, is just by the virtue of your cells becoming less efficient, it introduces that risk.

But also, I will say that another big one is inflammation. So inflammation tends to go up as estrogen is withdrawn. Also, there tend to be changes in people's weight distribution, so we have more visceral fat accumulation. Visceral fat is a lot more of an inflammatory fat. It tends to lead to more insulin resistance, which also increases the risk of breast cancer. So those types of things, yes. But as far as the specific data saying that we can tell you with 100% certainty that that is the logical pathway of what leads to breast cancer risk, I'm not personally aware of any study that has done that, but I think we wouldn't really be able to 100% say that there's something in particular that is making that happen.

Moderator:

Okay. So to wrap up the questions, you've given us great news on the usage of vaginal estrogen, you've given us a lot to think about when it comes to systemic estrogen, and you've touched upon lifestyle behaviors and risk reduction. Let's finish on, I'm going to ask you to add something about that, because I know we all had questions about hormone replacement therapy, but let's just emphasize how important that is.

Dr. Jordan Emont:

So if there is one thing that people should do to reduce their symptom burden and to improve their long-term health, and people don't always like this, but cutting out alcohol is one of the best things that you can do. If alcohol doesn't do anything for your life, you should stop drinking. There is no medical benefit to drinking any amount of alcohol. Now, the only thing that I will say is that alcohol often brings people together, and it's important to have social connections. So if that is the only benefit, then do it, but do it sparingly and try not to drink very much of it. But the reason that I say that is that very consistently, alcohol worsens sleep, alcohol worsens hot flashes, alcohol worsens joint pains, alcohol worsens mood disorders, alcohol worsens breast cancer risk as well. In fact, there's a higher risk of breast cancer drinking alcohol than would ever come from, for example, those synthetic progestin medications that I mentioned.

So that is probably the single most important thing that a person could do if they want to improve their symptom and their health. But all of the other things are incredibly important as well. So Mediterranean diet, which you can Google if you don't know what that is, but generally a plant-forward, lower in red meat, higher in fish content diet and lean meats significantly decreases your risk of cardiovascular disease, tends to actually improve a lot of menopause symptoms, and decreases the risk of breast cancer. Similarly, regular

exercise, one of the most important things you can do for your health, but also helps to decrease symptom burden and decrease the risk of cancer recurrence.

So these things are not nothing. I was just at another event today and they talked about longevity more broadly. And I think that we have all these conversations about, oh, this peptide and this cool new thing that this new device that came out, maybe the MonaLisa is a perfect example. It's this cool new thing that exists. But I think that the stuff that actually helps people live longer and feel better is usually the boring stuff. And so, doing the boring stuff well and consistently is the single most important thing that a person can do.

Moderator:

That's a great thing to end on. Okay. As we begin to wrap up, I want to thank Shari for sharing her story and Dr. Emont for not only your insights, but all of this important information. Thank you again to our summit sponsors, the Cooperative Agreement 24-0061 of the CDC, AstraZeneca, Eisai, GSK, Lilly, Pfizer, Smart State, and Weill Cornell Department of Genetics and Personalized Cancer Prevention. Thank you again to our Summit partners. We are putting a link to a survey in the chat box right now. It will take you less than five minutes to fill out and you can still listen. You can click now and still listen to the last couple of things I say. We'd be so grateful if you would fill that out.

I want to share a quick note about an upcoming webinar, the last of this year's summit. This Monday the 19th, we've scheduled a webinar on GLP-1s and cancer. I saw a question come in, I wish I could have asked you about microdosing GLP-1s. Please, whoever asked that, join us on Monday night. There's some really interesting information about GLP-1s and cancer, unexpected, at least for the average person information. So that's this Monday. And all the other webinars that were presented during this year's summit have recordings that have been posted on our website alongside transcripts. If you've missed any or want to re-watch, please check them out. The summit actually has its own page on our website, so let's post that in the chat box where you can check out all the programs, national, local. There's still a ton of local programs going on. You can register for webinars, learn more about our partners and our sponsors.

And please remember that Sharsheret is here for you and your loved ones. We provide emotional support, mental health counseling, and other programs designed to help you navigate the cancer experience. All are completely free, completely confidential, and open to all. There's contact information in the chat box right now. And as we say goodnight, please let's put the link to the evaluation in one more time. Thank you, Sherry. Thank you again, Dr. Emont, for a really enlightening evening. Safe travels to you and goodnight everyone.