New Developments in Breast Cancer Screening and Treatment

Breast cancer is the second most common cancer in women (although men can get it too). Some breast cancers are driven by inherited mutations while most are sporadic, driven by unknown causes or by environmental or behavioral factors like obesity, lack of exercise, or alcohol use.

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Breast cancer screening aims to reduce the number of women who die from the disease and the statistics tell us that even though the rates of breast cancer now are greater than they were in the early 1980s, fewer women are dying from the disease. However, the scientific evidence backing screening's benefits is mixed.

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We are talking to Dr. Esserman of UCSF Helen Diller Family Comprehensive Cancer Center about developments in breast cancer screening and new treatments.

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Full Transcript:

Priya Menon: Good morning everyone and welcome to Cure Talks. I'm Priya Menon and your host. We are into October and this month is all about breast cancer awareness and today we are discussing new developments in breast cancer screening and treatment with none other than Dr Laura J Esserman from UCSF Helen Diller Family Comprehensive Cancer Center. Joining Dr. Esserman on the patient panel are breast cancer advocates, April Stearns and Kelsey Smith. So to get the discussion started, we have with us Dr Laura Esserman, surgeon oncologist who has been co-leading the breast cancer oncology program at UCSF Helen Diller Family Comprehensive Cancer Center for more than two decades. Dr Esserman, it's such a pleasure to have you with us today.

Dr Laura J. Esserman: Thank you. It's so nice to be here.

Priya: So my first question is kind of a doubt clearance. You can say so while I was researching for today's talk, I found a very common discussion in various forums, which was about a difference between screening for breast cancer and early diagnosis. It would be great if you could help us understand the difference if there is one.

Dr Laura J. Esserman: Well, I think one of the things that people confuse as a screening and prevention in particular, so the idea behind screening really started in the 1980s and it came from our understanding that people with early stage disease did much better than people with late stage disease. Now back then, we all thought that breast cancer was simply one disease. And so it made sense that if only we could, the earlier we could find these cancers, the better off we'd be. This really became sort of the mantra for early detection saves lives. So the idea of screening is really to find cancers at a very early stage. That really is the purpose of screening. Screening is not prevention. It is really the idea that if only we could find every cancer at this really small stage that the problems with breast cancer would go away.

But unfortunately that did not solve all of our problems. The incidence of breast cancer has gone up over time and we have had an increase in the rise of these very small cancers without an equal drop in the risk of the big cancers. So some of the late stage cancers later stage cancers went down, but nowhere near as much. And what we learned from that was, Oh, there's also a bunch of small low risk cancers that may not, that may be different from these high risk cancers. So it's really just highlighted the point that breast cancer isn't one disease, it's many diseases and some of them are small and are never going to be destined to be killer cancers. And some are killer cancers even when they're small. So I think the issue is that our notions of screening have to evolve in their understanding of the biology of breast cancer has evolved and as our treatments are changing, so we're learning how to personalize treatments for breast cancer and we now have to learn how to personalize our approach to screening. And as well, that opens the door for us thinking about how do we personalize and, and think differently about how to prevent breast cancer, not just screen for it.

Priya: So what we're essentially saying is that screening is performed to find the disease before the symptoms begin and probably the goal is to detect…

Dr Laura J. Esserman: Yes before symptoms begin, but when it is still, this has to blow as a cancer, as a small cancer

Priya: Yeah. And the goal would be to detect that the disease at its earliest, and as you said, at the most treatable stage.

Dr Laura J. Esserman: Right. That was the goal. But there are, things never work out quite as you hope. And again, we designed this when we thought that every breast cancer was the same and that every breast cancer was on this path to slowly grow and become a bad cancer. That turns out not to be the case. So just different kinds of cancers that grow at very different rates. And so some cancers, again, some can, the best analogy I can make is do prostate cancer because people I think understand that. The rise of PSA screening has been very controversial because it led to the detection of many small prostate cancers, many of which would never really become a clinical problem if they were detected. And that led to over-treatment.

So over diagnosis, treatment and that again what's happened is it's not that all screening is bad and if we just have to broaden our understanding of what happens when you screen in any disease, when you screen, you will find more people with these early stages of disease, some of who are going to go on and get something bad, but many of whom may not. So we have to then develop plans and strategies to separate out who has the good risk cancers and the bad risk cancers. How do we evolve screening so that it's more purposeful and we're finding and the consequential cancers and reducing the risk and that way.

Priya: So Dr. Esserman, what are the current recommendations for breast cancer screening? And it'd be great if you could touch upon what age should screening begin and who should screen and some of the screening methods because these are some of the questions that we've received from our audience.

Dr Laura J. Esserman: Well that is the perfect question and I would say we don't really have the right answer to that, which is why we're running a big trial called WISDOM study. So there are at least seven recommendations from professional societies in the United States alone. None of which exactly agree. I think the consensus is that women over 50 should be screened. The question is, should it be one year, every one

year or should it be every two years; in the United Kingdom, they do it every three years. Around the world screening adults have very different, and the question is, should you start at 40, should you start, if you have a family history, when do you start? Some people say 40 some people say 45, some people say 50. The recommendations are all over the map. And I was recently talking to a healthcare professional who said, my gosh, my mom died of breast cancer screening.

