Transcript

Kendal Williams, MD (Host): Welcome, everyone, to the Penn Primary Care Podcast. I'm your host, Dr. Kendal Williams.

As you know, we did prostate cancer last time, and we're starting this series focused on cancer prevention and primary care. Today, we are going to discuss breast cancer. So breast cancer is obviously very common. It's something we deal with quite a bit in primary care.

And I have the pleasure of introducing two absolute experts in prevention and management of breast cancer. Dr. Christine Edmonds is an Assistant Professor of Radiology at Penn in the Department of Radiology with a focus on breast cancer imaging and diagnostic radiology. She did her medical school and residency at Penn and a fellowship at Memorial Sloan Kettering.

Christine, thanks for coming.

Christine Edmonds, MD (Guest): Thank you so much for having me. I'm really excited for the opportunity to do this.

Kendal Williams, MD (Host): Dr. Lola Fayanju is the Helen O. Dickens Presidential Associate Professor of Surgery at Penn. She is the Chief of Breast Cancer Surgery at Penn Medicine. She also directs the Rena Rowan Breast Cancer Center at Penn. She maintains an active research program in breast cancer, focused on disparities and aggressive breast cancer variants.

Her undergraduate degree was at Harvard and medical school and residency at WashU in St. Louis. She did her fellowship at MD Anderson in Texas before coming to Penn.

Lola, thank you for coming.

Lola Fayanju, MD (Guest): Really happy to be here. Thanks for having me.

Kendal Williams, MD (Host): And finally, I want to welcome back to the program my cohost and the occasional host of Penn Primary Care Podcast, Dr. Amber Bird.

Amber is an Assistant Professor of Medicine at Penn and the Associate Program Director in the Penn Residency Program in Internal Medicine. Hi, Amber.

Amber-Nicole Bird, MD (Guest): Thanks for having me back, Kendal.

Kendal Williams, MD (Host): We're going to focus in today's discussion on the prevention and early management of breast cancer, focused on screening primarily, especially mammograms and other imaging. But I'm going to do a brief overview of breast cancer and then I also want to pull in particularly our experts and guests on the epidemiology of breast cancer.

So from a high level, we know that breast cancer is very common. One in eight women will experience it in their lifetime. That's a 12 plus percent lifetime risk. There are 250,000 plus cases per year, translating at least in 2020 to

about 41,000 deaths. So if you remember prostate cancer is about 34,000 deaths in men. And so this is more than that and affects women primarily. Seventy-five percent of breast cancers occur in women over 50 years old, but can occur in the 30s and, very rarely, even earlier.

We know the basic epidemiological risk factors for breast cancer. We know it's higher in women with early menses and late pregnancy, particularly over 35.

It appears that stimulation of the breast with estrogen and progesterone without actual pregnancy and lactation is a risk factor. And we know that prolonged lactation reduces the risk of breast cancer. Hormone replacement therapy, which was popular a decade or so ago, we now know markedly increases the risk of breast cancer. There's also something about our Western culture that increases risk of breast cancer, because folks that come from other cultures where breast cancer is less common, quickly within a generation are experiencing breast cancer rates that are similar to the Western world.

We know that obesity, metabolic syndrome, diabetes increase the risk as does moderate alcohol use. We've defined some of the risk factors, genetically, particularly when it comes to the BRCA 1 and 2. But only 10% of breast cancer actually are in patients who have a family history. So it's still very common for people to present with no family history.

So with that, let me just stop and get sort of a high level overview of breast cancer from Christine and Lola: What are some of the elements of breast cancer that you think are important in thinking about breast cancer on a population level?

Lola Fayanju, MD (Guest): I'm happy to start. This is Lola. The good news about breast cancer is that the vast majority of women who are diagnosed with breast cancer will do very well. And it represents one of the real success stories in oncology.

Within breast cancer, we have a range from stage 0 to stage IV, stage 0 being non-invasive breast cancer, also known as DCIS. That by definition is confined to the ducts of the breast and therefore can not metastasize anywhere outside of the breast. It does not need chemotherapy. It may need radiation if a woman has lumpectomy and a person may benefit from endocrine therapy again if she has a lumpectomy.

And then stage IV disease at the other end of the spectrum is metastatic disease. That is breast cancer that has spread outside of the breast and regional lymph nodes. And the good news again is that very few people are diagnosed with stage IV disease at presentation, that is less than about 5% or 10%.

Unfortunately, we do know that there are significant disparities with regards to who is diagnosed with late stage disease versus early stage disease. And we know that Black women as well as Latinas are more likely to be diagnosed with higher stage disease.

