

[MUSIC PLAYING]

**MELISSA**

OK. Good morning, everybody. I'm feeling bad already, because I don't have any cute mnemonics, like Tanya did.

**MCNEIL:**

But what I do want to talk to you about is a boat that we are missing-- something that I want to try to empower us, in the next 40 minutes that I have with you, to try and make a difference in your practice.

And I want to thank my colleagues, who are in the section of women's health in the division of general internal medicine, for their help. And so this is sort of an amalgamation of a number of talks that we have given. So thanks to all of these folks who are active in our women's health section.

OK. Here we go. OK. So my objectives today are to, first and foremost, help you, as a provider, begin to estimate your patients' breast cancer risk. I want you to be able to identify factors that should prompt, number one, referral to a high risk breast clinic; number two, make you think a little differently about how you screen; and number 3, I want to challenge you that perhaps initiating chemoprophylaxis to prevent breast cancer is part of what we should be doing in primary care.

We spend so much time thinking about mammograms, talking to our patients about mammograms, obsessing over new guidelines-- should we or shouldn't we, who should get it, what mammograms should we get? And I'll remind you that when we do mammograms, we're finding cancers that are already there. If I can move you to a place where you think about initiating some of these agents for our women, we will actually prevent up to 50% of cancers.

That's a whole lot more bang for the buck than we get out of mammograms. So I want you, in order to be able to do that, to understand the risks and benefits of chemo prevention and know how to counsel for the appropriate selection of the drug. So I'm going to talk about risk assessment, screening, primary prevention.

I'm going to talk about two classes of drugs-- the selective estrogen receptor modulators, which are tamoxifen and raloxifene, and then the aromatase inhibitors, which are exemestane and anastrozole. And we're going to compare and contrast them. So the obligatory epidemiology slide-- breast cancer is the most common invasive cancer among US women.

It is the second leading cause of cancer death in women, second only to lung cancer. And our efforts in primary care, as I said, focus on screening. And this is despite the fact that multiple randomized placebo controlled trials-- the best science that we can bring to the table-- have demonstrated risk reduction in chemo prevention in women who are at increased cancer risk.

So that means two things. You have to figure out who those women are, and you have to get comfortable in prescribing. The current guidelines actually recommend that we incorporate breast cancer risk assessment into routine primary care to allow for an increased focus on the prevention, not just the early diagnosis.

So when we think about breast cancer prevention, there are four strategies. This is not unlike osteoporosis, not unlike thinking about the elderly and our frail patients and how we manage them. But there's a four-pronged approach. So there's lifestyle modification, enhanced screening, chemo prevention, and surgical prevention.

I would argue that our efforts to date have really focused on enhanced screening. Sometimes, actually, on the surgical prevention, we have a number of women who get an abnormal mammogram and just want those breasts off. But in reality, there's a lot more we can do.

In terms of lifestyle, healthy weight matters, because we know that the adipose tissue you have converts androgens to estrogens. And those estrogens then prove a risk factor for breast cancer. Exercise actually reduces breast cancer risk. And in fact, limiting alcohol to less than one drink a day reduces breast cancer risk.

And I want to sort of single out the alcohol piece. One drink a day is about the same risk as being on hormone therapy for five or more years. We spend a lot of time and energy and angst about whether our women should or shouldn't have hormone therapy, whether it's safe to put them on hormone therapy, how long we can give it. We're not talking to them about their alcohol consumption. So I want to put that in context for you.

Enhanced screening. Mammograms-- when do we start, how often do we do them, do we do adjunct screening, like tumor synthesis or ultrasound or MRI? And then finally, the SERMs. And that's where I'm going to focus most of my talk.

So in order to apply chemo prevention, you have to identify the population that's at risk. There are a number of risk factors that we know that increase a patient's risk for breast cancer. So let's take a look at them.

So patient characteristics-- age is probably the primary one. We've been talking all morning about-- age is just bad. It's hard to age. Bad things happen. So age is important, race ethnicity, height and weight.