I'm in the healthcare field and I don't know when to start or what tests to you. And this is very confusing for women. And so the University of California, San Francisco started up a network called the Athena Breast Health Network. It was originally the five University of California Medical Center campuses and now has extended to include Stanford Health in the Midwest and the University of Chicago in Illinois and Minnesota and Alabama. So we're really trying to put a network together to really tackle some of these big questions and we are really trying to answer the question, when should you start stop? How often should you screen and what modality and should we be integrating screening with prevention? So we're testing what some consider to be the gold standard, which is starting screening at 40 every year until 75 or 80 and we're testing that again, a more personalized approach.

Now what does that mean and why did we come up with this personalized approach? Our notion was that if all women don't have the same risk and all cancers aren't the same, why are we screening everybody as if they all had the same risk and where the risks are the state in cancer. But that didn't make sense to us. And what we wanted to do was take all we knew about breast cancer risk and put that together in a way that we really wouldn't be able to say much more definitively when they should start stopping. And how often did screen. So our personalized program includes doing a comprehensive genetic panel, and this includes looking for errors in nine genes that lead to a much higher rate of getting breast cancer. So BRCA1 BRCA2 PALB2, CDH1 etc. There's nine of those genes.

Now, they're not very common, but if you have them, they really do confirm high risk. This is something that we've learned over the last couple of decades. Why aren't we putting that into practice. As well there's information about the small variations that people inherit in their genes – that's the stuff that makes you a little bit different from your sister or a person sitting next to you. So it's there. But there has been a huge amount of work around the world trying to identify several of these, couple of hundred of these, what we call single nucleotide polymorphisms. It's a long, complicated thing, but all it means is little small variation. Together, we can put that risk together, we call it polygenic risk. Many genes – poly, genic – genes PRS. So that PRS score actually does differentiate people in the highest and lowest risk.

And so we're adding that to some of the standard tools, the breast cancer screening consortium risk tool. We add the information about screening, I mean by the genetic risk, breast density and other risk factors that people have. And we put this comprehensive tool in place to then tell someone, do you open up risk to start in your forties or should you wait until you're 50 if you're 50 or 40, should you do it every year or should you do it every two years? And are you really at an extremely high risk, in which case you should be screened every six months and with different modality and what the MRI, I think we may get to this later, but not everybody, I think we have to be careful not to use too much screening. MRI is, it's an expensive test and it has very sensitive and finds all kinds of things.

We're trying to also decrease the harms of screening. And we can get to that later, but there are harms from screening. And so the point is if we really understand people's risks, can we do more for the people at higher risk and do less, safely for the people with lower risk so that we don't so we don't unnecessarily expose people to harm when they're not gonna get much benefit. But where we're really wanting to look harder for the people who do have more risks because they're much more likely to benefit from screening. So this is the basis, this isn't the end. This is the beginning of how we change. And one of the important things we brought into this trial, the WISDOM study, that's an acronym that stands for Women Informed to Screen Depending On Measures of Risk.

The idea here is that we're going to start with the best knowledge we have today and every six months we improve our screening algorithm as information becomes available because it's a modern era trial saying we

know that information is changing all the time. When new information comes out, we change it. It's just like if you would come in last year and you had no family history and next year you come in and your sister got diagnosed, I wouldn't say, Oh, I'm sorry I can't take that into account because I started your screening last year and your sister didn't have breast cancer, no one would do that. That's not how we practice global medicine. Our trial should reflect more about what's appropriate for them. So, the U S preventive passports guidelines say to go talk to your personal physician to try and figure out what's right for you.

I would say if you're listening, go to wisdomstudy.org and join the WISDOM study and share your wisdom and help us find the right answer because this is one of the most important questions that women have. This is one of the most urgent public health issues because all women are told to screen and there's so much confusion, we want to really help unravel that confusion and get us on a path to learning how we can personalize screening. The other thing that we think is important is if you are at higher risk, there are things we can do to lower your risks. Sometimes that's lifestyle, sometimes that the medicines that we have like for heart disease, there are medicines that are approved for many people it's very easy to take. If we can do something to lower your risk, that's always better. That's even more important than screening.

And if you're super high risk and come from a family where a lot of people died of the disease, you want to really think about what all your options are. So I think that's our approach. We recognize that the options and the advice for women out there is not optimal. It's just confusing and we can't make that confusion better without putting together a modern era study. Because most of this data comes from 30 years ago when we didn't even know that breast cancer was – there was estrogen positive and estrogen negative and all this information, and there wasn't any treatment there. Today everything is different and we should be using all the information at our fingertips.