We also know that Black women are more likely to die from breast cancer at every age and every stage of diagnosis. Interestingly, Latina women are more likely to be diagnosed with late stage disease, but actually have a relative survival benefit as compared to white women. And with regards to Asian women, we also see a survival benefit relative to white women, but there is an increased frequency of some types of more aggressive breast cancer, including HER2-positive breast cancer.

So that is to say the picture of how breast cancer works in different racial, ethnic groups is complex. There's an

opportunity for improvement in all groups. That opportunity often begins with screening, that is having women get screened for breast cancer so that they can be diagnosed if they're diagnosed at an early stage.

And one of the challenges with breast cancer is that knowing when someone should start screening can be very confusing to patients because the guidelines feel like they're always changing and they differ slightly between different groups, such as the American Cancer Society, American Society of Breast Surgeons, USPSTF. So I understand why it can be confusing for both physicians and patients.

Really what matters is that women get a risk assessment, that is an assessment as to whether they are average risk and therefore should start getting mammograms at 40 or if they need to start earlier. And if earlier, whether that risk assessment and screening should include an MRI. But I will defer to my colleague, Dr. Edmonds, talking more about risk assessment and screening, but that's a bit of an overview on kind of breast cancer and how we see it in different populations.

Kendal Williams, MD (Host): That's very helpful. Christine, do you have anything to add?

Christine Edmonds, MD (Guest): Sure. That's a great overview by Lola. As far as what she said about disparities, both in terms of diagnosis and then mortality among different races and ethnicities, one recent development there that is critical for all of us to understand both in radiology in breast cancer treatment, but also in primary care particularly, we've always had data from the American Cancer Society saying that breast cancer is the number two cause of cancer mortality among women and among US women.

And just in the last two weeks, we have brand new data from the American Cancer Society showing that breast cancer is now the number one cause of cancer mortality for Black women, still number two across all women, but that's a critical difference and that says a lot about how we are screening or perhaps not screening or not adequately treating that population.

The other two things I will add to what Lola said are what I like to remind our patients and our ordering docs to correct a couple of very common misconceptions about breast cancer and breast cancer screening.

One is that we continue to see a lot of patients come into our clinic for screening or diagnostic imaging who have the misconception that breast cancer really is a disease of patients with a family history, and largely it is not. As you pointed out in your introduction, there are 10% to 15% with either strong family histories or genetic basis, but the large majority of patients we diagnose have either absolutely no family history or perhaps one distant relative. So we want patients to be aware of that, so that they don't skip screening on that premise.

And the other thing is, I know we will talk about all of nuances of the breast cancer screening guidelines as far as from one organization to the next, but it is important to remember that breast cancer rates increase very sharply right around age 40. That is part of the premise for beginning screening at 40. And then if you look at life years lost, that's impressive because 30% of life years is lost to breast cancer in the United States is from women who are diagnosed in their 40s.

But we still continue to see, in our practice, a lot of women deferring screening until age 50 or even beyond. And so we do like remind our patients and our providers of those facts, those statistics.

Kendal Williams, MD (Host): Amber, do you have anything you'd like to jump in with?

Amber-Nicole Bird, MD (Guest): So I would just say I think that both Lola's and Christine's points are illuminating to me, because I think one of the biggest challenges that we have in primary care is trying to have this nuanced discussion of risk. And I think we'll probably get into more of this when we start to talk about screening and how to screen and who to screen when.

But so often my conversation about when should we start screening brings in a lot of nuances about family history and patient preference. And I think I struggle a lot with bringing in disparities and thinking about how do I have a conversation that focuses on disparities and screens accurately in different patient populations. I'm glad we are kind of focusing on disparities and I hope as we talk to screening, we can hear a little bit more about how you think about this and how you counsel patients on when to start and what their risk is, understanding that some of the tools that we have to assess risk really might not accurately predict it in all of our patient populations.

Kendal Williams, MD (Host): So let's just jump right into screening, because that's obviously the topic we all want to talk about.

Most guidelines, including the USPSTF, will agree that women between the ages of 50 and 70 should be screened. It's I think fairly well known the USPSTF is conservative in their screening guidelines requiring a very high level of evidence before recommending anything. But it's the group in the 40 to 50 range I think that is the most controversial and worthy of discussion. I also want to raise the question and, Lola, you had alluded to this, breast cancer's shifting, right?

We're seeing some of the women who are presenting in their 30s. And what do we do in those situations? Should we be even thinking earlier than 40? So let's talk about the 40 to 50 range.

Lola, maybe I'll start with you. What do you think about that age group?

