Angelica Ladd:

So good evening, everyone, thanks so much for joining us. My name is Angelica Ladd. I'm community relations specialist at Dartmouth-Hitchcock health. Welcome to this Healthy Living Series presentation about Women's Reproductive Cancers: An Overview of Cervical, Ovarian and Uterine cancers. We are joined by Dr. Ivy Wilkinson-Ryan gynecologic oncologist at Dartmouth-Hitchcock.

And we'll talk with her in just a moment, but first I have a few housekeeping items. So first of all, if you would like to ask a question, please use the question and answer function. We should have plenty of time to get to your questions, but if for whatever reason we do run out of time, we'll do our best to get those answers for you, and post them on our Healthy Living Series page, which is, go.d/h.org@HLS, and I'll put that link in the chat for you.

Tonight's event is being recorded and will be posted on that same Healthy Living Series page, as well as YouTube. So you can rewatch it later this week, if you feel like you've missed something. It'll live there forever, so you have that option. We also have closed captions available for tonight's presentation. Just click on the closed caption icon for live captioning.

At the end of the event, you'll be sent a quick three minute survey. So I would be so grateful if you could take just three minutes to take that survey, because that helps us with future programming, and lets us know what we're doing well and what we might need to work on. So if you could do that, that would be wonderful.

And finally, on November 17th, we are hosting a Healthy Living Series on understanding epilepsy, and you can register for that today. And, again, that's at go.d/h.org/hls, and I'll put that link in the chat for you.

So now we can get things started after we got all that housekeeping out of the way. And presenting for us this evening is Dr. Ivy Wilkinson-Ryan MD. Dr. Wilkinson-Ryan is the division director for gynecologic-oncology and an assistant professor at the Geisel School of Medicine. One of her guiding principles is to give her patients the information they need to make decisions that are right for them. And so thank you so much, Dr. Wilkinson-Ryan for being here, and I will let you take it away.

Ivy Wilkinson-Ryan:

Thank you so much. I just wanted to start with my dog bursting in the door that doesn't quite latch. Sorry, everyone. I'm going to start my screen.

All right. So, again, my name is Ivy or Dr. Wilkinson-Ryan or Dr. Ivy, patients, people in the community, you're welcome to call me whatever you want. Tonight, I'm going to go over screening and prevention of gynecologic cancers. And like Angelica said, we're going to focus on cervical cancer, ovarian cancer, and uterine cancer, which are the three most common gynecologic cancers that we see here in the Upper Valley.

So what we're going to touch on tonight, we're going to go over a little bit of what is a screening test? And then, we'll go over the risk factors, prevention, symptoms, and screenings for those three cancer types. And cover the topics in ways that they fit, or I thought they might be meaningful the population or people in the community. And you'll see why we might leave some of those topics out for some of these cancers.

But just to make sure we're all on the same page. So I'm a gynecologic-oncologist, so I'm a women's cancer surgeon, and we also do chemotherapy for women's gynecologic cancer. And just make sure we're all on the same page with the anatomy. Angelica, are you guys able to see my mouth?

Angelica Ladd:

Yep. They should be able to see your mouse? Yes. I see it.

Ivy Wilkinson-Ryan:

Okay. All right. Okay. So this is the vagina, cervix here. The cervix is sort of the entryway into the uterus, but it really functions as its own organ that gets its own cancer. Here's the uterus and the uterus is lined by a layer of tissue called the endometrium, the fallopian tube and the ovary. And so tonight we're going to talk about cervical cancer, uterine cancer, and ovarian cancer.

So talking a little bit about screening tests. So tonight, I might take an absolute in ways that people might want to say, "Well, I know somebody who had a different cancer, it didn't quite work out like that." And please, a lot of times, I'll sort of generalized about the cancer as a whole, and there are sort of exceptions in cancer all the time. So please understand that I don't doubt what any family member has gone through, but they may have had an exceptional experience. I'm really going to talk to the more common experiences tonight.

So when we talked about a screening test, the principles of a screening test or the concept of screening test is a test that we give to an asymptomatic population to try to detect disease. That's really important. So if you go to your doctor saying, "I have a stomach ache," and they say, "Okay, let's get you a colonoscopy." That's not a screening colonoscopy, it's really for a symptom. Whereas, if you turn 50 and they say, "You need a colonoscopy," even though you feel fine, that's a screening colonoscopy.

It's really important that screening tests capture most patients who have the disease. And when I say most, I mean, almost all. Because when you go through a screening has to say, "I did my job and I got my regular pap smear." You're supposed to feel assured that you don't have cancer. And so you really need to make sure that that test is going to capture everybody who has the problem it's supposed to detect.

On the flip side of that, we're willing to let screening tests have what's called a high false positive rate. So in the example of a pap smear, it's really important that nobody with cervix cancer has a normal pap. Everybody with cervical cancer needs to have an abnormal pap, such that they get caught. But a lot of patients with normal cervixes, will have an abnormal pap smear, and they'll get a second test to figure out if it's really a problem or not. And so that's what that high false positive rate means.

