

Scott Redding: Welcome to the 3Ps of Cancer podcast where we'll discuss prevention, preparedness, and progress in cancer treatments and research. Brought to you by the University of Michigan Rogel Cancer Center. I'm Scott Redding. In this special episode, Michigan Medicine social media strategist Ed Bottomley sits down with gynecologic oncologists, Dr. Crapanshu Uppal and Dr. Rebecca Liu to talk about ovarian cancer.

Ed Bottomley: I'd like to introduce you to our panelists, Dr. Rebecca Liu and Dr. Crapanshu Uppal. If you guys could just give me a few seconds on your expertise in this field, Dr. Uppal?

Dr. Crapanshu U: So I'm one of the GYN oncologist. I'm an associate professor at the University of Michigan and I'm also a co-director for Michigan Oncology Quality Consortium, which is one of the collaborative quality improvement effort by the university to improve the quality of care for ovarian cancer. So I'm also associated with the medical school. We also run the fellowship in training the new generation of GYN oncologists.

Ed Bottomley: Fantastic. Thank you. Dr. Liu?

Dr. Rebecca Liu: I'm also a GYN oncologist at the University of Michigan. I've been at University of Michigan since 1999. I practice both at University of Michigan and St. Joseph Mercy Hospital and do research in ovarian cancer. I also work on the Michigan Oncology Quality Consortium with Dr. Uppal . We try to involve all of the GYN oncologists in the state to improve the quality of care for ovarian cancer patients. So I hope that you will participate with us.

Ed Bottomley: Thank you. Well I'm excited to have both of you with us here today. Let's go straight into the questions. So our first question, a straightforward one here, what is ovarian cancer? Perhaps it isn't a straightforward one. What is ovarian cancer?

Dr. Rebecca Liu: I don't think it's really that straightforward. There are many types of ovarian cancer. There's sort of a continuum. Some ovarian cancers are diagnosed in very young women. In their teens, 20s and some are diagnosed in women who are post-menopausal. When we think about ovarian cancer, I think most people think about epithelial ovarian cancer diagnosed in women around the age of 60 to 65. And it's also known as the silent killer. Which is a good opportunity to talk about symptoms of ovarian cancer. Most people call it the silent killer because the symptoms of ovarian cancer are very vague. People may have kind of bloating, indigestion, pelvic pressure. Maybe some sort of urinary problems. Which is everybody's had those at one time or another.

Dr. Rebecca Liu: The key with ovarian cancer is that these symptoms persist. And I like to think about this sort of how the people in the airline industry have a checklist when they go through their flights. And if anybody thinks that something is off, they stop and check it. So I think that people should really do this for themselves. You

know your own body. If you think something is off and your whatever doctor you see think ... says there's nothing wrong but you still feel like something's off, check it out. Go to your gynecologist.

Ed Bottomley: Thank you for that. Dr. Uppal, anything to add?

Dr. Crapanshu U: No, I think Dr. Liu's covered this but I think one thing I would like to add though is that as time goes by, we're recognizing that ovarian cancer, even though as a term, refers to one thing as we know it, but when you dissect it out, it has so many different entities to it. And then that also impacts on the survival where some cancers behave much more aggressively, whereas the others do not. And then there's another component of it where now we're recognizing that there's a large portion about one in five of ovarian cancer patients have a genetic component. So again, there are different reasons why women get it and this is ... even though it comes under the umbrella of the word ovarian cancer, these are multiple types of diseases which we lump together.

Dr. Crapanshu U: But more often than not, epithelial ovarian cancer is the one which we know as most often the most aggressive cancer.

Ed Bottomley: Thank you for that. So the second question we had, I feel like we've answered it a bit. What are the symptoms or signs? Do you have anything to add to that beyond what Dr. Liu said?

Dr. Crapanshu U: Yeah, no, I think the main issue here is that there have been studies done on this actually where we've looked at symptoms. Most notably Dr. Barbara Goff from Seattle where they looked at the symptom inventory on how many times the women have the symptoms and they came up with the answer that more than 12 times if you have abdominal pelvic pains, sensation of bloating. If you eat and you feel like you're full already. And these symptoms are happening more than 12 times in a month, this is suspicious for ovarian cancer. Now if somebody's had a history for a very long time for these symptoms, they might have another issue, but if you find these symptoms just like Rebecca said, even if your primary care doctor or the person you're seeing thinks that no further evaluation needs to be done but you know your body and you think that this needs to be escalated and further testing needs to be done, I think seeking another opinion is a right thing to do.

Ed Bottomley: Thank you. The next question that we have up, if I have symptoms, do I go to my gynecologist?

Dr. Rebecca Liu: Yes. So, we're subspecialists and the gynecologists are accessible to everybody. Gynecologists are accustomed to doing pelvic exams. Unfortunately, we don't have a good screening test for ovarian cancer yet. There is no pap smear that diagnoses ovarian cancer. There is no mammogram that we have. So the best thing that we have is a physical exam with your gynecologist. A pelvic exam. Now, many women think that after they're finished having children, they don't

need to go to the gynecologist anymore. But please go every month. I mean, every year. Nobody wants to go every month. Every year.

Ed Bottomley: Thank you.

Dr. Crapanshu U: Yeah. I think in the community, if the gynecologist is not available, the primary care doctors do take on this role and do a wonderful job. And they're trained to look for these diseases. So I think the short answer is yes.

Ed Bottomley: Okay. Thank you. Now, you touched on screening options. Could we talk about that a little bit more? What options are there if the screening options are limited?

Dr. Rebecca Liu: [inaudible 00:06:42].