Lola Fayanju, MD (Guest): So that's an age group where the ramifications of a breast cancer diagnosis are very profound because these are women who are often in the middle of careers, so not retired. They're often in that kind of sandwich generation where they both have children they might be caring for as well as older parents who they're starting to care for. And so it's a situation where these are women who often cancer blindsides them, because they may have just begun screening and really thought they were checking a box and not really changing their life.

So it's a group where we really need to have a lot of attention paid to not only the cancer diagnosis, but everything around it, how it affects their finances, how it affects their insurance if they're the policy holder, their ability to attend appointments, their ability to limit themselves in activities as required by some treatments they might receive, and what the sequalae of those treatments are and how much they can impact again their lives and their ability to comply and adhere to treatment.

In terms of diagnosing these women, it feels like they're being diagnosed early and earlier. I would say the good news is I feel like there's a much more public attention and awareness regarding breast cancer, such that women are aware of their family histories increasingly. And so they do start getting mammograms a little earlier. They do start self breast exams a little early. They do talk about their breast findings with their OB-GYNs and with their primary care providers. And they're more aware therefore of changes in their breasts, which is all a wonderful thing.

So that's us to say that I'm a very firm believer in that breast cancer screening should begin for an average risk woman at 40 and, again, for high-risk women may need to begin earlier. Again, not only because we want to catch cancer when it's early and curable, but because of just the huge ramifications for delay and how much more difficult

it is to treat late stage disease in people whose lives are at a very complex moment over the course of their lifetime.

Kendal Williams, MD (Host): So Christine, you see both the bad and the good with screening, picking up early cancers. But you also see a lot of the downstream testing and that's often what we hear is the downside of screening too aggressively. These don't have perfect specificity and so you have false positives and so forth. But it sounded from your comments earlier that you're very comfortable with the 40 to 50 range being screened aggressively.

Christine Edmonds, MD (Guest): Yes. I agree with Lola. I feel that it's very important to begin screening at age 40. That's what's recommended by the American College of Radiology, Society of Breast Imaging, American Society of Breast Surgeons and ACOG. They are for the most part in agreement about that. And I won't get into the weeds on data, but there is data behind that.

Obviously, randomized controlled trials are the gold standard for establishing that. That's tricky for something like breast cancer screening. Especially at this point, we can't really open new trials like that to really define what age it should begin, does this vary by race, et cetera, what should be the frequency? They require many years to obtain the data. They're are incredibly expensive. And we already have evidence that screening works. So ethically, they are challenging at this point, too.

But if you look back, we have some decent randomized controlled trials, sort of 11 major ones, over the course of medical history. And if you combine all of them, they show together a big reduction in breast cancer mortality on the order of 20 some percent and actually that's really just testing the invitation to screen.

If you look beyond that, that would actually translate to upper 30s or even 40% reduction for women who actually undergo the screening. Unfortunately, a lot of the data that shows specifically at what age you should begin screening is not from randomized control trials. It's from models, the Cancer Intervention Surveillance Modeling that the USPSTF uses. But consistently, we see that the greatest lives saved, greatest mortality reduction is from beginning at 40.

You mentioned overscreening and, yes, we hear a lot about that both in medical literature and also in mainstream media. That's a tricky one for those of us in breast imaging and particularly those of us looking at the science of screening.

Often, what you hear about as overdiagnosis is DCIS or ductal carcinoma in situ, so that's technically stage 0 breast cancer when the cancer cells are confined to the ducts, they haven't broken through the duct walls.

That's a pet peeve for some of us who look at the science of screening, because we don't know still what counts as overdiagnosed DCIS, meaning some DCIS has a fairly benign or slow course to it. Some, while it is stage 0, is a completely different actor.

And for example, if you just had a small focus on a screening mammogram one year, perhaps one year later, it has already spread to the point that there is microinvasion and it's even in nodes. We cannot differentiate that based on imaging at this point. And even on laboratory science, we're not good at it yet.

We know that there's a tremendous biological diversity among ductal carcinoma in situ. So we can sit here and say we're overdiagnosing some. Yes, we know we are. But I think until we can tell which ones are the ones we are overdiagnosing, that isn't a great argument against screening.

That being said, I do still recognize that there is some overscreening going on, maybe we will touch on this further later. But in brief, ultrasound has been used at a lot of centers around the country, growing over the last decade or so to screen women who have dense breasts.