Priya: Oh, that's awesome Dr Esserman. At this point. I'd like to actually take a question from the audience and it's on screening so that's why I'm just taking it at this point. She wants to know is there evidence to support the use of imaging modalities such as digital tomosynthesis, contrast mammography, MRI, etc for screening high-risk premenopausal women, (previous biopsy with atypia, family history, no children, no genetic risk factors) who have extremely dense breast tissue that appears solid white and mammogram images. She also wants to know if there is a metric for determining screening frequency and modality such as a lifetime risk score threshold and is there value in quantitative transmission ultrasound imaging. I know a whole bunch of questions there.

Dr Laura J. Esserman: Okay. I think I can handle that. Okay. Yeah, so those are all excellent questions. So the majority of people don't have really high risk. But if you do, the recommendation is natural to rely only on mammography, but it's to rely on mammography with MRI imaging. I think it's very clear that some kind of contrast enhanced imaging as value and what that, so there's two kinds of, let me break down the screening tests for you. So mammography takes ionizing radiation and it goes through the breast. And so anything that's in will reflect back and look white. The more of that you have, the harder it is to see masses. Now, one thing is true that mammography sees things called calcification. These are a little deposits of calcium, which are actually pretty common in the breasts. And so it's not the actual finding of the calcifications themselves, it is the way it's the pattern in which they're deposited and the way they're grouped or clustered.

And that you can see even in a dense breast, in a dense breast it often reflects cells dying in the center of something so that's why it's a good modality in that regard. But the ability to see masses or change in the breast cancer and the breast architecture is much less if you have very dense breast tissue. The younger you are, the more dense breast tissue you have as you get older. Your breast density gets less. Not always, but most of the time there's a lot of confusion about what it is you should be using if you have very dense breast tissue and there's a lot of fans of using ultrasound, but ultrasound in many ways is the same thing. It's taking sound waves just like ionizing radiation and the more dense your breast issue, the more it will look solid and the harder it is to find things.

The problem with ultrasound is you find a lots of things. The chance of a false positive is like 90% it's very high. The chance of a false positive with an MRI is like 40% it's still very high, so you don't want to use a lot

of these modalities and unless you've got a good reason for it, dense breast tissue alone is not a good reason. Dense breast tissue in the setting of higher risk is a good reason. And people at highest risk, our recommendation is every six months you alternate a mammogram and an MRI. And one of the reasons is that calcification is one way to find things. And when you have a contrast based test you're putting something in the vein that goes through the bloodstream and you're looking at the blood flow to the breast and often tumors will take up that contrast material much faster and then wash it out.

That's what we're looking for when you're looking at a contrast based test like MRI. Contrast enhanced mammography is another contrast based test. It's not used anywhere near as much here, but it actually is very promising and probably less expensive than an MRI. And there are some studies that are testing this. And I think it's a very promising modality. I think some kind of contrast based imaging for someone at high risk was high breast density is a good idea. And if your mutation carrier or someone who has that level of risk, you start at 10 years before the diagnosis of the youngest family member. So someone earliest it was 35 then you might start screening it at 30 or even earlier if there's a lot of breast cancer in the family.

When you're younger, we tend to use just the contrast based imaging tools because you don't want to be doing a lot of mammography before the age of 30 or 35. So that's how you think about it. And one of the things that we've tried very hard to think about is to make sure that we don't overuse these technologies. And so this idea, so there's starting to be recommendations that everybody was that breast tissue should out and get lots of these tests and sounds like a good idea at the surface. But you have to be careful because you don't really want to have all these workups or false positives. This is very frightening for people. And once you find one thing, then you can get to another. And so on. And one of the things I think is important for people to think about if you have a diagnosis where you've had atypia, that's a marker of risk, but it's also a marker that you would be particularly benefited from an intervention like taking Tamoxifen. Tamoxifen is a medicine that we use for young women that you can drop the breast cancer risk in half.

In fact with atypia you can drop that by two thirds or more and that actually beats screening any day. So I think it's important to use the information not to also think about what can I do to lower my risk. I feel that the rush to do tons of tests for people is a potential real problem for women. And, and we have to be careful not to overdo it with the testing. A lot of people don't realize it. I mean mammography seems like a simple, easy test, but when you look at across the country, we spend probably about $10 billion a year on screening. It's just one test and we want to use it wisely and make sure that we're not really frightening people unnecessarily. So we have to be thoughtful about it.

There are a lot of studies now on comparing these different modalities and how to combine them. At the current time, the standard for high risk women should be MRI alternating with mammography every six months – so once a year MRI once a year mammography. And again to look for the different ways that you can detect cancer. One is calcifications and the other is with the uptake of that contrast material. And that's why that's what we proposed. There's a lot of people who use ultrasound. Ultrasound is a fantastic diagnostic tool to investigate things that are wrong on MRI or mammography. It's not a great training tool even though it's used a lot but just something for people to know about. And then to talk about the last question and there's a very big study. So the team has studied that it's out to try and tell us whether tomosynthesis really adds a lot of value to screening and that likely as some, but probably not in the way that people think.