Dr. Crapanshu U: Yeah. So I think for screening, before I go into the details of the screening, I think you have to look at why do we screen for cancers, right? And what is the good and the bad of the screening, and I think that's the fundamental reason why we don't have a good screening test for ovarian cancer. When we're trying to screen for any cancer, what we want is a test which is accurate. Meaning, it's picking up the people, those who have cancer. And at the same time, we want a test which is not picking up people who do not have the cancer but the test is labeling them that maybe you have ovarian cancer. The unfortunate reality for ovarian cancer is that all the things we have tried in terms of screening, pick up a whole lot of women and label them as potentially having ovarian cancer.

Dr. Crapanshu U: And then we start on investigating and sometimes doing surgeries on these women, and eventually end up hurting more than helping in finding the ovarian cancer in the specific cohort of women [inaudible] label as possible ovarian cancer. So that's where the problem lies in. So we've had multiple attempts, most notable the test which women might have heard about is a ca-125. Now we use this test in treatment all the time, but as a screening, this test has not been very helpful. You'll end up about one in a hundred women will have a elevated CA-125 during the time of their menses or they have an infection or any other reason the test could be elevated. And now you're labeling them or you may have ovarian cancer and they might end up getting surgery. And as I've mentioned, that could be a problem.

Dr. Crapanshu U: So there have been other things which [inaudible] primarily another test called HE4. There's been another ... One other big thing is the pelvic ultrasound which is being looked at for screening. And multiple trials. Most noticeable one which was done in the United States called the PLCO trial was one of those trials where they looked at the CA-125 and ultrasound to screen for cancers. And again, the result was the same where more women underwent surgery but it didn't help in terms of the screening. So it's a long answer in saying, "No, we don't have a good screening test at this point of time." The Society of GYN

Oncologists, The American College of Obstetrics and Gynecologists does not recommend screening in women who are low-risk.

Dr. Crapanshu U: Now there's a whole [inaudible] category of women who are high-risk and we can talk about that later, where screening is indicated. But I think if you have no family history and no genetic predisposition of developing ovarian cancer, screening at this point of time is not recommended.

Ed Bottomley: Thank you for that. Anything to add, Dr. Liu?

Dr. Rebecca Liu: Well, I think that you touched upon this. If someone has high-risk for ovarian cancer, then we need to be more vigilant about looking for ovarian cancer in these patients. And those would be patients with a strong family history of ovarian cancer. Basically, all patients with ovarian cancer have genetic testing. Genetic testing means not only checking their blood for a germline mutation. That means you're born with this mutation and it makes you more susceptible to breast cancer. Usually breast and ovarian cancer. But now we know that we can test the tumor also for these mutations and if you have a mutation in the tumor, it gives you a whole nother avenue of treatment options. So it's very important that all of our patients get tested. Genetic testing. So those are the patient's family members of these patients should be treated in a separate category than the general population.

Ed Bottomley: Thank you for that. The next question we have coming up, are there different stages of ovarian cancer?

Dr. Rebecca Liu: Yes. All cancers have stages one, two, three, four. Usually stage one means that the cancer is limited to the primary organ. So ovarian cancer is limited to the ovaries. Stage two means it's spread to the pelvis. Stage three means it's spread into the abdomen. And stage four means it's gone to the liver or even the lungs, or further. Unfortunately, many times we see patients who come to us with stage three or four disease already because the symptoms are so vague and we don't have a screening. I would say that when we find patients with a stage one cancer, it's typically in those families with a family history and we are ... maybe they're having a prophylactic surgery. And then we found it by mistake. It's not very often that we find an early stage ovarian cancer.

Ed Bottomley: Anything to add, Dr. Uppal ?

Dr. Crapanshu U: No. I think this is ... most of the cancers have this similar structure of staging. Starting in the organ to going in other places. And as Rebecca mentioned that the unfortunate reality in ovarian cancer is most ... like about 75% of the patients are stage three or above. And that's something which is directly related to the fact that we don't have a screening test.

Ed Bottomley: Okay. Thank you for that answer. Next question we have up with regards to diagnosis. If I do have an elevated CA-125 level, does it always mean you have ovarian cancer? What else could it be?

Dr. Crapanshu U: Yeah. I imagine a few possibilities of that. Number one is that why was a CA-125 test done? Right? Was it done in hopes of screening for ovarian cancer? Or was it done for another reason? So that would be important. But then if it's elevated, it has to be put in the context of family history which will put you into a higher risk. But otherwise, there are a host of different reasons why CA-125 could be elevated. Anything which will irritate the inside lining of your abdomen will elevate the CA-125, whether it's an infection, endometriosis. Patients, even some of them who have fibroids which are growing could elevate CA-125. So it's a very non-specific test. It just tells you there is something going on in the abdomen. That something could be anything, not specifically ovarian cancer.

Dr. Rebecca Liu: I really want to reiterate that. It's very important that people don't think that CA-125 is a magic test, because pregnancy can elevate your CA-125. Any kind of liver disease.

Dr. Crapanshu U: Liver disease.

Dr. Rebecca Liu: Basically any kind of -itis, any kind of infection in the belly will make your CA-125 go up. So I know a lot of people put a lot of stock on that number, but it's not black and white. It's kind of a gray issue.

Dr. Crapanshu U: Yeah.

Ed Bottomley: Thank you for reiterating that. Thank you. Next question we have up. Now you've touched on genetic issues a few answers ago. This question is, if there is a family history of ovarian cancer, should I have genetic testing done?

Dr. Rebecca Liu: The first person to get tested should be the person who had the ovarian cancer. If that person is negative, then all the relatives, it's less likely that the daughters and the sisters would have that mutation. So that's the most important thing. If we're unable to test that patient, then we can do a family pedigree and basically take a very detailed family history and then determine by the results of that, that person should have blood testing or whatever.