So women with heterogeneously dense or extremely dense breasts have mildly elevated lifetime risk of breast cancer and there's a question of do they warrant supplemental screening. Ultrasound has been raised as a possible modality to do that. It's fairly cheap. There's no radiation, et cetera. Many of us, myself included, believe that that does fall into overscreening. It does not detect many additional cancers, and it has very high false positive rates. It leads to a lot of unnecessary biopsies, et cetera.

While I do think it's important to screen beginning at age 40, I also understand overscreening and what we need to look out for in that regard, too.

Kendal Williams, MD (Host): So let's talk about the imaging that you do suggest. So traditional mammograms is film mammography, right? That's not done anymore very often. Correct?

Christine Edmonds, MD (Guest): That's correct. Screen film or film screen mammography, the ones that you think about where radiologists were hanging up those films to a light, that is not done at all in the United States or at least it really shouldn't be anymore. And it has been replaced by digital mammography.

Kendal Williams, MD (Host): Right. Similar to chest x-rays have been replaced. But is digital mammography different than just-- we used to look at a chest x-ray in the film room, in a light box, and now we look at them on the computer, but digital mammography has more to it than just that, right? That transition.

Christine Edmonds, MD (Guest): That's exactly right. So digital mammography was developed to overcome a few limitations in particular with film mammography.

So primary benefit of digital mammography, other than the fact that it allows better storage of imaging data, which is of course critical, but it allows for the separation of the image acquisition and the image display. So anytime you separate those two processes in radiology, you can allow basically for optimization of both of those.

And so it allows for image processing of that digital data so that you can basically manipulate the contrast, basically how bright or how dark something is, and that is extra important for reading a mammogram in a woman with dense tissue where you're going to have limited contrast.

So the benefits of digital mammography compared to film are it primarily outperforms film in those who are younger, women who are younger, so under age 50, and those who have denser breast tissue. It has much better contrast resolution overall.

Kendal Williams, MD (Host): I saw sensitivities for mammography ranging from 60% to 90%. That's a pretty broad range for a well-known tool. What are we accomplishing now with digital mammography?

Christine Edmonds, MD (Guest): That range still persists. And digital mammography now includes tomosynthesis. So tomosynthesis affects that range. You have such a large range because there are many other factors that go into that besides tomosynthesis. So the sensitivity of mammography is notably increased by the

density of the breast. That's one of the arguments for why women with dense breasts may need some sort of supplemental screening.

And then there's a lot of reader performance variability, so how specialized the radiologist is, the volume that they read, that type of variability.

Amber-Nicole Bird, MD (Guest): I have a followup question about different screening modalities. This is both to Christine and Lola. There's different ways you think about this. I think mammography is our go-to. At Penn, we have access to tomosynthesis and I think that we feel pretty comfortable ordering that for patients once we've decided that screening is appropriate.

I think the question I have is, when we're thinking about risk, obviously there are patients who see us who are above average risk, either based on prior breast biopsies, family history, any number of things.

And certainly, a question that comes across our inbox frequently, and I will say even twice in my inbox this week, is should I be screening with something like a rapid MRI or should I be adding ultrasound to my mammography screening? And I'm just curious how you think about those additional screening modalities and should we be using a standardized risk assessment tool for that? Or is it based on breast density? Just any insight you might have for us on that.

Christine Edmonds, MD (Guest): So as far as basic screening now at Penn, and really the standard of care around the country now, is to screen everyone with tomosynthesis. So that has become the standard of care. It was approved in 2011 and, over the last decade, it has really replaced 2D cancer screening and that's for a couple of reasons. It cuts the recall rates and we also detect more breast cancer, including invasive breast cancer, particularly in women with dense breasts. So mammography is performed with tomosynthesis now.

Kendal Williams, MD (Host): Christine, may I just jump in with a question. Tomosynthesis is where you're cutting the breast IN multiple slices, right? Like a CAT scan. Am I thinking about that correctly?

Christine Edmonds, MD (Guest): You are thinking about that correctly. The technology is actually different than a CT scan. But similar to a CT scan, the reconstructed data presents a 3D image of the breast. And so it is obtained over an arc. It's step-wise, quick shots of the breast over a 15 or so degree arc, depending on the specific technology. And then, that raw data is reconstructed into a 3D image of the breast.

Kendal Williams, MD (Host): And we don't have to order tomosynthesis. It's just dependent on the screening center to which they go and whether, like Penn, they do tomosynthesis, right?

Christine Edmonds, MD (Guest): That is correct. You do not need to order it. And actually the large majority of screening centers in the US are using tomosynthesis for both screening and diagnostic breast imaging. And those that are not will hopefully be moving in that direction soon.