It's not, I don't think it's going to be the solution to people have extremely dense breast tissue where it adds and replace the IB contrast tools like MRI or contrast enhanced mammography. I think that there will be a role in the highest risk women with very dense breast tissue. But again, about 15% of people have very dense breast tissue, but when you look at people who have – so there's four grades of density of breasts – Fatty, Scattered fibroglandular density, Heterogeneously dense, Extremely dense – So that is classified as A, B, C, D – A and B and then C is they call heterogeneously dense, meaning patchy density and D extremely dense. So C and D that's half the population, that's a lot. So that's not very discriminating and so saying that we should be doing MRI for everyone. I mean we would be spending $50 to $100 billion to do that.

That's probably that we just don't have the, I don't think that's the right way to go. We need to be much, that again tells us we have to have more personalized ways of screening. Who's going to benefit, who has the risk, who is it worth for whom is it really worth doing all this extra workup. And I spend a lot of time in clinic talking to people who got down the screening cycle. I saw someone yesterday who had had nine biopsies. On her ninth biopsy, they found a tiny bit of insight to breast cancer and had recommended a bilateral mastectomy. That's not the goal of screening. You don't want to torture someone, she wasn't even 50. So the goal isn't to torture people until we find something and then take the breast off. That's not reasonable. But that is what happens. And people don't think about it and they say, Oh, why not just screen? So we have to learn how to use our information well and that's the motivation behind the WISDOM study to try and figure out how to tailor screening and prevention in a way that we get the most benefit for the people who have the most to gain and we minimize the harm in then people with low risk.

Priya: Thanks Dr Esserman. That was very, very well explained. I would at this point just being mindful of time, I'd like to bring in the panel. So we have with us April Stearns who is a writer and April was diagnosed at 35 years old with stage three breast cancer and four years later, April launched the Wildfire magazine as a way for young women to tell and read breast cancer stories. So April, you're on air, please ask your question.

April Stearns: Thank you Priya. Hi, Dr Esserman. I'm actually in your backyard in Santa Cruz, so it's a pleasure being on air with you. I really appreciate what you were just saying about the need to balance increased screening with common sense. To summarize, I am coming at this from, as Priya said, being a survivor of breast cancer myself. And I wonder if you could talk a little bit to us who've been diagnosed young and now worry about our own daughters. I was diagnosed at 35, I represent women who were diagnosed under 45 and so I hear every day from people who are concerned about their children coming up behind us and wonder about screening for, not necessarily as children, but as they get older. And I wonder if you could talk about maybe why 40 is the magic number and if self exam is actually still more or the most effective for people who are younger than that.

Dr Laura J. Esserman: So thanks so much for your question, April. And you, your story actually represents exactly the challenge with screening. And what our notion was in 1980 was again, that, all cancers grow slowly and that all we had to do with my them early in all would be well and that if you look at the risk, the risk increases with age. And so you have, if you're screening a million people and one of them has, might have cancer, that's not common enough to screen. So one of the principles of screening as the disease has to become, so breast cancer is very common, but the kind of cancer you had was a fast growing cancer. And fast growing cancers tend more often to happen in young women. And this is again one of the principles that's making us rethink screening that there are some types of cancers that grow very slowly where screening is good.

Or maybe there are some kinds of cancers that grow so slowly that they would never come to this level attention. So you don't want to find them inside to cancer might be one of those. The high risk for the high grade cancer, the kind of cancer you have, they grow very fast and they can actually come up in three or more months. So it's not that you were neglectful and didn't come in in time, it's just that you had bad biology and screening is not going to help us. And in fact, we're not going to screen our way into a cure for those kinds of cancers that in fact, I run another trial called the I-SPY trial where we're really trying to optimize the treatment upfront for the people who have cancers that are life threatening. The screening isn't going to be the solution there and we shouldn't, it's not helpful to us to hope that we are going to screen our way into a cure for that.

These kinds of cancers that are life threatening from the beginning, you have to figure out how to get the treatment right. So the best thing going forward would be to understand who is this for these kinds of cancers. One of the things that we're working on is trying to figure out for, so the I-SPY trials, really looking at people with stage three breast cancer stage two and three cancer particularly 2B, 3B I would say, who are the people at risk for that we actually are doing our investing in a big project to try and understand better, what are the predisposing risk factors, what will be if we knew that we could find those people, we would do

something early for them and the more we know about how to treat them, the more we're going to know about how to prevent them.

And we'd love to be able to come up with ways of prevention that don't include prophylactic surgery. For some women who have very early breast cancer, there is driven by BRCA1. But it's not necessarily that when you prophylactic surgery can be on strategy if you want to, if you come from a family where people have had their many cancers and people have died early, but that's a very, very unusual and small group of people. What we really need to get to is a better understanding of people who get the kinds of cancers you're describing because our current screening policy will not help us. But what we can learn from our studies is try and develop specific screening tools for people at high risk like them. That's what we're working on. That's why we hope that some of those genetic profiling, more comprehensive genetic profile will help us as well. There are new tests coming out about breast density and the types of density that you had may really help us identify people who are at higher risk. We don't have those tools today. But by saying that we're missing something and admitting that it's a problem and really working hard to find those solutions, that's how we're going to get there. And I certainly hope that we get there before your daughters need that.