Dr. Crapanshu U: Yeah. I think one of the other things I want to add to this question about genetic testing is that over a period of time our understanding is that one in five epithelial ovarian cancer, which is the most aggressive cancer, one in five of those patients when you screen them, will have a genetic component. So then we start drilling down into their family members and we'll find a lot of patients who have the same mutation. Specifically, BRCA1 or 2. Then we have an option or now they can undergo surgery. So either you remove the breast or remove tubes and ovaries when they're done with childbearing. When they decide with their provider the time is right. We can prevent a lot of cancers from happening.

The other thing I want to add here is the question about genetic testing is we're in interesting times because the FDA just approved some of the kits for California where you can do BRCA1 and 2 genes yourself. There is a lot of discussion happening in the community as to what does it all mean.

Dr. Crapanshu U: But our stand is the same that if you think there's a family history, there's a strong family history of ovarian cancer, talk to your doctor. Talk to your provider. And as Rebecca mentioned, going in and drilling down into the details of the family history and talking to a genetic counselor to figure out what tests are right. Because BRCA1, 2 are just the tip of the iceberg. There are other genetic tests which are available which predispose you to these cancers. So I think those are available to you because they are approved in the FDA and you can do those testings. But if those are negative and you have a family history of ovarian cancer, that doesn't take you off the hook. But it could be other things you need to be looked at and I think discussion with your doctor is important for that.

Dr. Rebecca Liu: I think it's really important for people to see a genetic counselor because if you have a test result, somebody needs to explain it to you. You know? It's really unhelpful if you have a yes or no. You don't know how to interpret it. So it's very important to speak to a genetic counselor.

Ed Bottomley: And I feel like this next question kind of flows perfectly on from that. If I have BRCA1 or 2 genes, should I get a hysterectomy if not diagnosed with ovarian cancer?

Dr. Crapanshu U: I think if you have a BRCA1 or 2 gene, you should be hooked in the system talking to an expert who takes care of patients who have BRCA1 and 2 genes. These discussions are often very nuanced. I mean, the risk of cancer is not a static thing. As you age, your risk goes up. And the risk is different for BRCA1 and BRCA 2. And having a discussion with a team which has the expertise in dealing with these issues will not only help you make this decision, but can also help you fulfill some ... if you are at an age where you are hoping to have children, then you can work with this team and see what is a best time where you can reduce your risk of having cancer but also fulfill your fertility.

Dr. Crapanshu U: Other having a risk reduction mastectomy is an option. But again, having a discussion with this team is super important. So answer of your question, should I be getting hysterectomy, that's a question we don't have the answer yet. That's a much more detailed question. Even when we do propose surgeries in patients with BRCA1 and 2, we usually remove tubes and ovaries and leave the uterus. However, there's some new research which shows that they have increased risk of endometrial or uterine cancer. But we don't have any Society recommendations on this. This question is actively being debated right now in our Society to come up with a question of whether hysterectomy is worth it or not.

Dr. Rebecca Liu: I will just add that our team is taking care of patients with BRCA1 and 2 mutations or even other mutations that predispose you to ovarian cancer are multidisciplinary teams. So they're surgeons and they're medical oncologists and radiation oncologists. And there's a whole team. Plastic surgeons. It's not just one person you'll see. You will need to see a whole team and get all of your options so they can make a good decision .

Dr. Crapanshu U: Yeah. And then the other ... last point I would like to make with BRCA1 and 2 is breast and ovarian are the most common cancers. But that also predisposes BRCA predisposes you to other cancers as well. So we have a focus in ovarian cancers so we always think about ovarian cancer, and we are here to discuss ovarian cancer, but we should not forget that these mutations predispose you to gastrointestinal cancers, for example pancreatic cancer. So that just highlights the importance of having a team which is used to taking care of these patients.

Ed Bottomley: Thank you. Thank you for that. And the final diagnosis question or the last one that we have up right now. Life expectancy. How long would I have to live after being diagnosed?

Dr. Crapanshu U: That is a very [inaudible 00:19:03].

Dr. Rebecca Liu: I'll give it back to you.

Dr. Crapanshu U: Yeah. I think it ... Let me circle back to the statement we made earlier, right? Ovarian cancer is not a one disease. So I think if you have a cancer which is not as aggressive and was diagnosed at an early stage, whether it was picked up because you were going to your doctor and they felt a mass during the exam, or you were having an ultrasound for something else, or it was caught at a later stage but still not an aggressive cancer, or you underwent the right treatments. The life expectancy could differ a lot. Rebecca could tell you. She's been practicing a lot longer than I, but I have inherited some patients from a few of my partners. They've had ovarian cancer and they're alive at 10 years, 15 years.

Dr. Crapanshu U: So it's not ... even though the numbers on the websites and everything will give you a summary that the statistics [inaudible] five year survival of ovarian cancer is 40%. That can be very misleading, and frankly, disheartening. Because this number includes a lot of women who are diagnosed later in the age, when they're older, and they are not able to ... they have other comorbidities. They have heart disease. If somebody is in their 80s and 90s, their risk is different than somebody who is diagnosed in their 30s and 40s. So it's difficult to put all this together. The number 40 to 45% in five years is a very oversimplification of the facts. So, I don't have a good answer to that question but I think it varies.

Ed Bottomley: You know, I think that is a good answer. And I don't feel like you should always be on the hope for bespoke answers to some of these very, very specific questions. But I really appreciate these answers.

Dr. Rebecca Liu: I also would reiterate that you will see all these statistics and numbers on websites, but it's not one size fits all. There's a kind of a continuum and we are always discovering new treatments. For example, now, immunotherapy is very hot. We didn't have that five, or 10 years ago, and I think we're starting to treat ovarian cancer more like high blood pressure. It's a chronic disease. We keep treating it. It comes back, we treat it again. We might have another treatment. We might have a clinical trial. And so the treatment now is different than it was five years ago, even. So ...