Lola Fayanju, MD (Guest): I just wanted to say quickly before we move on that anyone who sees a patient who has not had a tomosynthesis study, that is a red flag that wherever they may have received their screening is not providing centers of care. And one of the things we believe may be a contributor to disparities in diagnosis and stage of diagnosis is that we know that there is often inadequacy of mammography equipment as well as mammography interpretation, that is the presence of people like Christine, who can interpret tomosynthesis and the regular availability of tomosynthesis in a lot of medically underserved communities, which tend to be communities of color often with rural communities.

So even though we should not be really seeing any 2D mammogram, they still do sometimes come across our path and no doubt they will come across the path of many of the primary care and OB-GYN providers in the Penn system. So again, just be attuned to the fact that quality of mammography is actually really important and we think may be a contributor to disparities that we see in diagnosis.

Amber-Nicole Bird, MD (Guest): I agree. I think that's really helpful. And I think about the times where we're getting a scanned report and we're trying to decide if somebody has had adequate screening. It's helpful to just make a mental note for ourselves that we really should be ensuring that they got the kind of appropriate standard of care screening, which is 3D imaging, so that's helpful.

Kendal Williams, MD (Host): So let's deal with the issue of MRI. And then I want to go back to Christine and just what constitutes an abnormal mammogram. But let's first address MRI. So let me just say this, women with dense breast are the concern, right? Younger women tend to have denser breast, right? So in the 40 to 50 age group, that's where you're going to have the issue. Am I right about that?

Christine Edmonds, MD (Guest): You are correct. I will say that what is clear is that based on guidelines and what we see in clinic, the women that need MRI and more groups agree on this, are those who are considered at high lifetime risk of breast cancer. So those are women with genetic mutations, very strong family histories. And high lifetime risk is considered 20% and above. So those women qualify, meaning insurance typically covers screening MRI for those women.

Kendal Williams, MD (Host): So Lola, are there scoring systems that can help us determine who are in those highest risk categories, other than simply a family history?

Lola Fayanju, MD (Guest): There are a number of statistical models as Christina alluded to that allow us to assess whether or not someone is at increased risk for breast cancer. One of them is the Gail model. That's something that's limited to women who are age 35 or older, so it's not really applicable in younger women. There's a Tyrer-Cuzick model, which has also been adopted and sometimes referred to, I believe, as the breast cancer surveillance consortium model, and that incorporates family history as well as other factors, including exposure to estrogen, menarche, menopause, that kind of thing.

And so there are opportunities to use these types of models as Christine mentioned to assess whether or not someone's at risk or elevated risk for breast cancer. One of the challenges, a lot of these models were not built with a high proportion of Black patients amongst the subjects upon which the modeling was based. And so that is why there are sometimes skepticism as to whether or not people can frankly trust the outputs that are placed.

And there is some evidence that some of these models actually underestimate the risk of breast cancer in Black and Latino women as well as Asian women, again, due to the under-representation of individuals in the initial modeling cohort.

Amber-Nicole Bird, MD (Guest): It sounds like none of these risk assessment tools can perfectly estimate risk across Latina and Black populations. And so is there any way that you conceptually think about having that risk discussion or, and maybe this gets to Christine's comments that are to come on that like intermediate risk of 15% to 20%, like should we be considering a more aggressive screening strategy in Black and Latino women who fall into that kind of intermediate near high risk understanding that maybe the calculators aren't perfect?

Lola Fayanju, MD (Guest):): Yeah. I think that that's a reasonable conversation to have. I mean, this is exactly the

space in which shared decision-making is so important and where we need to encourage our patients to also go back and learn their family history, if there's any opacity to it, in order to make sure that we are providing as accurate a risk assessment as we can.

In some communities, there's a lot of reticence about describing or knowing the types of cancers people have had. People don't make the distinction between different types of "female cancers" that is uterine versus cervical versus ovarian, all of which have very different origins and genetic associations or none.

I think it's something we need to just talk about patients with, letting them know, yes, that there are certain groups that have higher rates of early as in premenopausal diagnosis, often late stage, not infrequently triple negative, which is an aggressive variant, but that obviously engaging in high-risk screening with MRI, for example, also may lead to more biopsies, more procedures, more uncertainty associated with those procedures and possible false positive.

Again, just having a conversation with patients, knowing, "Look, we have your back. We want you to have as good and healthy a breast history as you can. And that involves, if you have a breast cancer in your lifetime, catching it at an early curable stage and, yes, that might involve some additional biopsies, but really the priority is to keep you alive and whatever breast cancer you develop to be just a blip in your otherwise long life."

Kendal Williams, MD (Host): MRIs do have an out-of-pocket cost universally, right? Is that for all insurances?