It's very important that both the screening tests and the diagnostic tests are low risk, which is to say that, you can't do a screening test that involves a big abdominal surgery, that's not screening. That's not safe enough to put an asymptomatic patient through. If you get a screening test and it turns out that you screen positive, so if you get a mammogram, you feel fine, no lumps that you can feel, and you get a mammogram, and they say, "Ah, I see a lesion on your mammogram," or you get a pap smear and they say, "Your pap smear is not normal," the next test to actually diagnose, to actually get some tissue to look at it under the microscope and tell you what's going on, that next test also has to be low risks.

Because, as it is with screening tests, you're going to have a lot of patients who have an abnormal screen, but don't have any problems. And so you want to make sure you're not going to put them through a invasive or dangerous procedure just to find out that they didn't have the problem in the first place.

And then you need to determine that doing the screening test on a certain population is going to result in improved health in that population. And we run into this in ovarian cancer, which I'm going to touch on tonight. You can screen and screen and screen, but unless you're actually making a difference in the health of the population, it's not "worth," it doesn't justify the inevitable worry that people have get, the cost of it, the sort of potential low risk of doing a screening test. So even if it's an

easy screening test, there are still some risks and there's going to be a lot of anxiety on the patient's part. And if it's not going to help a individual's health or population's health, it's not a good screening test.

So with that in mind, we're going to go over these three most common gynecologic malignancies, and the screening tests or lack thereof for these diseases. Sorry, just going to walk you through an example of a screening test, and some are successful and some are less successful.

So screening for cervical cancer with a pap smear. So this is a successful screening test that we use in the United States. And so, for a pap smear, you screen asymptomatic women, so women with no problem, no abnormal bleeding, pelvic pain, no nothing. You go in for your annual exam, and get your pap smear, which might not be annual anymore, but you get a pap smear, where they just swipe some cells from the cervix. It's not comfortable, but it's not dangerous. They swipe some cells from the cervix, put it on a slide, and look at it under the microscope. And they've gotten so good that they can look at the cells in the microscope, and say, "This patient is fine," "This patient might have a problem," or they'll say, "I'm very worried that patient has a problem."

And they're prompting the gynecologist or your primary care doc to do another test, if necessary. They're propping that doctor to respond by potentially doing another test where they actually get a biopsy. Again, a non-invasive, a not very comfortable, but not dangerous process.

Just to go over, that's a good screening test, because it's performed on an asymptomatic population. Cytologists or people who read those pap, are very good at it, so they catch everyone. It does have a high false positive rate. So there are a lot of women who get a pap smear with an abnormality, who then ended up having a normal, what called colposcopy, or normal cervix. Both the screening test, which is a pap smear, and the diagnostic test, which is called a colposcopy, are very safe.

And it has resulted in improved health in the population. So we're able to catch precancer problems of cervix and prevent cervical cancer. And you can see a very big difference between countries that have pap smear programs and countries that do not, in terms of cervical cancer rates and deaths from cervical cancer.

So another example, just to walk through screening tests, would be screening for ovarian cancer, with a pelvic ultrasound, which is not a good screening test. And the reason is, is because if you have a pelvic ultrasound and there's an abnormality, only way to get tissue, to get something to look at under the microscope to figure out what was going on, is to do a surgery, to remove the ovary. And so in that scenario, really, that test is going to be sunk, because the diagnostic test is not low risk. You have to undergo a surgery and remove an ovary. That's not okay second, or diagnostic task for a screening test. And then the other issue which we will get into a little bit more tonight is that it does not result in improved health in the tested population.

So Angelica, my picture of my little screen of people, is gone black. Are you guys still able to hear and see me?

Angelica Ladd:

Yeah. Our participants are all still here. Yeah. You're just doing like [inaudible 00:11:36]. Oh, actually, you are frozen a little bit. If you want to restart your camera, and see if that will bring you back.

Ivy Wilkinson-Ryan:

That is not an option right now.

Angelica Ladd:

I can still see your mouse moving.

Ivy Wilkinson-Ryan:

Okay. And you can still hear me.

Angelica Ladd:

Yep. Oh, there you go. You're-

Ivy Wilkinson-Ryan:

That's should do it.

Angelica Ladd:

... moving again.

Ivy Wilkinson-Ryan:

There you go. Sorry. All right. As long as you guys can hear me... Angelica, I'll rely on you to speak up, if something goes wrong and you can't hear me and can't see my slides. Otherwise, I'll just keep moving.

Angelica Ladd:

Okay.

Ivy Wilkinson-Ryan:

Hopefully, I don't freeze in a very strange position. All right, so the first thing we're going to talk about is cervical cancer. So again, at the top of the vagina is a cervix and it's sort of that tissue that transitions between the vagina and the uterus. And although it's in continuity with the uterus, it functions very differently.

So cervical cancer is caused by HPV, or human papillomavirus. It is exceedingly rare to get cervical cancer without having HPV. And this is one of those cases where it happens, we in GYN-oncology have seen it, but it is very rare. So I'm really going to talk tonight as though you're not going to get cervical cancer, unless you have HPV. Other risk factors for cervical cancer, that patients can have some control over, are smoking, and the other risk is not undergoing the recommended screening. So the time that we see cervical cancer are really in women who have had an abnormal pap smear, and either they haven't gotten pap smears, or they've had an abnormal pap smear, but haven't gotten the appropriate follow-up for that.