Ed Bottomley: Thank you. And I think you read my mind a little bit because we're going to move on to treatment options. What treatment options are available?

Dr. Crapanshu U: So, [inaudible] start with this. One of the things which most of my research is in looking at whether women with ovarian cancer get the right treatment when they get diagnosed. The unfortunate reality in the United States is only about 60 to 70% of the women get the right treatment. So that's something we can make a lot of difference, because if everybody got the correct treatment, we would have a bigger chunk of women who would be cured from the disease right up front. And even when the cancer comes back, having had the right treatment before pushes the recurrences farther. So it puts you at a better track.

Dr. Crapanshu U: In general, for a cancer which is the most common scenario we see is generally women in their 60s to 70s. They would have cancer usually in the stage three disease. What they need at that time is a combination chemotherapy and surgery. So what we found in our research is sometimes they get the chemo but not the surgery. Sometimes the surgery is done but not the combination chemotherapy. They only get one drug. Those are the things which we can make a huge difference with by giving the right treatment. But generally, it's a combination of treatment and surgery. The other thing I want to emphasize in the treatment of ovarian cancer is who treats your ovarian cancer matters.

Dr. Crapanshu U: We, Rebecca, and I and our partners here in GYN oncology are obstetrics and gynecology trained specializing in only treating cancers in women. So we don't do anything else but treat these cancers and there's data to support that women who actually see GYN oncologists during their treatment have better survival. So even if they're getting treatment from closer to home, if there's not a GYN oncologist available, the guidelines both from the American Society of Clinical Oncology and The Society of Gynecologic Oncologists are that at some point, a consultation with a GYN oncologist should have happened. And then they could get chemotherapy closer to home with medical oncologists. But the surgery part, we're especially trained to do these surgeries. Sometimes these surgeries last for six to eight hours and how much effort is made in these surgeries directly translates to the survival in these patients.

Dr. Crapanshu U: So seeing a GYN oncologist and also participating in a discussion with your doctor, am I getting standard of care? And this line is relevant to any cancer. Am

I get the standard of care is something which people can do to improve their chances in getting treatment.

Dr. Rebecca Liu: I think we should highlight that there are websites where people can check to see that they're getting the standard of care treatment through the National Cancer Institute. Through the NCCN, there's a link for patients. There's a link for physicians. And they're kind of hyperlinks. So it will take you to other websites. If I have this, I should be getting A, B, C, D.

Ed Bottomley: Great. And for those watching live will get those links and post them up afterwards.

Dr. Crapanshu U: Yeah. And sometimes what is listed on that document may not be the right thing for you. But putting it out in front of your doctor and having a discussion, why am I not getting this, is helpful, because then you get the satisfaction that okay, my physician has looked through everything and they've made a choice of doing this because maybe my kidney is not doing as well as other people so that's why they decided to do a different kind of chemotherapy. But I think as patients we should ... they should not shy away from asking these questions and holding us to a higher standard. Are we doing the standard of care or not?

Ed Bottomley: Great. Thank you. Another treatment question here. With newer options, how do you treat ovarian cancer as a chronic disease as you mentioned?

Dr. Rebecca Liu: Well, we have many treatment options for chemotherapy and it's not a black and white question. I guess I'm going to revert back to our discussion about genetic testing, because that's most relevant. Since 2007, the National Cancer Institute has asked us to refer all patients with ovarian cancer to a genetic counselor. But only about one in five women are referred to a genetic counselor. We know that. But in the last year, some new treatments have opened up for patients with BRCA1 and 2 mutations that are called PARP inhibitors, and now that we have different treatment options for patients with these genetic mutations, more patients are getting tested, okay? So, these treatments are open to patients who have mutations genetic, germline mutations and also somatic mutations in their tumors.

Dr. Rebecca Liu: So you know what? If you didn't get tested, your tumor didn't get tested 10 years ago when you were diagnosed, we're going to test your tumor now because you might be eligible to be treated with these new medications that are oral chemotherapy agents. There are also immunotherapy clinical trials that are open, and this is really ... I think the new area of treatment for all cancer patients really retrain, reeducating your immune system to fight your cancer. It's, I think, very exciting.

Dr. Rebecca Liu: And a lot of these are oral medications that people can take at home. Sometimes they're taken in conjunction with regular chemotherapy. So, it's very nuanced. There are many clinical trials open. Again, there's another website.

clinicaltrials.gov which we will post. But it will list, you can search for your cancer type. Where you live. How far you're willing to travel. And then I guess we can mention different kinds of clinical trials. There are ... it's kind of confusing for people. So there's phase one clinical trials which means they're testing for side effects of a new drug. They might help you. We don't know.

Dr. Rebecca Liu: Phase two trials means that there's activity probably in your drug. We really want to make sure that it's going to work in ovarian cancer. Phase three trials are the best because that means we have a new drug and it's going up against the gold standard. So if anybody finds a phase three trial that they can get into, you need to try to get into that. So ...

Dr. Crapanshu U: Yeah, so I just want to clarify something about when we use the word chronic disease. I don't want people to think that ovarian cancer is treated just like diabetes. It's much more serious than that.

Dr. Rebecca Liu: It is.

Dr. Crapanshu U: But we often, in our conversations, we'll call it a chronic disease which is in some way, we're a little optimistic about it. When you go and talk to people maybe 20 years ago and you mentioned the word ovarian cancer, mortality was very, very high. Most women would not live as long as they do now. And partly because, as Rebecca mentioned, we have multiple different kinds of treatments. The drugs which have come up. So they go on living longer. Now the best thing is if they didn't have this cancer, but sometimes we get stuck with the hand we are dealt with. But even in those circumstances, if they're taking the drugs orally or once a week, they're coming and getting the chemo, and they go on and they can carry on for a number of years and do things which are important to them in their personal life, it gets labeled as something you live with. That's what the definition of a chronic disease is.