Christine Edmonds, MD (Guest): That's not quite right. So screening MRI for those with a 20% or greater lifetime risk is typically covered, or at least largely covered by insurance.

The out-of-pocket cost really comes into play when you're talking about women who don't meet that 20% lifetime risk, but want supplemental screening. And that's where we get into a little bit of a gray zone as far as what are the recommendations, because those recommendations continue to evolve.

So we think about sort of two main groups of women who might need some sort of supplemental screening, and what should that be. So one group is the women with dense breasts, heterogeneously dense or extremely dense breasts. We know mammogram has poorer sensitivity in those patients. So do they want MRI for supplemental screening?

The second group is those who have above average lifetime risk, but don't meet that 20%. So those on the order of 15% to 20%. And so for those women, they may elect to get a supplemental screening MRI. And that is often, around the country and including at Penn, in the form of what we call a fast MRI or an abbreviated MRI. So that's the protocol is much shorter than the standard full MRI. It takes about 10 minutes.

But there is typically at most places, including at Penn, an out-of-pocket cost for that. So of course, as soon as you introduce something like that, again, we are really increasing disparities as far as what populations can get what screening. So that's another down side of that.

Kendal Williams, MD (Host): Amber, did you want to follow up on MRI before I move on?

Amber-Nicole Bird, MD (Guest): That was really helpful. And I think using that kind of 20% cutoff is a good reminder for all of us. And I think using some objective calculator obviously can be helpful, but understanding the limitations of that calculator is really important. And I don't know about you, Kendal, but as I listen to both Lola and Christine talk, I think about how this needs to be an entire primary care visit just for the discussion of when to start

screening and how to screen, to really allow for good shared decision-making.

Christine Edmonds, MD (Guest): I think it really does. It's a big subject. And I think one of the things that frustrates Lola and me is that the USPSTF's guidelines are not really doing a good job of appropriately guiding the ordering physicians, the primary care physicians in this area. So it is really placing the burden in the lap of the primary care doctors to figure out how to appropriately screen their patients.

And even the USPSTF took it so far as to, a year or two ago, say that they were really going to make efforts, for example, to create guidelines and measures that counter the systemic racism that affects cancer screening and cancer diagnosis. And yet the USPSTF guidelines that are there for breast cancer, some of the newer ones that have come out for colon cancer, et cetera, really don't get us there.

And if we look at all races of women, perhaps some patients and providers think there's some flexibility about when to start screening, and maybe that is correct among some populations 40 versus 45. But when we look at the fact that Black women have 40% higher breast cancer mortality, and when we understand that they have notably higher rates of diagnosis under 45, and that they are diagnosed on average four years earlier than white women, the fact that the USPSTF either doesn't make screening a blanket statement beginning at age 40 for everyone or, at a minimum, create some race or race/ethnicity-based guidelines is really putting a lot of burden on the primary doctors to figure out what to do.

Kendal Williams, MD (Host): So the fact that African-American women are diagnosed four years earlier, that's not a result of overscreening, right? That's a result of the biology, correct?

Christine Edmonds, MD (Guest): It is definitely not a result of overscreening, because we know they are presenting at more advanced stages. Black women are presenting at more advanced stages and carrying worst prognoses, including worse mortality. So therefore, that means that is not a problem with overdiagnosis or overscreening.

It is part genetics. We know Black women are predisposed to get triple-negative breast cancer, which is an aggressive form of breast cancer and it also lacks some of the targeted drug therapies that have been developed for other types of breast cancer. However, we're learning more and more recently that most of the differences in terms of breast cancer mortality are not due to genetics. And I'm sure Lola can add to that.

Lola Fayanju, MD (Guest): Yes. People often try to ascribe differences in mortality between Black and white women to higher rates of triple-negative breast cancer in Black women, which is true. There is more triple-negative breast cancer in Black women. And there are some alleles in the genetic makeup of breast cancer that are commonly found among Black women. One of them is the Raf allele that we believe may contribute to increased likelihood of triple-negative breast cancer, which is a very common variant in Sub-Saharan Africa, where 40% or 50% of breast cancer is actually believed to be triple-negatives.

But it's very important, one, to realize that race is a social and not a biological construct. And that frankly, what it means to be African-American is much more than the genes and much more than your ancestry in terms of where your grandparents and other ancestors came from. And so that's important to realize.

The second thing I will say is that some studies have shown that while there are higher rates of triple-negative breast cancer and it's a more aggressive cancer in Black women, the actual disparity in mortality is most pronounced hormone receptor-positive breast cancer. That is the breast cancer that patients are technically supposed to do the best with, that is where we are seeing the greatest disparity. And that was seen in a paper published by Erica Warner,

who is an epidemiologist at Harvard. I believe it was published back in 2015 or 2016.