In terms of your family history-- the degree of relation, the age at diagnosis of the family member with breast cancer, and then other related cancers that kind of go together, like ovarian cancer and uterine cancer, the reproductive and/or hormonal history, age at menarche, first birth, menopause, the use of hormone therapy. And then there's your breasts. Do you have increased density?

By the way, the increased breast density that we spend a lot of time and energy and angst dealing with-- our radiology colleagues send those letters mandated by the state, saying, oh, you have dense breasts, this increases your risk, please talk to your primary provider. None of us know what to do with breast density. There's no data to support it. And that risk is the same as one drink a day.

So these are risk factors that are not terribly strong as standalone. Prior breast biopsy, benign breast disease, and then the history of chest radiation, which is a big one. So here's the slide on the magnitude of risk. These are the relative risk, greater than or equal to two times, relative risk of 1.5 to two, and a relative risk of one to 1.5.

So relative risk of two comes with a first-degree relative with breast cancer-- so family history is important-- extremely dense breasts-- not heterogeneously, but extremely dense breasts. Just less than 25% of the women that we do mammograms on. And then a biopsy finding that increases your susceptibility, which is LCIS or a biopsy with proliferative atypical hyperplasia.

These are high-risk biopsies. And these guys clearly need chemo prevention. There's not really any doubt about that. Generally, they're managed by the high risk breast folks.

So relative risk 1.5 to two-- a second-degree relative with breast cancer. So first-degree-- your mom, sister, daughter. Second degree is your aunt or your cousin. So you got to go to that level when you take the history. And actually, just a prior breast biopsy, even if it was benign.

And then we have the sort of lower level risks-- the null parity, the age greater than 30 at first live birth, or heterogeneously dense breasts. So again, each of these, as standalone risk factors, is not terribly scary. But as I'm going to talk about, there are ways to put them together to give you a cumulative risk.

So what are my goals for breast cancer assessment? The first and foremost is, I want you to identify women who would benefit from referral to a high risk breast clinic or genetic counselor. This is probably the most important thing you can do, because these women clearly benefit from chemoprophylaxis or even surgical treatment-- primary surgical mastectomy.

Now, let's start with our first case. We have Colleen. She's 69-- she's 60. She's getting younger all the time. She's 60.

And she's presenting for her annual visit. And she's worried about breast cancer. She has a paternal aunt and a paternal uncle diagnosed with breast cancer at age 53 and 67, respectively.

She has a mother and three sisters. They're all without breast cancer. Her mammograms have been normal.

On the surface of it, this doesn't feel that scary, right? It's nothing in her immediate family history. These are all second-degree relatives.

So what should you tell her? A, because her first-degree relatives have not been altered, she's not at increased risk; B, her family history suggests she may be an increased risk, and this risk can be estimated by using the Gail model; or C, her family history alone is enough to say she's at increased risk, and she should be sent to a high risk breast or genetic counselor? And the answer here is C.

And here's why. First thing to appreciate is that less than 5% of all breast cancers are hereditary. The high risk mutations-- the BRCA1 and 2-- have enormous lifetime risks of breast cancer. Li-Fraumani syndrome-- 50% by age 60. There are other tumor syndromes that, in fact, are rare but carry the increased risk.

The identification of these syndromes is huge for women, because, first, they all have a lifetime incidence greater than 20%, which is the indication to start yearly MRIs and aggressive prevention strategies, like mastectomies. Most providers would offer women in any of these categories, mastectomy.

So a woman with a family history suggestive of hereditary breast cancer-- and I'll talk about those guidelines next-- you're done. That's all you have to do. You take the family history. If the family history flags scary, you send to high risk breast.

So what I'm going to say-- I'm going to challenge you at the end to make one change in your practice. And if you just make this change, you will have made a difference in the lives of your patients. The risk factors for hereditary syndromes warrant immediate referral.

And these are risk cancer-- breast cancer assessment tools don't work in this population-- so family histories alone. So what are the indications? Somebody in the family is known to have a high risk genetic pedigree, greater than two breast cancer primaries in a single individual. So mom had two breast cancers.