Dr. Crapanshu U: But two and two are not equal. We recognize that. But I think still, we find this exciting that women with ovarian cancer can go on and live longer than what they did before.

Dr. Rebecca Liu: I mean, I guess I should clarify because I'm that one [inaudible] treated like a chronic disease. I mean, the best case scenario is you treat somebody and they're cured.

Dr. Crapanshu U: Yes.

Dr. Rebecca Liu: You don't see the cancer. The next best scenario is you treat somebody and their disease is stable. It doesn't change, but they can still live their life and they have a good quality of life. They can do the things they want to do.

Dr. Crapanshu U: Absolutely.

Dr. Rebecca Liu: If you're treating somebody and their cancer is not responding to the treatment, that's when we need to change. Yeah.

Ed Bottomley: Thank you. Thank you for that. One more treatment question. After treatment, what's the likelihood of ovarian cancer recurrence?

Dr. Crapanshu U: High. Very high. But at the same time, people ... so, when somebody gets the treatment, they've gotten the right treatment or they've gotten the standard of care treatment, what we see is that at five years, for somebody with advanced cancer, somewhere from three to four women would be alive and an even smaller fraction would be completely cured. So it is really important to continue following up with your doctors so they can keep an eye at it and make sure that if the recurrence was discovered that it's discovered early enough so that the treatment can be started. But it does put you at a difficult place, right? Because you're living in the shadows of this disease where you're always thinking, "Is it going to come back?" So I tell my patients all the time that for our perspective, when we are done with the treatment, we believe that everybody is cured until they are not.

Dr. Crapanshu U: Right? Because otherwise it becomes very difficult to carry on with your life thinking that this is going to come back.

Ed Bottomley: Thank you for that.

Dr. Rebecca Liu: We do keep a really close eye on patients, so after they finish their initial treatment, we'll see them very often, every three months. And then as time goes on, the risk of a recurrence drops off so we will space out their appointments and we try to accelerate a little bit when we reach different milestones. So, but we keep close contact with our patients.

Ed Bottomley: Thank you. Thank you for that. We're going to move on to some more of our questions now. What kinds of support groups are there for people with ovarian cancer?

Dr. Rebecca Liu: There are multiple support groups. There is ... I think I'll mention MIOCA. Michigan Ovarian Cancer Alliance. It was started by a patient at the University of Michigan who was a nurse and her daughter, Pam Dahlmann is also a nurse, and they started this enormous network, I think, that [inaudible] not just University of Michigan patients, but patients from all over the state. And they've had information courses for patients that are free of charge will have support. People who come and give talks about treatment options. Genetic counselors have given talks. We'll have talks about alternative medicine at these meetings. And they meet monthly.

Dr. Rebecca Liu: I know there's a [inaudible] club meeting on the other side of town, so there's multiple groups, but I think it's really important for patients to feel like they're

part of a community and they're not going through this process alone because it's very difficult to go through alone and they need the social support of people that are going through it at the same time. Not only their family members and friends but other patients. I think it's very, very helpful for them.

- Ed Bottomley: Thank you for fielding this broad range of questions. The next one that we have up, are there ways to prevent ovarian cancer?
- Dr. Crapanshu U: Yeah. I think one of the good things about preventing is obviously we don't have to deal with any of this disease related issues. And when I say you can break this question down into two different categories. One is general lifestyle things that you can do which will reduce your risk for all cancers. And then there are things you can do specifically in ovarian cancer. So I can answer both of them. The lifestyle things which are in general keeping your weight in check. Because there was a report just now recently that in women, the overweight is becoming the number one reason of developing more cancers, even more so than smoking. So that's number one. Regular exercising. Maybe rigorous exercising for about 30 minutes.
- Dr. Crapanshu U: Something which makes you wind it. You can't have a conversation. So that kind of exercise. But after talking to your doctor if it's safe to do so. And then eating healthy, going through some of the websites [inaudible] NIH and seeing what that entails. It's a huge conversation is general. But all those healthy lifestyle issues will reduce your risk of developing any cancer. But ovarian cancer specifically, we know one intervention which is definitely helpful is oral contraceptive pills. So if you're premenopausal and there are no contraindications to starting oral contraceptive pills, then oral contraceptive pills can reduce your risk of ovarian cancer.
- Dr. Crapanshu U: The pills make ... the ovary forms a cyst when it ovulates every month and the oral contraceptive pills by design reduce that and have ability to reduce, on a population level, the ovarian cancer. So that's one something specific. Do you want to add something other for ovarian cancer prevention?
- Dr. Rebecca Liu: Well, I would say, people might say, "What makes me at high-risk? What makes me at low-risk for ovarian cancer?" Basically, the less you ovulate, the better for ovarian cancer risks. So birth control pills decreases your number of ovulations you have. Somebody, Andy Berchuck at Duke did a study. He counted number of lifetime ovulations and if you had many more lifetime ovulations, you were at a higher risk for ovarian cancer. So if you've had more children or if you breastfeed that also decreases your risk of ovarian cancer because it stops ovulation. For some reason, tubal ligation also decreases your risk. We don't really know why but now we think that ovarian cancer might start in the end of fallopian tube, so removing the fallopian tube has something to do with it even if the ovary is still there.