The symptoms of cervical cancer are... It's pretty hard to detect based on symptoms. Typically, what women will see some abnormal vaginal bleeding. In particular, what you'll see described as post-coital bleeding, so some spotting after having intercourse. And some women will develop pelvic pain as a symptom that leads to the diagnosis of cervical cancer. But, again, another theme you'll see tonight, is that women in your reproductive lives and post-menopausal lives, have a lot of gynecologic symptoms. Every period is cramping or bloating and feeling distended, having some nausea. And then you may, in your entire reproductive life have abnormal bleeding, and that's a symptom of cancer, but for you, it's totally normal. So it is worthwhile keeping in mind that a lot of the symptoms of these cancers are just what women experience day-to-day anyways.

So cervical cancer, we talk about pap smears already, but cervical cancer is the gynecologic cancer that does actually have an effective screening tool, and that's the pap smear. This is our HPV virus over on the right. Oh, man. All right, so join me in the weeds for a little while. There are a lot of assets or biology about HPV that makes cervical cancer easy to screen for. So one of the primary components of HPV that make it easy to screen for is that it takes a long time, like years between an HPV infection and cancer, so you have time to screen.

So down here, these are the results you could get on a pap smear. These results, the second tier, are the results you would get when you take your biopsy. This little picture is a cartoon of what one would see under the microscope, and then this is sort of a timeframe of these changes. And this picture here is a picture of the skin. It's a picture of what you would see under the microscope for the skin that covers the cervix.

And so you start here with normal epithelium, or normal skin. When you first get an HPV infection, so the studies are that like up to 50%, or at least 50% of reproductive age women have been exposed to HPV. I've seen statistics in the '80s, really, if you are sexually active, you have to assume you've been exposed to it.

The vast majority of women kick it out, their body fights it off, and they don't have HPV harbored in their cervix. The difference between women whose bodies fight it, kick it out, and women whose bodies sort of let it in, and let it hang out. We really don't understand that difference. So what happens when you initially get an HPV infection, and you'll see some changes to the cells called koilocytosis, and that's just the way they look under the microscope. As it persists, you start to get these precancer lesions CIN1, 2, and 3.

If you have koilocytosis or this precancer level one, your pap smear likely comes back as atypical cells of undetermined significance or low grade squamous intraepithelial lesion, both of those are low grade pap smears. If you're getting pre-cancer level two or precancer level three, which is the highest, then we're going to start to see high-grade pap smears. And that's really when the cytologist, the person looking at the pap smear is saying, "Doctor, you need to look closer. I think something's wrong." And then after precancer level three, we start to see cancer.

But, again, not every patient marches like this. Not every patient marches like this in continuity. So there may be a lot of time in CIN1 and koilocytosis, and then CIN3, and then it regresses and then comes back. And a lot of patients will get CIN2 and kick it out, and it'll never come back. So it's really hard to predict who's going to do what. The fact that it takes a long time to develop into cancer, if that's where it's headed, gives you an opportunity to screen.

The other piece to keep in mind here is that, if it's possible with some of the participants tonight, used to have annual pap smears, and now their doctor's telling them that "You need pap smears every five years," which sounds crazy, if you're used to hearing once a year, that you don't have cervix cancer. But it's really the research that led to the acknowledgement of how much time it takes, one, and that you don't get cervical cancer without HPV, and our ability to test for HPV, that's let us space out those pap smears. So if you do not have HPV and you've never had HPV, the chances of you get getting HPV and getting cervical cancer in the next five years are exceedingly low. And so that is why, in certain populations, we've spaced the pap smears out to three years or five years.

And so that is what this slide's about, what happened to my annual pap smear. And so we can now test for HPV, and so we understand, now, we can risk stratify patients based on their HPV. So if you don't have HPV and you've never had HPV, you're not going to get cervix cancer within X amount of time. And that amount of time is really determined based on your age group. And then the other principle, that once the patient had HPV, it takes years to develop precancer.

So I do want to talk for a moment about prevention of HPV, because now that we understand that you can't get cervical cancer without HPV, it sure seems like it's worthwhile to prevent HPV, and we can. So there is an HPV vaccine. The one in the United States protects against the nine most common strains of HPV. It's approved for ages nine to 45, in males and females. The best coverage is if you get vaccinated by age 12. With the HPV vaccine, I don't know enough about the vaccine world to really understand how this works at other vaccines, but I know enough about the HPV vaccine to understand that, as you get older, your body does a less good job of what's called zero converting or building up antibodies.

And so if you get the vaccine as a younger human, you will have a better vaccination. You'll be have a more efficacious vaccine. The reason we love the vaccine is because, preventing exposure to HPV is very difficult. So looking today, trying to update this statistics, what I found was a study showing that 50% of reproductive age women got exposed to HPV, in the course of a year, I think it was a study at a college. But some statistics has said as many as 80% of the female population, if you are sexually active, you will get exposed to HPV. And, again, we really don't know who holds onto it and whose body kicks it out, and why.