April: I appreciate that. Thank you. I have another question for you. And it goes back to something that you were saying a few minutes ago. And this is with the idea that there are kind of two different ways of screening or times when screening is necessary. And one, like you were saying is before diagnosis and the other is later. I've been fortunate enough, lucky enough to be living no evidence of disease for seven years now. And my oncologist has a similar feeling about lots of vigilance. It sounds like as you do where if we look hard enough, we will find something. And so his point of view is that he doesn't want me living in constant fear of what scans will say. So he has a more minimal approach where I do mammograms. I was doing MRIs. Now I do mammograms yearly on the one breast that I have remaining. And then we do other types of things like MRI and CT when I have specific concerns. But I wonder if you could talk a little bit about that post-treatment scans and vigilance and how to balance the common sense with not overdoing it.

Dr Laura J. Esserman: Yeah, I think these are excellent questions and I have to say I agree with your oncologist in the same way. What happens is you don't want your life whittled by fear when you have a very high risk cancer. And I don't know the specifics of your cancer and we can't get into that on the phone here. But what I would say is for many women, these very aggressive high risk breast cancers, the biggest risk of recurrence is usually in the first five years depending again on the biology. There are some, if you have a hormone driven cancer, this of lower grade, your risk isn't as high, but it persists a much longer period of time. But those aren't fast growing. So if in the aftermath of a very aggressive cancer that really wasn't easy to find, it's reasonable to get an MRI once a year in that early post-period of follow up, maybe up to five years.

But then after that, and it also depends on the breast density, but after that, you have to say, well, what's my risk of developing another cancer in my lifetime? Especially if you've had a mastectomy on one side, you're really looking at the other, that's in the setting of the breast remaining. But once you'd have that breast is removed, you have to say, what's my risk of getting cancer on the other side? And it's a little bit different for the tumor types. So again, we need wisdom for screening after breast cancer as well. And we're working on a pilot for that.

For screening after breast cancer as well. And we're working on a pilot for that. That's based on your tumor type, your breast density and other risk factors again, so we can try and create some rationale. I mean real rationality to how we screen because especially if you've had cancer, if you get called back and people get, it's like post traumatic stress disorder. Some people are called back and it's just debilitating for people and you have and it's been proven that you at this time screening, knowing all these looking for metastatic disease. If you know the ASCO guidelines, the American Society of Clinical Oncology guidelines say very clearly that you shouldn't be doing screening tests cause it's all they do is ruin your quality of life. If you have a specific symptoms that will come up with in two months.

So it's, and finding it early doesn't make your treatment any more effective. So, constantly looking at trying to find something is not good just because you have risk. So these are the things that have to be separated. And if you're not a mutation carrier and there wasn't another reason, once you've gotten, you're in your mid forties an annual mammogram is probably all you need. And that's, again with the specifics, that's one of the things that your oncologist knows you and knows your risk factors. That's the right kind of conversation to have. And doing more may feel better until you get called back. One of the things we know is that after 10 years of screening, 50% of people will get called back. So as will even at the fall class rate isn't super high.

Cumulatively when you're doing something frequently that leads to a lot of trauma and a lot of call backs and 75% of what we call people back for turned out to be a biopsy even turned out to be nothing. So I think the stakes are even higher when you've had a cancer, when you get called back, it's just so frightening. So we just need to do better. And I do think that our technology is going to improve, the kinds of tests that we can use will improve. And the ways in which we can screen for recurrence is gonna improve a lot over time and needs to.

April: Absolutely. Well, thank you for that. I really, really appreciate that approach.

Priya: Yes. thanks April. I think we'll just go over to Kelsey and if we have time we'll round up back to you.

April: Thank you.

Priya: Yeah. so our next panelist is Kelsey Smith and Kelsey was diagnosed with stage two breast cancer in 2014 or the age of 29. She started the CanSurvivor Network, an advocacy organization focusing on elimination of financial toxicity caused by a cancer diagnosis and she also hosts a weekly podcast which chronicles stories of survival, second chances and ingenuity. Kelsey, you're on air, please ask your questions.

Kelsey Smith: Hi everybody. Thank you so much for having me on this show today. It's so nice to meet everybody. Dr Esserman, I have a question for you. I'm kind of piggybacking off of April's question. We kind of discussed the fear and as a patient advocate for not only my own sake, but also to kind of keep my constituents informed, rather I tend to go through with some of the screenings. So for instance, I'm undergoing the BCI testing right now to determine what my risk of recurrences within five to 10 years is. So I do like to screen, however one word that is very well known within our community and our culture is scanxiety. So from a provider's perspective, what kind of advice or what do you think we should do to help lower patients scanxiety around these screening tests and such?

Dr Laura J. Esserman: So one of the things that I try and tell my patients is that I said, look, if I'm going to screen humans with an MRI, if I'm going to even get an MRI, I'm going to give, I want to prepare you for what can happen and I want to prepare you for what you might read from the radiology report and what my job is as a provider to interpret those results. So even if you have cancer you can say, okay, here's what will happen with that MRI. It could be that the rest of the breast, everything is completely clear and we just see this one cancer. That's possible. It could be on the other hand, that we see something very obvious that's cancer and clearly needs to be worked up. And then there's all the stuff in between, which is the most likely that there's going to be some stuff that might be cancer that we have to work up, but not necessarily.