- Dr. Rebecca Liu: And all of the healthy lifestyle choices you said. Really reducing your weight is key.
- Dr. Crapanshu U: Yeah. I think that Rebecca brings a really important point that women who ... this is applicable to a very specific population. If you're done with childbearing and you were having a C-section and in the C-section you were asked a question, "Do you want to have more children?", and the answer is no, in the past we would tie the tube. Now we just take the entire tube out. I think that's something which we think we reduce the risk of ovarian cancer because there's some newer research which is coming up which is showing that a lot of these ovarian cancers actually start in the tube. So this is still an area of active investigation.
- Dr. Crapanshu U: We don't yet recommend that women, once they're done childbearing, go and electively remove their tubes. This is still an area of active investigation. There are no recommendations on that yet, but definitely in the high-risk population, if you have a strong family history, again, talking to the genetic counselor, you will definitely be steered towards a direction where tubes and ovaries are removed once you're done childbearing. So I think these are all possible ways of reducing ovarian cancer.
- Ed Bottomley: So you both mentioned weight as a prevention. Can it affect your recovery as well?
- Dr. Rebecca Liu: Recovery from treatment, yes. I think that obesity is associated with so many different things that affect your health. High blood pressure. Your risk of heart attack. All these other things. This all contributes to how we can treat you. Our treatment is sort of limited by what you can tolerate, physically and emotionally. But physically, also. Some of the drugs affect your heart. So if your heart is not in good condition, we can't give you that chemotherapy. We have to consider all the different parts of you. Not just the cancer. We have to consider you as a whole. So, even just recovery from surgery is really improved if you have good physical health going into surgery. We know that if you are a walker and you regularly walk at even just two weeks before surgery, you're going to do better with surgery.
- Dr. Rebecca Liu: So being physically active is always a plus. Reducing your weight. There's some ... some people ask, "Is sugar bad? Does cancer like sugar? Is it okay if I eat candy?" I think that everything in balance is a good rule of thumb.
- Dr. Crapanshu U: Yeah. I think the obesity is a huge topic in this setting, but I think overall, I would say we poorly understand the obesity. We don't know why some people gain more weight than others. That's an area which is heavily being investigated right now that how we can stop the obesity crisis we have. But the short answer is, yes, those who are already at a higher weight, at every stage of the treatment, it is slightly more difficult for us. That doesn't stop us from doing our best, but

overall, if you were to compare patients in terms of their surgical outcomes, patients who are overweight, there's higher risk of infection in the incisions. Surgery in general is a little bit more difficult.

Dr. Crapanshu U: So that does affect their outcomes. Later on in the treatment when we have chemotherapy, then it is really important that ... some of the work done in the University of Michigan by Dr. Griggs, who's one of the medical oncologists here, showed that patients who were higher weight got less chemotherapy because the protocols which had a weight restriction or limit were not giving the entire amount of chemotherapy which was recommended for these patients.

Dr. Crapanshu U: So there are lots of nuances in this. But yes, that can negatively affect you. So it should stay on people's radar in terms of prevention that by taking an active approach in their weight management, they can reduce risk of lots of different diseases. Not just ovarian cancer.

Ed Bottomley: Thank you for that. The next question. Do supplements or vitamins help reduce the risk of getting or having a recurrence of ovarian cancer?

Dr. Crapanshu U: Well, do you mind if I take this one?

Dr. Rebecca Liu: No. Please.

Dr. Crapanshu U: Yeah. You know I say this because this is a question which is very ... I'm very passionate about this subject. And the reason for this is, that the evidence supporting this is it's close to zero. There are two aspects to this. Number one is, I would recommend people who are really interested in knowing about this conversation is Frontline from PBS did a huge one hour documentary on supplements in the United States. It's not an FDA regulated market. And specifically in that commentary, there were two issues they mentioned.

Dr. Crapanshu U: Number one was when you're taking supplements there was an issue that are you getting the supplement which they are claiming is in there? And the second thing was the efficacy. The dosing. Especially in vitamin D, some of the brands which were selling it had wide ranges of it. The other issue is, we have not had any study which shows that by taking these vitamins and minerals and that people have reduced the risk of cancer. As a matter of fact, study after study which has come out has shown that these interventions are not helpful. Now, if somebody is deficient in a vitamin because of a reason, because the diet they choose or maybe they have some GI malfunction and their physician thinks that they should be supplemented for that vitamin, I am not talking about that population.

Dr. Crapanshu U: I'm talking about in general, people who are able to eat a healthy lifestyle. So I think the last thing I would say is, that if you have a cancer, and if we presumed that your cells in your body did really well with vitamins, so will the cancer cells.

You're feeding them in addition to yourself. So, no matter how I look at it, I personally cannot come to a conclusion that these things are helpful. There are no recommendations from our societies that people should take supplements to prevent or treat cancer with minerals and vitamins. So, I am not in the favor of that. But I think this is a question which will surface again and again and there's an active ... Yeah.

Dr. Rebecca Liu: I think it's very confusing to people because when they get diagnosed with cancer, all of their friends and family will say, "Oh, I heard you should take this, this, this and this." And if you have an inflammatory state, you're more likely to have cancer. And I do think that inflammation is associated with cancer. But it's important to recognize it. We don't have a FDA for herbal supplements, okay? Even if it says you're getting curcumin, you don't know what the soil conditions were. What it's contaminated with. It's not regulated the way other medications are regulated. So it's always a better idea to get these nutrients through your food than by taking supplements.

Dr. Crapanshu U: Yeah. So I usually tell my patients that if you want to do and you think that this is important to you, don't spend a fortune on it. Make sure you're getting it from the right source and make sure that they're not making you sick. Anything, including other supplements which Rebecca mentioned in treatment of cancer. Sometimes we'll get questions like, "I've heard online that this particular thing is really good for treating cancer." I don't know. We don't have a study to support for or against. So in that setting, if they're taking it and they feel good, I just tell them that if you start developing side effects which were not in line with the chemotherapy we are giving you, then obviously the next thing to be blame would be the possible supplements. So yeah.

Dr. Rebecca Liu: It's also important that you tell your doctor what you're taking, because some of the things, if you're taking very high doses of antioxidants, it may counter at the effect of the chemotherapy.

Dr. Crapanshu U: That's really [crosstalk 00:44:00].