And so there's some improvement in that statistic with condom use. So you do see a reduction in the transmission of HPV with condom use, but it doesn't prevent it the same way condoms really prevent like gonorrhea, chlamydia. HPV is just much more willing to spread. And it really has to do with just skin touching. So just a little plug for the vaccine.

All right. So that was cervical cancer talking about screening for cervical cancer. I'm going to touch now on ovarian cancer. So we're going to travel from the cervix out the fallopian tube, and then here's the ovary.

So there are a lot of types of ovarian cancer, and I'm going to be primarily talking about a disease called epithelial ovarian cancer. It is the most common type of ovarian cancer. Included in that diagnosis is fallopian tube cancer, and a disease called primary peritoneal cancer. And we all just call them ovary cancer. When we want to not list all three, every time we talk. And so just to be clear, I'm talking about epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer, and they all sort of fit together there.

So the risk factors for ovarian cancer, the more lifetime ovulations, the higher your risk for ovary cancer. And so when you ovulate, if you have regular periods, regular mensies, you are almost certainly ovulating. The more times in your life you do that, the higher your risk for ovary cancer. Which is just to say, when we did these big population studies, women who had more lifetime ovulations were at higher risk for ovary cancer, or were more likely to ovary cancer.

The presence of intact fallopian tubes, and that's sort of just a backwards way of saying that we've found that women who have had hysterectomies or have tubal ligations or had their tubes removed, have lower rates of ovary cancer. If you have a family history of ovarian cancer, and specifically, it's ovarian cancer. So we haven't found that patients with a strong family history of breast cancer, who do not have any mutations, have a high risk of ovary cancer.

And then having mutations such as BRCA mutations or Lynch Syndrome, do increase your risk of ovary cancer. There is a long list of other mutations that you can inherit that can predispose you to ovary cancer. And we'll talk a little bit about genetic testing after this, or towards the end of the ovary cancer section. But for shorthand, I put down BRCA and Lynch syndrome, which are two of the more common genetics, positive ovarian cancer.

In terms of preventing ovarian cancer. Well, you just look at the risks and what can you do to reduce those risks? So decreasing your lifetime ovulation. So for instance, if you have many children,

then you won't ovulate as much. If you breastfeed, a lot of women don't ovulate while they're nursing. Nothing you can control, but if you start your periods late, or you go through menopause early, that decreases your risk of ovarian cancer. If you take birth control pills, most women don't ovulate on the birth control pill.

The other data that's come up recently as a Mirena IUD also decreases the risk of ovarian cancer, sorry. Removing the fallopian tube, so this is some newer data. We know if you had a hysterectomy or we know if you have your tubes tied, then you have a decreased risk of ovarian cancer. But we've just recently started to talk about taking the tubes out of women as a way to reduce their risk of ovarian cancer without taking out the ovaries. That's something we're really reserving for the BRCA positive population, or women with a very high risk of ovary cancer. But I put that in there because it is worth asking, if you're going to get us tubal ligation, if you don't get your tubes tied, to ask to get your tubes removed, and not just cut and burned. And then, of course, removing the ovaries, we're seeing a little extreme, but is a procedure we do fairly frequently to reduce people's risk of ovarian cancer.

All right, back to some basic science, again, bear with me as we get into the weeds here. But the more recent science, and this just figures from 2015, so it's still pretty old, but the more we've looked and the more carefully we've looked, we're starting to settle on the idea that a lot of ovarian cancers actually start in the fallopian tube. And the connection to ovulation is that, when you obviously, which is a normal physiologic process, in order to release the egg from the ovary, you have to break down the ovarian capsule, and your body makes sort of noxious chemicals to do that. And then once you ovulate, those little chemicals are sitting right there in your fallopian tube, the fimbria, or the little fingers at the end of your fallopian tubes are bathed in that fluid.

And over time, with multiple exposures, you can start to get some mutations in the fallopian tube, because of irritation from that fluid. And in some patients, those mutations will just accumulate and accumulate, and eventually turn into a malignancy. Now, I don't want anybody who's ovulating to be thinking like, "Oh God, I have to stop this process right now," because all things considered, not a lot of women get ovary cancer. The lifetime risk of the average woman in the United States is about one in 70 or between one and two percent. And so I don't want anybody envisioning their tubes being mutated right now. But that is the process that we think happens in some women that really triggers the ovarian cancer to form.

So ovarian cancer classically was called, I hate the word, silent killer, but a disease without symptoms. And it's not true, but here we are back at like symptoms every woman gets their whole life. Which is, the symptoms that are most common for ovarian cancer are abdominal pain, abdominal swelling, or bloating, and urinary frequency. The other issue I will say that these studies that try to detect symptoms of ovarian cancer are fraught with what's called recall bias. So if you asked a group of women who have ovarian cancer, did you have any symptoms? They'll be like, "Yes, of course I did." But they're sort of biased by the fact that they've now been diagnosed with this terrible disease, and they can really hyper-focus on what they've been experiencing. Whereas, had it not led to the diagnosis of ovarian cancer, it might've been pretty run of the mill bloating that they kind of get anyways and they would've blown it up.

