00;00;00;02 - 00;00;31;02 WNPR (radio voice) Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital. Welcome to Yale Cancer Answers. The director of the Yale Cancer Center is Dr. Eric Winer. Yale Cancer Answers features conversations with oncologists and specialists who are on the forefront of the battle to fight cancer. Here's Dr. Winer.

Dr. Winer 00;00;32;09 - 00;01;05;07 Today, we're focusing on one of the most important and potentially empowering aspects of cancer care, and that is prevention. Increasingly, we think about prevention and wonder whether we can apply different types of interventions, whether they're medications or behavioral approaches to limit the number of people who develop cancer. Joining us today for a discussion on cancer prevention and risk factors is Dr. Melinda Irwin, the Susan Dwight Bliss, professor of epidemiology and associate dean of research at the Yale School of Public Health.

00;01;06;01 - 00;01;37;14 Dr. Winer Dr. Irwin is also the deputy director of the Yale Cancer Center, and we work together quite closely. Melinda has been a leading researcher on cancer prevention for over two decades. Her work has focused on weight loss and exercise and a variety of other approaches that we can consider as we try to reduce the risk of developing cancer. Melinda, thank you so much for joining us today.

00;01;38;06 - 00;02;12;00 Dr. Irwin Thank you for having me.

Dr. Winer All right. So why don't we just get right to it? And can you talk a little bit about what cancer prevention means practically for listeners? Can we really prevent cancer? And of course, we ultimately hope to eradicate cancer. But in this short term, what kind of steps can people take?

Dr. Winer Yeah, that's a really important question whether we can truly prevent cancer. 00;02;12;15 - 00;02;37;14 I like to think we can definitely lower our risk for developing cancer. But as you know, one of the strongest risk factors for cancer is aging. And so as we age and you know this better than anyone would say breast cancer, that if a woman lives into her ninth decade or something, she likely could develop breast cancer, especially with the way we're able to so effectively screen for cancer.

00;02;37;27 - 00;03;07;23 Dr. Winer So when we talk about cancer prevention, we're really talking about how do we lower our risk of developing cancer? And we definitely have research and data and programs focused on how to lower our risk for various cancers. And of course, the way we lower risk will vary from one cancer to another.

Dr. Irwin Correct. So for like lung cancer and in fact, for all cancers, tobacco explains about 30% of mortality from cancer. 00;03;07;28 - 00;03;40;08 But it might be a higher factor with, say, lung cancer or other cancers than breast cancer, because tobacco is not really associated with breast cancer.

Dr. Winer And let's just focus in on tobacco for a second, because I think that if we look at the statistics there, we can see just how much progress has been

made. So tobacco still is a cause of cancer mortality, but how much has that decreased over the years as we've had fewer and fewer people smoke?

00;03;41;04 - 00;04;07;20 Dr. Irwin Yes. So smoking or tobacco use was at an all time high, let's say in the 1960s, I think it was about 40% of the population was smoking. And today it's about 10% of the population that smokes. And so that's an amazing improvement. Much of that could be because of policy changes in that people can't smoke in public places, on airplanes, in restaurants.

00;04;07;29 - 00;04;33;17 Dr. Irwin And that reduction in tobacco use has led to about 50% of that 30% reduction in cancer mortality rates. So, you know, cancer mortality was at its peak in the 1990s, and since then we've had a 30% decrease in cancer mortality rates. Well, what explains is that 30%, 50% of that decrease is tobacco control. So significant improvements in tobacco control.

00;04;33;28 - 00;05;02;02 Dr. Winer And it is interesting how tobacco use has gone down so much. And it's been really a multi-pronged approach that people have taken to reduce risk. I mean, all of the ad campaigns and then, as you mentioned, eliminating tobacco use in public spaces, in restaurants and bars and all sorts of public spaces where in fact, people used to just light up all the time.

00;05;02;09 - 00;05;30;10 Dr. Irwin Mm hmm. Yeah. Yeah. One of the thing I want to go back to that's important. When we talk about cancer prevention, we often think about preventing the incidence of a new cancer. But there's also prevention. Once you've been diagnosed with a cancer, like preventing a recurrence or preventing a new primary or preventing mortality. And when we talk about tobacco and say lung cancer, it could be that there's a strong association between those two.

00;05;30;10 - 00;05;55;19 Dr. Irwin But what we really need significant more research on is among those who smoke and they're diagnosed with lung cancer. It is really hard for them to quit. And in fact, some might continue smoking during adjuvant treatment, during chemotherapy, which does not improve their outcomes. And so I think we need to actually do a better job on how to prevent something like tobacco among those diagnosed with cancer.

00;05;55;26 - 00;06;24;17 Dr. Irwin That's an area that's under examined.

Dr. Winer Right. And we know that if you continue to smoke, if you've been diagnosed with lung cancer, then in fact, your mortality is higher.

Dr. Irwin And in fact, if you quit smoking after diagnosis, you actually can increase your survival by two years.

Dr. Winer Yeah. It's quite dramatic. So let's talk about other approaches to cancer prevention.

00;06;25;02 - 00;07;05;06 Dr. Winer And I have a feeling we will take up most of the rest of the first half of this show talking about this particular the risk factor and steps that are taken. But why don't we talk about weight and being

overweight and what that does in terms of cancer risk and how we might change that?

Dr. Irwin Yes. So up until this year, it's been documented in hundreds of studies that obesity or having a high body mass index, that's your weight adjusted for height is associated with 13 cancers.

00;07;05;12 - 00;07;32;07 Dr. Irwin But now there's new research showing that a high body mass index or high obesity is associated with 18 cancers. And there's a lot of research right now going on. Is it really body mass index? Is it you know, what is it really? And so I think there's a research shifting to really talking about adiposity. You could be in the normal BMI range that have high adiposity levels.