And here's the one I think we miss, because we don't take first, second, and third degree histories-- greater than or equal to two breast cancers among first, second, and third-degree relatives on the same side of the family. So it doesn't count if mom's sister had one and dad's sister had one. It's got to be the same side of the family.

Greater than or equal to one ovarian cancer primary puts folks at high risk. First or second-degree relative with an early diagnosis-- less than 45-- and anybody in the family with male breast cancer. So if we think about Colleen, she has two relatives on the same side. And one was a male breast cancer.

So she's got a high risk family history. And she goes straight to a high risk breast cancer referral. So again, if you do nothing else for me, learn these criteria, and take a history, and refer one appropriately.

OK. Case 2-- Charlotte. Charlotte is a 63-year-old postmenopausal woman who presents to established care. Her mother was diagnosed with breast cancer around her age. She has no personal history of breast problems.

And there are no other relatives with breast cancer. Menarche was at age 12. And her first baby was at age 32.

On mammogram, she has a BI-RADS 2, which is benign, and she has heterogeneously dense breasts. So she got the letter saying her breasts are dense and she should talk to you. You want to actually be thoughtful in answering this question, so you decide that what you should do is really try to estimate her risk of breast cancer.

And the good news is that there are some easy-to-use risk stratification tools. So which of the following? You should not use a general breast cancer risk assessment tool, because she has a first-degree relative with breast cancer. We should refer her. You're going to know that's not right, because we just learned that two slides ago.

You do not need to use a breast cancer risk assessment tool, because she's at increased breast density and she's already at high risk. You should calculate a Gail model to calculate her breast cancer risk. And the BCS model should be used to calculate a breast cancer [INAUDIBLE]

So the answer here, really, is that the BCSC model is the only risk assessment model that incorporates breast density. And we know that one of her risk factors is her breast density. So I'm going to walk you through our risk assessment models.

So this is the second thing I want you to think about implementing in your practice-- is to do a breast cancer risk assessment in your women who don't flag for high risk breast. And here's how you do it. These assessment models-- it's kind of like the FRAX. Dr. Greenspan was talking about the FRAX for estimating the risk of a fracture with a given osteoporosis.

These models help you more accurately predict whether a patient is high risk or not. And the reason it matters is, it's going to change your therapy for that patient. So these models estimate the risk for breast cancer, using a variety of the factors that I talked about. They compare the woman that you're assessing to an average woman of the same age. Depending on the model, they estimate five, 10, or lifetime risk.

And just to reiterate, they should not be used for women who flag positive for the hereditary risk factors. If they flag positive on scary family history, you're done. You don't have to do any more.

So what is at high risk? Well, anyone higher than average. There are two numbers out there in the literature that serve as the threshold for initiating chemoprophylaxis. The initial chemo prevention studies were all done with a five-year risk greater than 1.66.

The US Preventive Services Task Force released guidelines recommending the primary prevention of breast cancer in primary care and suggested a 3% risk. And for us, in our practice, we use the 3% risk. The 3% risk feels very comfortable. It's a significantly higher risk. It's easy to counsel women on.

So what are the models? The Gail model is the National Cancer Institute Breast Cancer risk assessment tool. The BCS model comes from the Breast Cancer Surveillance Consortium risk. It's a prediction model.

There is another model called the Tyrer-Cuzick model, which is extraordinarily cumbersome and really not used in primary care. If you refer someone to the breast cancer risk clinic, they will use the Tyrer-Cuzick. But I'm not even going to talk about it today, because it's not something we could use in our settings.

So the Gail Model was developed in 1989, modified in 1999. It calculates five-year and lifetime, up to age 90, risk. A Gail score of greater than 1.66 was the criteria for the enrollment in both the SERM trials and the aromatase inhibitor [INAUDIBLE] prevention trials. So realize, I'm recommending that you use a 3% cut-off.

If you choose to use a 1.67, that's OK. That's just a little harder to counsel. And I'll talk about that in a minute.