And there's a bunch of stuff, it's just going to light up everywhere. And that doesn't mean that you have cancer everywhere. Well, one of the complaints that people have about MRI and the use of MRI, it has pushed people to, it is blamed for the increased use of bilateral mastectomy and prophylactic mastectomy, taking the other breast up on the other side. And I think that's pretty clear. I think once you start sticking you're needle in and checking things and looking here and looking there, it can get you there. But we have tons of data that breast conservation works before we even and that the use of MRI doesn't necessarily improve your ability to find other things that increases the mastectomy but what it does is change your local recurrence rates, meaning that a tiny little things here and there, even if they turned out to be cancer are

probably dealt with by radiation or whatever your treatment is.

So you have to, we have to put that perspective and I think it's really important for providers to warn people to say, and if someone is super, super anxious, you really have to weigh whether you should get a screening test that has a really high sensitivity, but it's not that specific. Meaning if it finds something, it doesn't mean it's necessarily a cancer, cause a lot of these things that have to be worked up or there may be some things that are kind of like a little bit little that I need, just don't work them up. There's a lot of stuff I don't work up. Now that doesn't mean the radiologist will write a report calling it that. The radiologists are going to write a report where they describe everything they see. They're not writing it for you, they're writing it for them and they're writing it because that's the standard in which they are trained and that they don't want to take any risks.

They just want to describe everything. It's the clinician's job to interpret it. And they radiologist always say anything there recommend biopsy, but that doesn't always mean that you have to have a biopsy, if something's really obviously wrong, yes you want to get a biopsy, but lots a little distals you can't often work all that stuff up and it's just so anxiety provoking. So I think you have to have a conversation with people to say that there's lots of stuff that lights up in the background and a lot of times that stuff just goes away, especially when someone's high risk, if they take Tamoxifen, the next MRI they have, things are much quieter and easier to see. So there are, I think it's important for people to be prepared and to know that and that every little thing that lights up isn't something.

Kelsey: Very good. Thank you. Thank you very much. Yes there is. There's definitely a lot of scanxiety, so that's a great, great answer.

Dr Laura J. Esserman: And if you're getting a PET scan or any of these other things that lots of things light up. One of the reasons why we recommend PETCTs at UCSF instead of CT bone scan, everything else is because it's one test. And if something lights up on one test and it's like it's one test to combine the two modalities, PET and CT and if something lights up on the test, but there's no finding on the CT or something's on the CT and you don't see anything on the PET, you know it's nothing and you can drop the number of false positives in half by doing that. And it's so much better for the anxiety of a patient. So that's unfortunate that it's, we've gotten into a cycle where these are not covered by insurance, but in fact it's a much more cost effective way to scan someone.

And we're working on trying to get awareness in the insurance company which has published something to show that it drops the false positive rates in half and it actually is cost effective. And so this is a much more patient centered tool and so we're trying to get a change, a sea change in the way people look at it. But it's very important if you get a scan and then you find that some like one centimeter thing on the adrenal gland or something over there, you're not looking for it. It's round. You gotta stop if that's not what you went for. People have to remember that the patients have to remember it, the physicians have to remember it.

Kelsey: And that is a great segue into my final question. And I want to bring up the fact that screenings, yes, like you had mentioned they can be they can be quite pricey for patients, but sometimes they can, they can paint a better picture of the patient's diagnosis to help with treatment. And so how are cost barriers being evaluated to expand access to care?

Dr Laura J. Esserman: Gosh that's such a great question. And this is something that I worry about a lot that increasingly I'm seeing people have health plans where they're paying at 20% copay. That's one thing if you're a hundred dollar test, another thing if you're getting a $5,000 test or a $3,000 test. And so I think that it's important for people to ask and not be afraid to ask, what's my copay and what is this going to cost me? And if it's not covered, why is it not covered? Is it really important and what am I going to pay personally and can I afford that? And to talk to your physician about it, not to be afraid or not to think about it. You're not being compliant. It is, physicians often have absolutely no idea what patients face in terms of copays, really depends what your insurance is.

If you're in a closed system like the Kaiser, you may not see that. But in a lot of the commercial insurance plans, you can be charged what amounts to be $1,500 from one of these scans, an MRI or something. And so you need to know that upfront and to know and to really sit down and think about it. What are you likely to gain? What's the cost? And it's not just getting the scan and if you find something that lights up so the things that we often buy is sometimes only 5% of those in the setting of cancer turn out to be a cancer. So that's a lot of workup and you're paying 20% copay for all that. This is something we all have to think about is this society. And I think it's important to just be aware so that you're not caught unaware of.