Dr. Rebecca Liu: If you're taking a lot of garlic and fish oil, those are blood thinners. We need to know that you're doing that before you go to surgery. So always bring your bag of pills to the doctor's office so we can look at them.

Ed Bottomley: Thank you. Thank you for that. And the next question we have up, can you get pregnant after diagnosis and treatment?

Dr. Crapanshu U: Yes.

Dr. Rebecca Liu: Yes.

Dr. Crapanshu U: If during the surgery the uterus and both ovaries were not removed. In younger patients, if specifically within the spectrum of ovarian cancer, they are much more likely to have cancers which are low-grade. Not as aggressive. But even high-grade, super aggressive cancers can happen in women in childbearing age. And in those settings, sometimes it's a shared decision making on fertility preservation. One thing I would say is that if they are in this unfortunate scenario, that they have ovarian cancer and they're about to embark on a treatment, seeing a fertility expert is really important.

Dr. Crapanshu U: Now, if somebody's had the treatment, they are free of disease, they have a uterus and ovaries, even one, the next question then is, did the chemotherapy affect their ovaries in a negative way that they're not functioning? Most of the treatments we do in ovarian cancer are not as toxic to the ovaries. So generally, they recover the function and if they're menstruating, yes, they can have children.

Ed Bottomley: Thank you for that. The next question we have up, can talc powder give me ovarian cancer?

Dr. Crapanshu U: Want to go for it?

Dr. Rebecca Liu: There's a lot of discussion about this and I think we don't know. We don't really know. I think this conversation's been going on for many, many years. And I don't think anybody's really doing rigorous research on this because how can you do the research on this? You know? There's no model. You can't have a control group and you can't expose patients to talc on purpose, because we just don't know. There's not really great animal models for ovarian cancer other than chickens and any ... There's not a good way to study that. So we don't really know.

Ed Bottomley: Thank you.

Dr. Crapanshu U: Best to avoid it, I guess, would be the answer at this point.

Ed Bottomley: The next question we have up, are there environmental causes for ovarian cancer? [inaudible 00:46:37].

Dr. Rebecca Liu: I think this is all along the lines of talc. There's no specifics about this. We can't say that if you live in this area, you're in danger of having ovarian cancer. We cannot say, for example, like lung cancer, if you smoke you're going to get ... you're at high risk for lung cancer. We can't really say that about anything for ovarian cancer. We just don't know. So, you maintain a healthy lifestyle and you eat more fruits and vegetables than processed food, that's all we know.

Ed Bottomley: Thank you. What is the difference between ovarian cancer and an ovarian cyst?

Dr. Crapanshu U: It's ... I'll go back to those Venn diagram analogies like where they say, "All dogs are animals but not animals are dogs." All ovarian cancers can have cysts in them but all cysts are not ovarian cancer, if it makes sense. So you can cysts which are not ovarian cancer. You can have normal cysts. You can have cysts which are completely benign. They have no cancer in them. But regardless of that, if you have small cysts on an ultrasound which was done for whatever reason, women in their premenopausal years will always have cysts. Generally, the gynecologist will repeat the scans unless they're very large cysts. In those settings, nevertheless, I think the short answer is that they should be investigated. If somebody's done an ultrasound and there are multiple cysts, it could be a polycystic ovarian disease.

Dr. Crapanshu U: So a cyst is basically saying that there's a small enclosed area with a little bit of fluid inside of it. Now, whether it's an indication that this cyst is ovarian cancer or not, sometimes it is and when you serially follow these, you do an ultrasound and it's growing and that's how some patients get referred to us that they had cysts and they're growing and they've done a CA-125 level in this patient. It's elevated. All of these things are pointing that they might have cancer. We'll typically go in and remove these and figure out whether this is cancerous cysts or benign cysts. More often than not, they are benign which is good, but no cyst should be completely ignored. But if it's a discussion with the doctor and they think that this is not a cyst, [inaudible] be worried about, then let them take care of it.

Dr. Rebecca Liu: And all women have cysts because every time you ovulate, you make a cyst.

Dr. Crapanshu U: A cyst.

Dr. Rebecca Liu: So, it depends on the context. How old are you and where are you in your menstrual cycle and how big is it, how long has it been there. So it's a conversation to have with your gynecologist, and the gynecologist, if they need us, they will call us and say, "Could you please see this patient? Tell me what you think." And then we have a conversation about it. So ...

Dr. Crapanshu U: And we get much more alarmed when the cysts are happening in somebody who's postmenopausal because ... just because they're in that age group, the ovarian cancer is more common and after you're done ... you're postmenopausal and you're not making cysts regularly on the ovary, why should there be a cyst? So we get a lot more alarmed in that setting.

Ed Bottomley: Thank you. We're into the final 10 minutes here. So we've got a couple of questions left. This one is looking forward. Where do you see the future of ovarian cancer diagnosis in treatment going?

Dr. Rebecca Liu: I think there's a lot of excitement about looking for screening tests. So as we mentioned earlier, there's no pap smear or a mammogram for ovarian cancer,

but people are finding out that if you have a certain type of bacteria in your system, you're more likely to have colon cancer. I think we're going to find that with ovarian cancer and I think it's not really the bacteria but it's your immune system. What does your immune system do with different types of infection? And how does your immune system get rid of abnormal cells? So I think that screening and treatment is all going to come down to how can we kind of tune up your immune system. I think that's a really big area of research.

Dr. Crapanshu U: Yeah. I think if you break it down into like three different buckets. There's a bucket of what Rebecca mentioned about this pre ... before you develop the cancer. The prevention strategies and early detection. That's like this one area. And I think that's the area we have to focus the most on. Because for everything you do, you'll prevent the cancers and you don't have to deal with the aftermath of what happens. The second bucket is this is the part where I do most of my research is that once you've developed the cancer, making sure that everybody is getting the right treatment. So if you can imagine a world where 100% of women got the standard of care when they got treated, or they got genetic testing all the time. Their family members who tested positive got their tubes and ovaries removed at the right time after a discussion with their physician.