And so up front, I'm going to say, I don't care which model you use-- Gail or BCSC. I will tell you up front, most of us like BCSC model for two reasons. One, it doesn't care when you had menarche. And most of us, when we're seeing 60 or 65-year-old women, I'm actually really not asking that as part of my review of systems. So if I decide to do a Gail model, I have to go back in and take additional history.

The other reason we like the BCSC is because it incorporates breast density, which we know is a significant risk factor. So here are the Gail model risk factors-- age, race, known genetic syndrome, first-degree relative with breast cancer, age of menarche, age of first live birth, a history of previous high risk breast pathologies-- DCIS or LCIS-- just a history of a breast biopsy, and then prior chest radiation.

All right. This is what the Gail model looks like. You just Google "Gail model." It comes right up. And it's a series of yes/no questions that you enter. And it will calculate, for you, your risk.

So if you look at the right-hand side of your screen, you see that for our patient here, this woman, at age 63, her risk was 3.2%-- five-year risk of developing breast cancer. The average woman of age 63 is 1.9%. So in fact, this woman would meet our criteria.

Now, what happens if we do the same patient with a BCS model? So it's different data. This one was developed in 2008, modified in 2015. It'll give you a five and a 10-year risk. There's a wonderful app you can download on your phone. It's super easy to use.

It does incorporate breast density. And it's more comprehensive for benign breast pathologies. The downside to the BCSC-- it was not the model used in the actual chemo prevention trials.

So there are benefits to each of these models. The US Preventive Services Task Force is neutral on which one. And from my perspective, I just want you to use one. I don't care which one you use.

I like the BCSC because I think it's easier and because it helps me manage breast density. So when my patient comes to me and says, oh, I got this letter and I have high breast density, what are you going to do-- I say, well, let's calculate your score. And in fact, there are a number of articles in the literature that suggest that breast density is one very small risk for increased breast risk and that what really matters is the overall breast risk. And this is how you find it. You use a calculator.

So the risk factors that are in the BCSC model-- age, race, first-degree relative with breast cancer. Part of the reason I like it is because it doesn't make me go back and ask the reproductive history questions that I'm usually not asking in my postmenopausal women. It does want to know the breast density.

It wants to know if you've had a surgical history. And it does want to know about prior breast biopsy and results. And it doesn't really care about your medical history.

So if we take Charlotte's risk-- and again, if you look at this-- just the visual of the BCSC model-- there are way fewer questions that you have to ask. And again, like I said, it's an app you can do on your phone. So in our patient, the number's a little bit different. She comes up with a score of 2.84%, which is a little bit less than she got, still above the 1.67%.

Now, what you also know is, if you wait a couple years, it'll go higher, even if nothing else changes, because age is such a potent initiative. And that's actually a pretty important thing to remember, because with all of our chemo prevention interventions, we only treat for five years. So knowing when to start and when to stop is helpful.

So which model? I don't care. BCSC is easy to access online or with an app. I like it because it includes breast density. The Gail, you can calculate it without the breast density. And remember, it is better validated in the chemo prevention trials.

Just pick one. Pick one. Get comfortable with it. Use it.

So risk assessment-- step 1, look for a high risk family history and refer-- the guidelines, or a brief genetic screen-- and do not use a risk model in these patients. Step 2, assess risk factors. And step 3, calculate risk.

So if you do nothing else after this lecture, if you do these three things, I will be successful in my intervention, because these women who have high risk factors can certainly be referred to the high risk breast cancer clinics. We're going to overwhelm them if we refer everybody with these lower level risks. But if you're uncomfortable prescribing, I'm OK with that. I'm OK overwhelming my breast cancer colleagues, because what I want is you to identify these patients. And if nothing else, maybe you tell them they should drink less alcohol if their risk factors are high.

All right. So your patient is high risk. Now what? Weight management, alcohol intake-- think perhaps about enhanced screening, tomosynthesis. Certainly, most of us who get our mammograms send our patients to the [INAUDIBLE] system. They're pretty much doing tomosynthesis on everyone.