And I know that a lot of patients can experience a significant out of pocket cost of the diagnosis of cancer. And that's something we all have to work on. There are, most communities how funds in ways in which you can get support and get help if you can't afford it. But I think it, everyone has to stop and think about it. If it's like, Oh, well, well it might be nice to have, but it's not really indicated. If it's going to cost you a ton of money and it's not really indicated, don't do it. If it's really important, then you shouldn't do it. And that's, but those are conversations that everybody can have with their physicians and should have with them.

Kelsey: Yes. And I will say too, I do believe that that also needs to happen within these corporations and having these talks about what kind of clinical trials and things, are we going to invest in per (unclear)? Because the thing is as you continue to if you have a misstep, you have to go backwards and then that incurs additional costs. And that gets rolled into the cost of some of these tests and some of these screenings. So, yeah.

Dr Laura J. Esserman: And I have, and one of the plateau in our WISDOM study, one of the things that we're trying to do is we're trying to get the insurers to cover the cost of the test because it actually turns out that when you personalize things, it's not more expensive. It's actually in the long run, a better way to spend resources because you're spending more for the people that need it and less for the people that don't. And we have a bargain where we're trying, you were funded by the patients that are coming through the research Institute started by the Affordable Care Act that the core eight but their deal is that we have to work with the insurers to cover the cost of the test. So we've tried to put this forward as a coverage with evidence development or coverage with evidence progression with the idea that many of the things that we do today don't have enough evidence like, okay, use evidence based medicine because it's really not appropriate for what we know today or the pace of change in science.

So what we need to do more of is put studies and trials together where we are generating the evidence and everyone has a stake – patient, physician, insurers advocates. Everyone's at the table saying, look, we need to generate this evidence. We'll all look at it. We'll all make decisions, but we all need to go forward and try and make it better. We don't want to stick with what things, how things were 10 years ago. We want to move into the future and help generate the evidence to do a better job. So I think this is a really important change for how we think about doing things better going forward. And some of the trials where we're trying to optimize care where we can learn early on, who's getting a good response, figure out who needs more therapy and who needs less. This is really important that the insurer should get, it just comes to the table and started helping us to fund those studies so that everyone has the data and we can more rapidly get these tailored approaches to patients.

Kelsey: Yeah. Thank you for that. Thank you very much.

Dr Laura J. Esserman: Well that gets to the issue, April you had about toxicity, right? And how do you manage that?

April: Yes. Yes, definitely.

Dr Laura J. Esserman: And I think this is like what we tend to do with medicine is when people have high risk, everyone gets worried and frightened and everybody then gets everything we give. We don't want to leave any stone unturned, which is all the darts at the board. So all, everybody, everything. And at the moment you're so afraid and there's so much risk. That's all you can think about. But people live a long

time where the consequences of that neuropathy in their hands where they don't have the right sensation, the fatigue, it can take years to get better suddenly immune side of no one.

It's a lot. It's a lot. And calls it collateral damage from, and their treatment. Right. So I think I had actually, it's essential that we do better than just give everybody everything that we can personalize our treatments to and the I-SPY trial, one of the things we're working on is trying to figure out, well, who needs what? How can we learn about these signatures and the tumor that tells, well this person needs immunotherapy or maybe this person needs a DNA repair damage. Then maybe we can figure out how to get less toxicity let's talk to it. . And we know if we start the treatment first, if you have a big cancer, you shouldn't go to the OR. I'm a surgeon. I'm telling you that that's not the right thing to do. What you, because if your cancer's going to tell you, you gotta know what's going to treat it best.

And so what you're looking for is what can make that tumor reduce or go away. And we can use those and early end point and if your treatment of a small amount of treatment gets you to that great end point, stop and go on and skip some of the other toxicity. But if not, we want to work. We're working in Iceland to try and give people multiple shots on goal to figure out how do we do it. We start with the least toxic, the most toxic. Do I know that that's the right way. Of course not, but that's what we want to test because that would have dropped it. Maybe everybody doesn't need everything and patients care about that toxicity, right?

Priya: Yes, absolutely. Thank you April and thank you Kelsey. Dr Esserman we have some questions that have been sent in by our audience and I think we could go over some of them. We did cover a couple of them while we're discussing earlier, you touched up on the WISDOM trial and screening modalities etc. So one question that's just come up is how different is a treatment and prognosis in breast cancer in males as compared to breast cancer of females?

Dr Laura J. Esserman: So breast cancer in men, if it does occur, but at a hundredth of the frequency and women. So it's really quite uncommon. So if it's one in 12 women who get breast cancer, it's about 1i n1200 men who in their lifetime would get a male breast cancer. And again, it's not frequent enough that we would screen for it. And this actually comes back to one of the questions actually April that you asked me that I did not answer and that is everybody should be aware. You asked about self breast exam, especially in your 20s and 30s and it is really important if you're screening and you have a normal mammogram on three months later you feel a mass in your breast and it's new and you know it's new, go get that checked out. And if you are a man and you feel a new mass under your breast tissue or your nipple tissue, you don't be embarrassed.