And again, just to make sure we're all clear, these are the symptoms of ovary cancer. There are also symptoms that lots of women experience their entire lives with every menstruation. It's worth noting that a lot of women undergo a urologic or gastrointestinal workup before they get diagnosed with ovarian cancer. Which is to say that they talked to their primary care doctor, their OB/GYN, and they start looking at either their bladder or their ureters or their colon or their intestines in some capacity. So a lot of patients will have had a colonoscopy and urine tested. And then finally they get an ultrasound or CT scan, and we can see that there's a suspicious mass there.

So while ovarian cancer does have symptoms, it's hard to tease them out. And what really stood out in the studies of patients who were monitored for symptoms. And then you look at the women who got ovary cancer, the ones who didn't, is the women who got ovary cancer, it was the persistence and severity of their symptoms. So if you had bloating and urinary frequency with every period, your whole life, and you get it your next period, don't worry. It would be that, if you start to get those symptoms, but they just persist. It's sort of new, the way that they're hanging around, and sort of getting progressively worse, and that should prompt a call to the doctor.

So ovarian cancer screening, so here's one of your fails, there is no effective screening for the general population. So we have tried. We have tried so hard to come up with a good screening protocol, doing studies of hundreds of thousands of women to try to figure out, can we prevent this cancer? Because it is often diagnosed at a very late stage, and it's very hard to cure at that late stage. But as we talked about in the beginning, those principles of screening, we can't get ovarian cancer screening tools to fit into those principles.

So for instance, one of the tools we've tried to use, that we talked about earlier, was ultrasound. And what we found is that with ultrasound, one, if you find a problem, the only way to actually get tissue to look at it under the microscope, to figure out what's going on, is to take the ovary out. That's unacceptable in women who have not gone menopause. It's certainly unacceptable in women who want to have kids, but also, there are complications from taking the ovaries out. They're rare. It's a relatively straightforward procedure, but if you do it enough, you're going to run into some complications. So it's not a good enough diagnostic test.

The other thing we found is that when we tried to do annual ultrasound, is that when we looked at the population getting ultrasounds and the population not getting ultrasounds, we saw the same number, in the same stage of ovarian cancers, which is say the cancers seem to pop up between the ultrasound intervals. There are some labs you can check. One's called a CA-125 or a cancer antigen 125, one's called a ROMA, and one's called an Ova1. I'll go through these, and keeping in mind that we've also tried to integrated screening tools using ultrasound and CA-125. And we can't get there for the general population. We have not got a good screening test.

But a CA-125 or cancer antigen 125 is a protein in the blood. Everyone has some CA-125 in their blood. It's a normal protein that your body produces, but it can be elevated in ovarian cancer patients. The issue is, is that it's normal in about 50% of stage one ovarian cancer, so it's not a good enough screening test on its own.

So ROMA, which is, Ooh, I forget, the R stands for risk, and the O probably stands for ovary, but that is an algorithm. It's a proprietary algorithm that we... I don't belong to that company, so I don't really know what the algorithm is, but it involves your CA-125 level and your age. And it's meant to detect your risk for ovarian cancer, as you get your CA-125 measured over time/.

And then the Ova1, and I bring up the Ova1, because it's something that people in the population might have heard of, but the Ova1 was developed to help women who have a cyst. So if you have an ovarian cyst that your doctor tells you should come out, the Ova1 can help determine if the cyst should come out with a regular OB/GYN, or if you need to see a specialist like me, who does GYN-oncology. And so the Ova1 can help determine, who's best to take that cyst out, or the risk of there's going to be an ovarian cancer.

So, again, we have tried to do these multi-modal approaches with the CA-125 and ultrasound at various integrals. And there's been some glimmers of hope, we can diagnose women in an earlier stage, but when you look at the general population, we're not helping people live longer, and we're not saving any lives. And it causes a lot of stress and worry. So we're not there yet for the general population.

The other thing I want to bring up here is, there are online risk assessment tool that I think's horrible. So I took one, when I was a fellow, and I was in my late 20s and I hadn't had children and I entered all my information. And it said, "You should consider getting a hysterectomy to prevent ovarian cancer." And I was so upset. And so just be very careful when you're looking at risk assessment tools online, and you want to know your risk of ovary cancer or they exist for breast cancer and colon, because it might tell you some pretty absurd recommendations. And then as physicians, we're like, "Oh God, did you do the..." The patient's coming in crying, because need a hysterectomy, and we just feel so bad, because they just did a online risk assessment tool.

If you have a genetic predisposition to ovarian cancer, so if you have a BRCA mutation or similar mutation or Lynch Syndrome, then we think we can make a difference by doing ultrasounds and CA-125, because your risk is high enough that all of a sudden you cross some threshold for a good screening test. For what it's worth, in my practice, I see a lot of women with BRCA mutations, and the ultrasounds still generate a ton of worry. Because as you can imagine, every time you go to ovulate, you make a little fist like a normal egg looks like a little fist. And so depending on when in your cycle, you get the ultrasound, you might be seeing a fist every single time, which is terrifying in a woman who's been diagnosed with a BRCA mutation, or has a high lifetime risk of ovary cancer.