But that is considered enhanced screening. So that's, again, something that you might offer for an increased breast density as an enhanced screening. The guidelines about how often we do mammograms are pretty variable. Sometimes what I do-- I subscribe actually to the American Cancer Society guidelines, which says, yearly, 45 to 55, every two years after 55 in women of average risk.

So one of the things you can sometimes do is just go to every eighth year after 55 if the risk is increased. And then there's always the question of ultrasound in some of these women. The data has not been terribly supportive of that.

Our radiology colleagues really like it. So that's a talk for another update. And then we'll think about chemoprophylaxis.

So just a word-- greater than 20% lifetime risk for breast cancer-- these are the really high risk patients. BRCA, radiation to the chest as a young person, a very atypical but benign biopsy, and a very high family risk history-- if you calculate a risk greater than 20% lifetime, these folks should get an annual mammogram and an MRI. Insurance will pay if the risk is greater than 20%. At moderately increased risk for breast cancer-- and we talked about what that means-- consider annual screening, starting at a younger age, and/or tomosynthesis.

Now, what I want to spend the rest of my time with is talking about chemo prevention, because this is where I think, as primary providers, we are the most uncomfortable. So I want you to look at this slide, which highlights these missed opportunities that we have. 10 million women eligible for you to think about using chemo prevention.

There are two million women who actually would benefit from it. Their risk is high enough that they would benefit from it. And they don't have contraindications to the medications.

And then look of that teeny, tiny, little yellow bar of how often we're prescribing this. Everybody gets their mammograms, which finds cancers that are already there. So I'm going to talk to you about chemo prevention and the magnitude of the benefits.

So there are recommendations out there that we should be doing this. The US Preventive Services Task Force, in 2013, came out and recommended that we should use tamoxifen and/or raloxifene. ASCO, in 2013, recommend tamoxifen, raloxifene, and one of the aromatase inhibitors.

And the National Cancer Networks, in 2016, recommended tamoxifen, raloxifene, and either of the two aromatase inhibitors. So let's talk first about the SERMs. The SERMs are Selective Estrogen Receptor Modulators. They have differing estrogen effects on differing tissues.

So in some tissues, they're pro-estrogen. In some tissues, they're anti-estrogen. Both are FDA-approved for chemo prevention.

And I was going to comment on Dr. Greenspan. She said raloxifene is not indicated for osteoporosis. I would argue, except in your patients of high risk breast cancer, because then it becomes a two-for agent. I can help your bones, and I can prevent your breast cancer.

So if we look at the two drugs, both of them are anti-estrogen on the breast. The biggest difference between tamoxifen and raloxifene is that tamoxifen is pro-estrogen on the uterus. So when you give tamoxifen, you are giving a weak, unopposed estrogen. So the risk of endometrial cancer does go up a little bit with tamoxifen. And then raloxifene actually has better bone protection than tamoxifen. So some of this is about risk benefit.

Now, the dose-- tamoxifen is 20 milligrams daily for five years. You can use tamoxifen either in a pre or postmenopausal patient. The adverse effects-- clotting, like any other hormone-- BTE-- endometrial cancer, like I just talked about, and, actually, cataracts are something that tamoxifen has been associated with. Raloxifene is a drug we, as internists, tend to feel a little more comfortable with, because we've probably used it at least somewhere along the line for osteoporosis.

The dose here is 60 milligrams, again for five years. You only can use raloxifene in postmenopausal women. And the biggest risk is venous thromboembolic disease-- so fewer side effects from raloxifene.

The benefits, if we look at them together-- I want to just get to my last slide. This is the STAR trial, which was actually-- Pittsburgh was one of the lead sites. And this compares tamoxifen to raloxifene, because that's really the question you want. Both are helpful in head-to-head trials against placebo.

Tamoxifen seems to be a little more successful in preventing invasive breast cancer. There are five more cases with tamoxifen than with raloxifene. However, it has more clotting. It has more endometrial cancer. And it has cataracts.

So you've got this dilemma that tamoxifen is probably more potent, but it has a lot more side effects. So how do you weigh those risks and benefits? Well, here's Judy. We're going to have to answer her question.