Don't be afraid to bring it up. That's actually one of the things that that happens why I think a lot of men who might find things saying, Oh I don't need to, this won't happen to me or someone who is 29 Oh this one happened to me. If you have a new math, it can happen. So the messages to be aware of your body, you don't have to do a 30 minute breast exam. You can do a two minute breast exam and just have a good sense of when you're getting a shower once a month, just get in the habit of just feeling your body and just seeing is there something new. Get to know what your body feels like. So everything in it, breasts are lumpy-bumpy, so lumps and bumps are fine, but is there something new that's different and clearly growing you'll notice it, 50% of women still come in have detected their cancers themselves. Many of those are in between screens. So that's just as important as screening. Be aware and make sure you bring that to your attention. Every little thing you get to be familiar with your body and if you see something that they were different that persists, not something that's there for one day or five days or three weeks, but something that's there for more than a month or is really changing is not going away. Bring that to the attention of your physician. Male or female.

Priya: Thank you Dr Esserman. So we have our next question and it is I am enrolled in UCSF's I-SPY trial, and interested in how you see the progress of the trial going so far. What have you learned? What new drugs look promising?

Dr Laura J. Esserman: Well, great question. So we actually have tested now almost 18 different drug

combinations and the people who have been on the arm, our treatment and we have doubled the chance of the tumours go away. So there's no question that they are all medicines. And in fact one of the immune agents has just shown in a confirmatory trial that you can really dramatically improve the chance of getting a complete response and the triple negative breast cancer tumors. And so this is really exciting. The regimen that they used is actually a little bit of the kitchen sink regimen. We think that in our trial we had almost as good as without as much toxicity. Again, we think the next step in the trial is to be able to figure out how do we start to tailor giving different combinations of patients.

Different treatments and learning how they're working and testing some of the less toxic, hopefully less toxic treatments, but then to also work on trying to tailor for every patient based on their tumor subtypes or prediction of DNA repair problems or immune signaling ways that we can start to optimize combinations of therapies. That's what's next. So trying to optimize treatment based on your tumor biology and then if you get to a complete response by measuring as you go, you can stop and not give more than you need. That's the next phase of I-SPY that we're moving into. I think that there are the kinds of things that are happening is that there are ways to enhance immune signaling. I think those combinations look very promising. There are also ways to enhance DNA where when, if there's already a defect in the way you repair errors in how the cells turn copies of themselves. That's DNA repair deficiency or something like that.

If you if you have that kind of tumor, there may be ways in which you can kind of hype that up really, cut off the blood supply, make that worse, and then you can come in with one of these more targeted agents. So I think there's really exciting things and then we know that there still are some tumors that just don't respond to any of that at all. And what's going to be the rescue for that? How do we learn to target patients who have leftover tumor? And one of the things we can do with that is then maybe that's where some of this stem cell, I think that's where all the science and biology of the last 20 years is going to help us really start targeting drugs to specific cancer. So we can get not too much, not too little but just right. So the idea, if you have more risk and less response, you get more therapy. But if you have either less risk or you have a great response to therapy, you can do less. So that's the essence of personalizing medicine.

Priya: Thank you Dr Esserman. Actually we have quite a few more, but no time. I guess. I just have one more question before we wrap up today's show. And this is like I don't know how many folks who are listening know that Dr Esserman loves to sing and things to all her patients before surgery, sometimes the song of their request, Dr Esserman, I think that this is amazing. When did you start doing this?

Dr Laura J. Esserman: I actually started doing that almost 23 years ago when I was actually in a situation where everyone was really stressed in the OR including me and I just couldn't think of anything else to do. And I had just seen the Phantom of the Opera the night before and I asked my patient if she liked music, suddenly I started to sing to her, her favorite song from the show and her, she was on the blood pressure monitor and her systolic blood pressure dropped 40 points. I think mine probably did too. Anyway, I thought and so then I started singing a few songs and then I realized, you know what, I could do is I love to sing and I've been a musician all my life, my hobbies. That was really best to have someone pick a song and it's really meaningful to them and learn that song for them. And that's so comforting and it's just such a lovely, it's a very lovely moment that you can have and you take people away from the fear of being in an operating room or in a difficult situation and feel comforted. That's the art of medicine. It's one of the things that I love to do.

Priya: That's a beautiful gesture Dr Esserman. Thank you so very much. And we've learned audience that the screening is looking for signs of disease before a person has symptoms, sometimes a screening test finds cancer that is very small or very slow growing. These cancers are unlikely to cause death or illness during the person's lifetime. The goal of screening test is to find cancer at an early stage that can be treated and maybe cured. Thank you very much. Once again, Dr Esserman for your time and for all the information shared. I think this one hour just flew by and we still have questions left. We welcome you again. It was a great hour. I think we still need more. We take you up on that one.

Dr Laura J. Esserman: Thanks so much for your question. Great to be on with you too. Thank you Priya.

Priya: Thank you. Thank you for your participation and April in Kelsey, you brought in the patient perspective onto the table and to the discussion. Thanks a lot for that. We also like to thank UCSF Helen Diller Family Comprehensive Cancer Center and the audience. This talk will be available on curetalks.com so please visit our website for details on upcoming talks. Thank you everyone and have a great day.

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