That being said, we do meet some threshold for a reasonable screening test. So if you have a genetic predisposition to ovary cancer, we are likely to offer that you can do ultrasound and CA-125, until you get your ovaries out.

All right, I'm going to pivot now to endometrial cancer. So the endometrium is the lining of the uterus. It's a cell layer that lines the uterus. It's the layer of the uterus that build up every month when you produce a bunch of estrogen and then shed every month to give you your period, when your body realizes you're not pregnant.

In terms of the risk factors for endometrial cancer, so excess estrogen, that layer that endometrium builds up in response to estrogen. And if you produce a lot of estrogen, then the signals of the endometrium is to just keep building, just keep making new cells. To the point that, oftentimes, a mistake is made and something transitions into a cancer.

Other risk factors include diabetes, Lynch Syndrome, which is a genetic disorder that predisposes you to ovarian, sorry, endometrial cancer, and then Tamoxifen use. And I bring that drug up, in particular, because Tamoxifen is a drug that's often used for patients who have had breast cancers, and in the breast is an anti-estrogen. But in the uterus is a pro-estrogen.

A little bit more about this excess estrogen concept. So one of the things that your fat cells do is that they turn other steroids in your body into estrogen. And so, one of the big risk factors for endometrial cancer is being overweight or obese. And that is primarily the population that we see this disease in. It is typically, a very low grade, so not very aggressive cell type, and early stage. Whereas ovarian cancer, where it's hard to catch in stage one, uterus cancer is easy to catch it, we usually catch them stage one.

And so other sources of excess estrogen would be, if you take estrogen, if you take hormones. So if you've gone through menopause, but you are losing your mind from hot flashes at night, and so your doctor goes to give you some hormone. If you still have a uterus, it's really important that you take both estrogen and progesterone, because the progesterone protects you from getting endometrial cancer.

In terms of prevention, so you want to do this things that decrease the extra estrogen you have around. So weight loss can help, not taking the estrogen drugs can help, control or prevent diabetes, and then undergoing a hysterectomy, obviously. But I just didn't want to miss the obvious, which is that,

if you've had a hysterectomy, you don't have any risk for endometrial cancer, and don't need to worry about it.

So in terms of endometrial cancer symptoms, so the symptoms of endometrial cancer have to do with abnormal bleeding. And so, we can imagine if this is the lining that builds up to give you your periods, as it builds up and builds up and builds up and builds up, and something turns into a cancer, it starts to grow really irresponsibly. So sort of all higgledy-piggledy, the cells will divide, and they'll try and make new blood vessels. And they don't do a good job. They're not very organized about it. And those blood vessels fracture easily, and so you see some bleeding. And so the most common presentation we see is that women have gone through menopause and come in saying, at 65, "What the heck I got my period again." And so we can do a biopsy and determine if they have an endometrial cancer.

In premenopausal patients, it's typically irregular bleeding. And so this gets really tricky as you get into your 40s and as you approach menopause, because it's very rare that women, ovulate every month and menstruate every month, and then just like that stop ovulating and stop menstruating and never have a period again. There's usually a couple years where their periods are much more irregular, they're more spaced out, some are heavy, some are light. If that patient comes to my office and says, "They're having that irregular bleeding," then they have any risk factor for endometrial cancer, I am likely to do a biopsy to try and figure out if that's what's going on. It might just be normal for them, but I like to check.

And so theme or my little can't would be, don't ignore irregular bleeding. And it's always very tempting, as women, to ignore your gynecologic symptoms because the exams are unpleasant, the symptoms are unpleasant to talk about, and we just sort of like to keep charging along. But it is very important that you don't ignore irregular bleeding. And if you start bleeding after you've gone through menopause, it's not just a period, you need to go see a doctor for it.

So endometrial cancer screening. So we do do screening for women with Lynch Syndrome or genetic predispositions of endometrial cancer, but we do not do screening for the general population. And the reason is, is that endometrial cancer causes bleeding so often that you don't' need to screen, you can detect it early. And if you do a good job as a physician to pay attention to what your patient is saying, you can detect it early enough. So we're not seeing these cancers at really advanced stages.

The diagnostic procedure, I included a picture here. This is called an endometrial biopsy pipelle. So it's about the width of a coffee stir and in the office, just like during a normal speculum exam, you can put this through the cervix, into the uterus, and you pull the stylette back and create a little suction, and suction out some cells from the uterus, and that's what's happening on the picture on the right. It is not very comfortable. It's very crampy, but it is something that we can accomplish in the office.

All right. So my take home points tonight, don't ignore your body. I can't tell you how many patients I've seen, who are women with families are just doing their thing, and trying to keep their lives going and their household going. And you just spend a lot of time, and you're young and having your periods and just ignoring the signals from your body, because they're uncomfortable, but you just have to keep going. And as you get older, do not ignore them, especially changes. So, if your periods, it is what it is, but if it starts to get much worse, those symptoms persist way past when you have your period, you need to definitely talked to your provider about that.