Dr. Crapanshu U: Now we've reduced the number of cancers. So that's where I focus. And Rebecca's had a lab for a long period of time. Dr. McLean who's one of our partners who's actively studying. Kathy Cho is another of our Michigan Medicine ovarian cancer researcher. They are focusing on newer treatments that why some cancers stop responding to chemotherapy. How can we reverse that mechanism that they continue to be sensitive to chemotherapies or trying to develop newer drugs. So in all three buckets, there's a lot of activity which is happening. And then the immunotherapy question and I think there's lots of clinical trials which are coming in the pipeline, how they do in ovarian cancer is a question to be determined. But we're optimistic in this.

Ed Bottomley: There was a statistic you gave earlier about the percentage of patients who aren't getting the correct treatment. Could you give that to me one more time?

Dr. Crapanshu U: Yeah. So in our research, we've looked at from the National Cancer Database that 60 to 70% of the patients are not getting standard of care treatment. And when you look at it, especially, there's a lot of disparities in cancer care. There's disparity of race. There's disparity of ethnicity. There's the biggest disparity in ovarian cancer we see is the geographic disparity. If you are from a rural area where there's no access to a GYN oncologist, or frankly, an oncologist, it is much more likely that you will not be getting a standard of care. Because it's difficult to travel 10, eight hours. And we see this first hand. A lot of our patients are from the Upper Peninsula. We try to work with the physicians over there and there are amazing people out there.

Dr. Crapanshu U: They refer patients to us and co-manage the patients with us. So it's we see the challenges in how difficult it is. In other states I think similar challenges are happening. And then the last disparity is the age disparity. When you're older, sometimes standard of care treatment's not given. People don't do aggressive surgery. Now I'm not advocating aggressive surgery on people who are older and they have a high risk from having complications during the surgery, but there's a population. As population is aging and people are healthier, the chronologic number should not mean anything.

Dr. Crapanshu U: What we should take into account is how is their functional status. If somebody is 80 and they're driving their car and they're going shopping themselves, they're living alone, they're doing everything, they should get the treatment the same way somebody in their 50s would. But we, time and time again, we see as you age, you don't get the same treatments. So that's something we can do now as opposed to hoping for newer treatments to come and newer tests to show up.

Ed Bottomley: Thank you. And as we wrap up this live chat, let's have one final question. If you could do a brief recap. Give me some more statistics of ovarian cancer. When to see a doctor. Prevent tips. Anything else you'd like to share for our final five minutes. [crosstalk 00:54:35].

Dr. Rebecca Liu: I want people to remember that you can cut your risk of ovarian cancer in half by taking the birth control pill for at least five years. If you don't have a contraindication to have. That's important to know. Don't ignore the symptoms. Ovarian cancer is not really a silent disease. Really pay attention to how you're feeling. See your doctor. See your gynecologist regularly. I don't know. Do you have more to add?

Dr. Crapanshu U: No. I think these things with the genetic testing we've talked about, these are really important and I would urge people to be a participant, an active participant in their treatment for themselves or their loved ones if they unfortunately have this disease. And saying, figuring out from some credible websites what should be done and is it being done? And if not, having a conversation with a physician, why not? And as I mentioned before, there might be good reasons why it's not happening, but that knowledge is super helpful. So in addition to all this, one other thing before, since we are running out of time, I want to mention is, a lot of things we mentioned where the research is necessary for example in the early testing phase or in treatment or making sure people are getting the right treatment, these research endeavors need money. And money comes from some of the National Institute of Health, NCI, National Cancer Institute grants.

Dr. Crapanshu U: Our group has shown and represented this data in Society of GYN Oncology is there's a huge disparity in funding in ovarian cancer. For how lethal this cancer is, we get a fraction of money to study this cancer as opposed to lung cancer or

breast cancer or prostate cancer. Now, whenever I talk about this, I get an argument that, "Yeah. But those cancers are really common." But one thing people forget is, that the number of women we are losing with this cancer actually put it really high on that list. And the number of life years lost because a lot of women develop this cancer in their 50s and 60s. If life expectancy in the United States is 80, we're losing 30 years of life.

Dr. Crapanshu U: So we ... people should get ... reach out to their elected members and say that, "There should be some equitable form of distribution of NIH dollars in studying these diseases." Otherwise, what's going to happen is that we'll have cures in other cancers but not in this disease. And that worries me, and we'll be left behind and unfortunately the gynecologic cancers are being left behind. We found the same thing in endometrial cancer which is a uterus cancer, and in cervix cancer. We need money to be able to do this and frankly, what we're asking for is grants. These are scientifically [inaudible] grants, not donations. So this is super important in this field.

Dr. Rebecca Liu: It's very important. We need to do these large clinical trials. National trials. Not just in one institution. Trials that include patients from all over the country, because ovarian cancer is not common. So we need to be able to study large groups of patients.

Dr. Crapanshu U: Yeah. We have no shortage of brilliant minds. And what they need is some money to help their research efforts so we can move the needle on this cancer.

Ed Bottomley: Well, thank you. I think that wraps up today's chat. Thank you both for your time and expertise. Guidance through all these nuanced answers. I think this has been very, very valuable.

Scott Redding: Thank you for listening. And tell us what you think of this podcast by rating and reviewing us. If you have suggestions for additional topics, you can send them to cancercenter@med.umich.edu, or message us on Twitter at [UMRogelCancer](https://twitter.com/UMRogelCancer). You can continue to explore the 3Ps of Cancer by visiting rogelcancercenter.org.