She's 53. She's postmenopausal, seen in follow-up of a breast biopsy which revealed mild ductal hyperplasia. It is not atypical, so it's not a high risk pathology. But it does mean she had a breast biopsy, which increases her risk.

You calculate her Gail score. And it's 3.8%, which is pretty high for a 53-year-old. She wants to discuss her breast cancer risk.

The good news is, she has no contraindications. She's not had a clot. She's not had a TIA or any other kind of CVA.

She has no endometrial cancer. And she doesn't have cataracts. So what do we recommend?

Tamoxifen? Raloxifene? Either/or, do a shared decision making moment with this woman? Tamoxifen is better but more risk. Which do you want to go? Or this decision is way above my pay grade, and I'm sending to the high risk breast. I'm hoping that after today, we change that answer for you.

So the answer here really is to recommend raloxifene, because even though she's otherwise healthy, the risk benefits of tamoxifen are a little challenging. And why do I say that? Well, again, we talked about-- this just reviews the risks and benefits.

There is a decision aid available in the literature by an author named Friedman, who actually built tables looking at the risks and benefits and doing a summary score. He compared the benefit risk profile stratified by the presence or absence of a uterus-- because if you don't have a uterus, then the endometrial cancer risk goes away-- and race. And he did it based on a five-year predictive breast cancer model using the Gail model.

And so I want you to just look at this table. And what you see here is that there's blue, there's yellow, there's gray. So here, the blue; here, the yellow; and here, the gray. The blue suggests-- and this is the raloxifene versus tamoxifen.

And what I want you just to take away from this, all things being equal, there's way more blue and yellow in the raloxifene category than in the tamoxifen category. So I'm not asking you to be perfect when you go forth and try to implement this in your primary practices. I just want you to do it, because you will make a difference. So all things being equal, raloxifene is almost always the better drug in a postmenopausal patient.

All right. So back to Judy, she could be eligible for either SERM. But the risk benefit of raloxifene wins for her. But now, we never figured out Charlotte.

I'll remind you, she was 63, postmenopausal, white. Her past medical history was significant for osteoarthritis and a provoked DVT. So she's not a great candidate for a SERM, because she's had a venous thromboembolic event.

She's never had a DEXA scan, because she's 63. She's under our guidelines at 65. Her Gail and BCS are both above average. And we're a little anxious about raloxifene.

So is she a candidate for chemo prevention? Yes, I would offer either and do a DEXA scan at age 65. Yes, I would offer either and add vitamin D and calcium. Yes, I would get a DEXA scan first and then discuss chemo prevention.

And given her history of DVT, she is not a candidate for aromatase inhibitors. And so we know that one's not true, because DVT is not a risk factor. The answer here is, you at least want to know what her bone health is before you start an agent that increases the risk of developing osteoporosis.

So the aromatase inhibitors inhibit the endogenous conversion of androgens to estrogens. They are only indicated in postmenopausal women, because their mechanism is by inhibiting conversion. So if I have ovaries that are still making estrogen, I don't block the estrogen effect.

The NCCN recommends the use of either. ASCO recommends exemestane for five years. I will comment, it is currently not FDA-approved, but it is widely used for this indication. How good are they? I want you to look at-- these are both versus placebo with exemestane and anastrozole.

Number needed to treat-- over seven years to prevent breast cancer. It's pretty small-- certainly in the order of magnitude that we make these decisions. But what I really want you to look at is this hazard ratio.

The hazard ratio over seven years for using exemestane is 0.35. That's a 65% reduction. For using anastrozole, it's 0.47, which is a 53%.

This is a huge difference. This is way better than anything we do when we obsess over their mammograms. We are clearly not providing the best care for our women to not be offering them this therapy.

OK. What do you do with your bone mineral density? We know AIs have deleterious effects. We know that bones actually get worse in as little as two years.

There is one study that stratified women based on their bone [INAUDIBLE] density. And those with osteoporosis actually received a bisphosphonate as a prevention when you're giving it. And this attenuated it.