You shouldn't have hormonal symptoms when you don't have hormones. So when you go through menopause, that is the process at which your ovaries stop making estrogen. So if you have bleeding after menopause, it's not from a period. It's not from a cycle, it's abnormal. If you have bloating and cramping after you've gone through menopause, that's not normal. Those are hormonal symptoms, but you don't have any hormones. So you got to talk to your physician about that.

Find out your family history. So I think we'll go into a little bit more about genetic testing with the Q&A, but I think there's a lot of like, "Oh, the women in my family did been talking about these things." Try as best you can to nail down those older family members that don't want to talk about it, and try to figure out what your family history is, particularly the cancer history. Because it really matters, not every cancer is the same, it really matters, in terms of your risk, who had what cancer.

Not all bleeding is a period that sort of goes back to this concept of like, if you don't have hormones, you shouldn't be bleeding. But at the same time, if you have a period, one month it's five days, and then three months later you bleed for one day, it's not another period. That's not from ovulation, that's not [inaudible 00:41:26], that's something you need to talk to your doctor about.

Pap smears test for cervical cancer, and that is it. Routine labs that your primary care doctor offers, sorry, that your primary care doctor orders, do not test for ovary or endometrial cancer. So I have a lot of patients that come to see me that say, "Oh, I'm so surprised. I just got my labs done. And they were fine." Those labs look at your cholesterol. They will get your thyroid. They look at your bone marrow and your kidneys, but they do not test for cancer. These cancers do not usually show up in routine blood tests. So don't think that because you got those tests, you're all good, and you can ignore symptoms. All right, that's it. I'm going to stop sharing.

Angelica Ladd:

Hi. That was great. Thank you so much. We have a few questions. So we have questions about that HPV vaccine. So you said it's for women ages nine to 45. Can women over 45 also get that vaccine, or is just doesn't work as well after age 45?

Ivy Wilkinson-Ryan:

It's not FDA approved after age 45. So you would have a hard time finding a provider who would give it, and I think you'd have a hard time finding an insurance company that would pay for it.

Angelica Ladd:

Gotcha.

Ivy Wilkinson-Ryan:

For what it's worth, I think the rates of that zero conversion or getting that protection, they go down with ages, so I think it'd be really unlikely that it would be helpful... Or it would be less and less helpful after 45. That's the issue with that, it's just not FDA approved.

Angelica Ladd:

Thanks. And then do estradiol vaginal suppository or cream lead to increased risk of endometrial cancer?

Ivy Wilkinson-Ryan:

Yeah, they can. So that's using estrogen, and -a lot of patients use vaginal estrogen for lubrication after menopause for various symptoms. And so we really try to minimize the use of that cream. What I often do is I'll start patients on some regular dose like use it nightly, but then over time, try to really decrease the amount that you need that cream or use the cream, so you can get to the point where you have symptom control. And really with like infrequent use, we don't think it increases your risk of endometrial

cancer. If you're using it a lot, like if you're using a significant amount nightly, then you might want to talk to your doctor about using some progesterone to then protect that endometrium.

Angelica Ladd:

And again, if you do have any questions, you feel free to use the question and answer function here in Zoom, and we can get those questions answered for you. We did have some questions that were submitted ahead of the program. And you probably touched on them, but maybe we just reiterate. So are you more at risk of gynecological cancer if you haven't given birth to a child?

Ivy Wilkinson-Ryan:

So that really probably falls into just the ovarian cancer. Having a newborn myself, not a newborn anymore, but a one-year-old, I don't think that having a child is really justifies the ovarian cancer prevention you get. It's a lot. It's a lot to do.

Angelica Ladd:

It's a big commitment.

Ivy Wilkinson-Ryan:

But, yes, if you have more kids, you do decrease those lifetime ovulations and you slightly decrease your risk of ovarian cancer.

Angelica Ladd:

Okay. So that would be like kind of the same as going from like some from of birth control and then not ovulating, like the Mirena and that kind of thing.

Ivy Wilkinson-Ryan:

Exactly. Exactly.

Angelica Ladd:

Reducing ovulation. I had a question about cervical cancer and HPV. So HPV always causes cervical cancer? That is like the main cause of it.

Ivy Wilkinson-Ryan:

No. It is that if you have cervical cancer, it is exceedingly rare to have cervical cancer without HPV. HPV is very common and most patients who get exposed to HPV don't get cervical cancer. And so the most common, the most likely scenario, if you get exposed HPV, is that your body just fights it off and you never really know. There's a whole cohort of women who will get HPV and sort of lingers and hangs out in the cervix and drive them crazy, but they don't get service cancer. And then there's the more rare patients who actually develops [inaudible 00:46:05] cervix cancer.

Angelica Ladd:

Okay. And then we touched on that one. And so we had a question that was interesting, because I don't really know, but what is the research on why HPV persists despite LEEP in older women?

Ivy Wilkinson-Ryan:

Right? So this is... Go ahead.

Angelica Ladd:

And then the second part was, what should our sexual partners now?

Ivy Wilkinson-Ryan:

That's a great question.

Angelica Ladd:

That's a [inaudible 00:46:35] question.