Notably, when there are disparities for triple negative breast cancer, much of that is explained by differential receipt of chemotherapy, in part believed because there may be less well tolerated side effects amongst Black women, in part because there may be concerns about dosing relative to whether we're basing on body surface area and higher rates of obesity among Black women.

And also that we know that there is often disparity and bias related to how chemotherapy is administered to people who are either overweight and/or people of color. So there are a lot of things going on here and I'm always very keen to point out that biology is a very small part of the larger picture, that much of what we're seeing and what's driving disparity are things that we can actually do something about.

Amber-Nicole Bird, MD (Guest): Thanks, Lola. That was really, really insightful. I guess the other thing I will say is like hearing that and hearing about all of the downstream things that can happen that can worsen disparities, I think makes the onus on primary care even stronger to really think about how we can catch things early enough to intervene in a way where hopefully we're not getting to the point where we have to look at treatment-based disparities.

And I know that's a big ask, but I think it just, again, reemphasizes, to me at least, in our primary care-based discussions, the importance of really thinking about the appropriate timing of screening and how we're screening and assessing risk in a realistic way for our patients, because if we can catch things early, then hopefully we can prevent some of those downstream disparities.

Kendal Williams, MD (Host): So there's one thing I don't want to finish without discussing, and that is what happens when a patient is sent to you, Christine, and has a mammogram that needs follow up, that needs a biopsy and so forth?

We all get those reports back to us that a patient is being called back for additional imaging or even a biopsy. Is that loop always closed? I always have a little bit of nervousness that it's closed and I send a note to my patients saying, "You are going back, right?"

But can you kind of take us through that process a little bit and let us know if that loop is being closed all the time.

Christine Edmonds, MD (Guest): Sure. That's a really important question. Fortunately, our practice, as do most practices, have some sort of data manager that is part of the practice that is working hard to close that loop. And in the vast majority of cases, the loop is closed. In a very small proportion, unfortunately, it is not.

So what happens when we recall the patient, the patient is notified via a letter. A lot of them also, of course, are getting their results via myPennMedicine, et cetera. There are many attempts made to reach both the patient and the ordering provider, if they do not call back within a timely manner, 30 days, to schedule their follow up diagnostic breast imaging. So two letters are sent. Letter is mailed to the provider. Voicemails are left with the patient requesting callbacks. And so that is tracked in our system and that's part of the beauty of our reporting system.

So we actually enter electronic what we call a BI-RADS 0, meaning the screening is incomplete. We need more information from a diagnostic imaging assessment. And that zero gets tracked through our tracking system and our data manager is keeping track of that, so we are aware when that patient has not returned. And many attempts are

made both to reach the provider and the patient to get them back, and that is usually successful with some rare exceptions.

Kendal Williams, MD (Host): So readings are not done at the majority of centers at the time the patient is-- there's not a radiologist reading these at the time. They're reading them later, and then patients are called back, right?

Christine Edmonds, MD (Guest): That is variable around the country. And there are advantages and disadvantages to doing it both ways. We do a portion of our screening as what we call same-day screeners, so the patients wait for their reads. We often, assuming we can accommodate it, give patients that option, to wait for their results. And so it's really variable from one place to the next.

Kendal Williams, MD (Host): And finally, can you give us some guidance as to when just a screening mammogram should be ordered versus when a diagnostic mammogram is more appropriate?

Christine Edmonds, MD (Guest): Sure. So screening mammograms should be for asymptomatic women who are age 40 or above, and we recommend that they undergo them annually. Diagnostic mammograms should be ordered. What we prefer is that it is ordered along with an ultrasound and then the radiologists can use their judgment to either do one or both, but diagnostic mammogram and ultrasound should be ordered when the patient has a sign or symptom.

So if the patient or the provider feels a lump; if the patient has nipple discharge, particularly unilateral; if there is focal breast pain. Diffuse breast pain or non-focal breast pain is rarely attributed to breast cancer, so we don't really recommend diagnostic imaging for that. So if there's any sort of sign or symptom like that, then it should be a diagnostic imaging study.

Kendal Williams, MD (Host): Occasionally, a patient will come back to me and say, "I need diagnostic mammograms ordered when you order my mammogram." And those are patients with a history of breast cancer or history of lesions that need to be followed up on and so forth, right?