So this is starting to get a little complicated now. So what I'm going to do is walk you through what I want you to take home. So Charlotte-- no concern for osteoporosis or osteopenia on her DEXA. So you're good. You don't have to worry about it.

And you can prescribe either of the aromatase inhibitors, one milligram daily for five years. But in three months, she's now having hot flashes, because, actually, either the SERMs or the aromatase inhibitors can give you hot flashes. So I want to talk, just for the last couple of minutes, about the management of the side effects.

We don't start very many women on chemo prevention. And those we start, only 60% will complete their five years. And the reason is because we don't ask about or manage the side effects.

Both SERMs and aromatase inhibitors can cause hot flashes. So I have to be honest, if I have somebody really early in their menopause, and even if their risk score flags high but they're having a lot of hot flashes, I will delay starting my five years until I get them to a little bit better place with their menopause. We certainly would ask you to avoid hormone therapy, obviously, in these women, because in a high risk breast, we wouldn't give hormone therapy.

Paroxetine, citalopram, and fluoxetine can inhibit the benefits of tamoxifen. So we don't use those drugs. But remember, the non-hormonal management of hot flashes includes drugs that we're very familiar with, like gabapentin and venlafaxine. So these agents can work great.

The arthralgias are sometimes a significant problem for our patients on the aromatase inhibitors. Analgesics-- but often they're ineffective. What has some good data is duloxetine, or Cymbalta. This is like, exercise is good, vitamin D is good, weight management is good. All those things are good. But often the aromatase inhibitors are limited by their arthralgias.

So the management considerations, in addition-- obviously, if you're on tamoxifen and your vision goes bad, you better be looking for cataracts. If there's vaginal spotting, you do prompt evaluation. We don't recommend doing screening vaginal ultrasounds on tamoxifen. But any postmenopausal bleeding would initiate it.

For SERMs-- either of the SERMs, raloxifene or tamoxifen-- these are hormones. So we take them off these agents if you anticipate surgery. And obviously, you think about VTE and CVA. So putting it all together, high risk assessment-- if yes, refer. If no and they're postmenopausal, do a Gail or a BCSC.

It is too complicated in the primary care setting, if you're uncomfortable with this stuff, to do this in premenopausal women. So everybody should get a family history. And if they're postmenopausal, you should calculate a Gail or a BCSC.

If they're increased risk-- greater than 3%-- consider chemoprophylaxis. If they're not, business as usual. If you do that family history and they're premenopausal and they have contraindications, do SERMs. Look for modifiable risk factor reduction.

You can consider tamoxifen. But most of those are done in the high risk breast clinic. Most of us are uncomfortable with that.

If they're postmenopausal and have contraindications to SERMs, and where they don't have a uterus or have osteo-- no uterus and no osteoporosis, think about raloxifene. Raloxifene is the one we're most comfortable with, and you get the additional benefit to their bones. If they have a uterus and no osteoporosis, you can use raloxifene or an aromatase inhibitor.

There is some shared decision making involved here with your patients. So you need to know the risks and the benefits. But I'm going to-- I don't quite have the cute mnemonics that Tanya have, but I'm going to give you what I think is a cookbook to how to do this.

Step 1, family history in everyone, and if high, refer. Step 2, if the patient's postmenopausal, calculate a score-- Gail, BCSC. I don't care. If they're premenopausal and have a concerning family history, referral to the high risk program.

If they're postmenopausal and that five-year risk is greater than 3%, I would like you to discuss chemoprophylaxis. If they're interested and you're uncomfortable, refer. If they're interested, I'd like to push you to think about it.

Assess their risk for using an aromatase inhibitor by measuring their bone density. If the bone marrow density is more negative than minus 1.5, start raloxifene. If it's not any evidence of osteopenia, start an aromatase inhibitor. The aromatase inhibitors are extraordinarily well-tolerated. And then, finally, monitor and manage the side effects.

So my challenge to you is to leave this today and do something. Take an enhanced family history. After you do that, try calculating some scores.

And then consider starting treatment. And if you only prescribe raloxifene for postmenopausal women with good bones, you'll be doing a service to our patients. OK. And with that, I'll quit.