Ivy Wilkinson-Ryan:

And so, HPV is the worst, it's such a pain in the cervix. It's such a pain. And so there's a lot of patients for whom, they get it, their body hangs on tight, and then they can't kick it. So you get to LEEP, which is supposed to excise it, and still you're still testing positive for HPV. And the only modifiable risk factor is to quit smoking, if you're a smoker, but otherwise, it's like not super helpful risk factors, like old age, where you're, "Thanks a lot, I can't do anything about that." And so why it hangs out in some women, like why you'll have an HPV positive pap smear after Leep, in some women, and then in some women, the LEEP is effective enough to kick it, we do not understand.

Angelica Ladd:

That's interesting. And then, could we just run through what the screening tests are for the cancers? Just one more time, just so we have a good grasp. So like pap smears are for cervical cancer, right?

Ivy Wilkinson-Ryan:

Yeah.

Angelica Ladd:

Okay. And then ovarian cancer, there's no good screening.

Ivy Wilkinson-Ryan:

No.

Angelica Ladd:

Okay. And then-

Ivy Wilkinson-Ryan:

No. So for ovary cancer and endometrial cancer, in the general population, there's no good screening. Sorry. The chat just came up asking about the partners, and, sorry, I forgot the second half of that question. What to tell your partner? Whatever you want, which is to say that HPV is so common that if you are of reproductive age, if you've had intercourse, you have likely been exposed to HPV. So it is responsible for what we call anogenital cancers, so anal cancer, you can rarely see penile cancer, you can see them head and neck cancers from it. And those are the cancers that, obviously, affect male

partners. It's really rare to transmit it through female same sex partners. And so what you tell your partner is sort of an individual choice.

We with gonorrhea and chlamydia, they can cause really acute illnesses, and for our patients get really sick, whereas HPV does not cause those problems. And so the other thing is that it can come and go, and so it's like if you had an HPV infection once, if it showed up in your pap smear once, but it never shows up again, do you have to tell your partner you had HPV? We really don't totally understand. And so we don't have like a universal recommendation for what you tell your partner. I think that's really a personal decision. Whereas like, I would say like, "Yes, if you know you have active chlamydia, you need to disclose that to your partner." It's not quite the same for HPV.

Angelica Ladd:

All right. Do we have any other questions that are from the audience? I'm not seeing any.

Ivy Wilkinson-Ryan:

Angelica, I did want to touch onto the genetic part, because-

Angelica Ladd:

Please.

Ivy Wilkinson-Ryan:

... I sort of kept referencing the genetics, and I realize I didn't take a minute to really dive into that. And so there are genetic mutations that you can inherit or hand down in a family that will predispose you to ovary cancer or uterine cancer. And they can be sort of hard to detect, but it is worthwhile talking to your primary care doctor about, if you have a strong family history of cancer, if you have a lot of cancer in your family, whether or not you qualify for genetic testing. And the way we do that, at least Dartmouth, is you meet with the genetic counselors, they go over with you your family history, what it makes them test for. And they'll talk to you about the implications of genetic testing. So what that means, for instance, if you want to apply for life insurance, after you have a genetic test that comes back with mutation, make sure that your insurance will pay for it, and then they'll go ahead and run the test.

That is the appropriate way to get genetic testing. Right now, there's all those direct to consumer genetic testing is 23andMe, and I can think of a couple of other private companies that offer some, like they'll check some BRCA. They don't do a good enough job to say that you got good genetic testing, and you don't need to worry. They really only test for, I think, it's the three most common BRCA mutation, but it's not enough. If you have a family history of ovary cancer, it's not good enough genetic testing to meet standard of care.

And so the way to get genetic testing is to talk to your primary care doctor, your OB/GYN or whoever provides most of your basic healthcare, have them go through your family history with and either... So there are algorithms for who gets genetic testing.

Angelica Ladd:

Great. Thank you. I think you covered a lot of really important information tonight, Dr. Wilkinson-Ryan, thank you so much. If we don't have-

Ivy Wilkinson-Ryan:

Absolutely.

Angelica Ladd:

... any other questions tonight, again, you have the opportunity to ask questions through the survey. If you submit the survey and if you're looking at it and you think, "Oh, I wish I had asked that," you can submit your questions through the survey, and we'll get that answered for you, and put it on a Q&A on our web page. I do owe you the link to that webpage, so let me grab that for you. And Dr. Wilkinson-Ryan, do you have any final thoughts before we sign off tonight?

Ivy Wilkinson-Ryan:

I don't. Thanks everyone for joining.

Angelica Ladd:

Awesome. So thank you so much everyone. I'm putting that link right in the chat. If you want to copy that, that's where you can find this video later this week. We will have it posted on that webpage, also on YouTube. And we're so grateful for your time tonight. Thank you so much for coming. Thank you, Dr. Wilkinson-Ryan for your time. We appreciate you and your expertise. Thank you so much.

Ivy Wilkinson-Ryan:

Thanks everyone.

Angelica Ladd:

Have a great night-

Ivy Wilkinson-Ryan:

Thanks, Angelica.

Angelica Ladd:

... everyone.