Christine Edmonds, MD (Guest): That's right. So if a patient has a lesion that needs follow up, that is typically lesions that we consider to have less than 2% chance of malignancy. And we actually have great mammographic data to tell us which specific lesions do in fact have less than 2% chance of malignancy. Those fall into what we call a BI-RADS 3 category or probably benign and we follow those at six-month intervals for a period of time.

And, yes, so anyone who is having a lesion followed up, those get diagnostic rather than screening imaging. And as far as patients who have a prior history of breast cancer, that's a little bit more of a gray zone, because there isn't good data to guide whether those patients need screening versus diagnostic and, if they are getting diagnostic after say breast cancer treatment, when they should be returned to screening.

So that is a combination of patient and clinician preference and also what the patient's individual insurance will cover. Many insurances will cover them to be in the diagnostic imaging pool for at least a few years after breast cancer treatment, although there isn't much data to suggest that diagnostic imaging is needed over screening.

Kendal Williams, MD (Host): Well, we always finish our podcasts by giving our guests an opportunity to say one last point to the Penn Primary Care community. I'll just go around. Amber, maybe I'll start with you in terms of things that you have gotten out of this discussion you think should be highlighted.

Amber-Nicole Bird, MD (Guest): I think just being more thoughtful about how I set aside time to have a

discussion about initiation of breast cancer screening, particularly in younger women and particularly when I'm counseling women who are Latina or Black and thinking about how we use those risks calculators. I'll be honest, those conversations are often really fast.

And so this is a good reminder to slow down and to make sure it's an intentional part of the agenda and that it really involves some careful shared decision-making, particularly for younger women.

Kendal Williams, MD (Host): How about you, Christine and Lola?

Lola Fayanju, MD (Guest): I think one of the most important things to realize is that risk assessment can and should be iterative as well. The extent to which a woman is able to engage with that process of risk assessment when she's 25 versus when she's 35 versus when she's 45 will vary for a lot of people, depending on what other competing concerns are in their lives.

It's important to also reassess people's family history because things can change. They may not volunteer that a sister or a cousin or their mother has been diagnosed with breast cancer, and changes the calculations slightly as well.

Not infrequently, I'll meet a patient who their sibling has been diagnosed with breast cancer and that sibling is young enough that they should have been getting genetic testing and they have not. And so, you can actually influence the trajectory of care for the loved ones of your patients that can also impact their ability to make informed decisions about risk assessment and screening.

So again, that is to encourage women to know their family histories, to not be squeamish about having candid conversations with their loved ones about both breast cancer, as well as gynecologic cancers and other cancers that may be caused by a known genetic predisposition. And to then just have an iterative relationship with them with regards to assessing the need for high risk screening and then to, of course, encourage women to get screening every year based on their risks categorization.

Kendal Williams, MD (Host): Christine?

Christine Edmonds, MD (Guest): I will agree with Lola's point that I do think reassessing family history and doing that frequently is critical. I can only imagine how challenging that is in a primary care environment when there are many aspects of the patient's medical history and health that you're addressing.

But we do see quite a lot of patients that come into our imaging clinic for screening or diagnostic imaging that we learn have something significant, a family member who is diagnosed with a genetic mutation or a very young mother or sister diagnosed with breast cancer. That really means the patient should be getting evaluated for what she needs for her now higher risk breast cancer. And that can include genetic testing, supplemental screening with MRI, or even just beginning mammography early sometimes.

And so I do think I agree with Lola. It's very key to reassess family history periodically.

The one other thing I will add, and that is because we've talked about how and when to use supplemental screening MRI, and we've also talked about the disparities, is that not just at Penn, but around the country, we know that certain patients of color, Black women in particular, don't get supplemental screening nearly as often. We found that to be true in our own patient population here at Penn. We have an abbreviated MRI with an out-of-pocket cost and that population getting that is predominantly white.

And so our Chief of Breast Imaging here at PCAM started a clinical trial that is abbreviated MRI screening specifically for Black women. And as part of that, the cost of the study is covered. So we're hoping to learn from that study, both more about the value of this screening tool in the population in Black women.

But this is also a good opportunity for Black women, if they want supplemental screening and they have dense breast tissue specifically, to get this at no charge. So this is also something that we want our ordering providers to be aware of, because it's a unique and potentially impactful study going on.

Kendal Williams, MD (Host): Well, this has been a terrific discussion. I really appreciate the three of you coming on. This obviously could go on for another podcast. We are going to do a second podcast on breast cancer, focused mostly on management and treatment and downstream treatment as well. Hopefully, we'll have you back for that.

Thank you, everyone, again for joining the Penn Primary Care Podcast. We'll see you next time.

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