00;07;32;16 - 00;08;03;03 Dr. Irwin So, you know, that's kind of where we're at is trying to figure out the amount of of body fat or adiposity that increases your risk of developing a certain cancer. And in much of this risk is because of hormonal changes that occur inflammation, immune markers, metabolic marker changes that that occur with more adiposity or more body fat.

Dr. Winer And are there certain patterns of being overweight that are that lead to greater or lesser risk?

00;08;03;03 - 00;08;33;01 Dr. Winer You know, people often talk about. Trinko obesity. So having a lot of excess body fat in, in the middle, you know, over your abdomen. Is that associated with a greater risk?

Dr. Irwin Yes. So there's as you said, you know, sort of the pear shaped versus the apple shaped body. But then more importantly, is the subcutaneous body fat that's right under your skin versus the visceral adipose tissue that's around your internal organs.

00;08;33;07 - 00;09;05;10 Dr. Irwin And as we age, we actually have a shifting or a reduction sort of in our subcutaneous body fat under our skin and an increase more in the visceral adipose tissue. And so that increases our risk of cancer.

Dr. Winer And so is that part of the reason why some older people, this loss of subcutaneous body fat, some older people simply lose weight as they get older, that the normal body weights go down with age.

00;09;05;27 - 00;09;35;01 Dr. Irwin Yes. So there's also another term called sarcopenia obesity. Or if you just take Sarcopenia, that's as we age or just people having a loss of sort of lean body mass or muscle mass, and yet no change in sort of adiposity. And then the circle. PINNICK obesity or people who have a high amount of body fat with the loss of muscle because as we age, unfortunately we lose muscle and bone as we as we age.

00;09;35;01 - 00;10;08;21 Dr. Irwin And we're not often losing body fat. And in fact, we're increasing in the visceral, adipose tissue.

Dr. Winer While I often say that obesity or being overweight in general is

probably next to tobacco, the biggest cause of cancer risk. And my assumption is that as smoking rates continue to decline and in fact just the use of tobacco, all sorts of different types of use goes down.

00;10;09;09 - 00;10;44;11 Dr. Winer That that obesity will ultimately become the major cause preventable cause of cancer.

Dr. Irwin Yeah, that's right. And it's really difficult because you can quit smoking or never start smoking. You don't need it to be a part of your life at all. But we have to eat. We have to eat. We cannot stop eating. And so on a kind of population level or a societal level, how do we shift our food environment to make it where we're eating healthier foods?

00;10;44;11 - 00;11;18;17 Dr. Irwin We have access to healthier foods that are available to us because we can't just say we're going to quit eating. Now, we can try to reduce our added sugar intake. We can try to reduce our in our meat intake, but it ends up then being about access and availability of healthy foods in our environment. But so it's a lot more difficult of a behavior eating and say exercise on our weight than eliminating tobacco or even, you know, abstaining from alcohol because you can't abstain from eating.

00;11;18;17 - 00;11;52;29 Dr. Winer That would not be good for you.

Dr. Irwin So it leads to different sort of behavioral interventions, different policy level interventions, community based interventions that are necessarily necessary in obesity prevention, in treatment for cancer or for any chronic disease. Then the behavioral interventions that are applied to tobacco.

Dr. Winer Do you think that the public is aware of the association between being overweight and cancer risk?

00;11;53;18 - 00;12;21;00 Dr. Irwin I don't think so. I think the public is very well aware of obesity, diet, poor levels, physical inactivity with, say, diabetes, cardiovascular disease, but not with cancer and definitely not with the 18 cancers associated with that with obesity. And so there's still a lot to be done in that regards of informing and disseminating research findings to the public.

00;12;21;00 - 00;12;48;20 Dr. Winer And of course, a major risk factor for being overweight as you get older, which is in some cancers, the major association, for example, in breast cancer, being overweight when you're younger has always been a little bit unclear the impact on risk, whereas people who are older and are overweight clearly have an increased risk. I think some of that's changing.

00;12;49;00 - 00;13;17;01 Dr. Winer But being overweight when you're younger also predicts for being overweight when you're older.

Dr. Irwin Exactly. So the studies, the research studies can look at just one point in time your weight or your BMI, but they can also look at weight change over time. And those studies that look at weight gain or weight change predict various cancers rather than just looking at BMI at one point in time, maybe in your earlier years.

00;13;17;21 - 00;13;40;08 Dr. Winer All right. Well, we're going to have to take a brief break at the moment. When we come back, we're going to talk about some of the more recent research, including a study that looked at the benefits of exercise in reducing the chance that a person with colon cancer would have a recurrence of that disease. So we'll be right back.

00;13;40;08 - 00;14;17;03 Dr. Winer And again, we'll be joined by our guest, Dr. Melinda Irwin.

WNPR (radio voice) Funding for Yale Cancer Answers comes from Smilow Cancer Hospital, which provides a multidisciplinary approach for treating appendix cancer, including advanced surgical techniques like hypothermic intraperitoneal chemotherapy. Learn more at Smilow Cancer Hospital dot org. The American Cancer Society estimates that more than 65,000 Americans will be diagnosed with head and neck cancer this year, making up about 4% of all cancers diagnosed when detected early.

00;14;17;04 - 00;14;55;08 WNPR However, head and neck cancers are easily treated and highly curable. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital to test innovative new treatments for head and neck cancers. Yale Cancer Center was recently awarded grants from the National Institutes of Health to fund the Yale Head and Neck Cancer Specialized Program of research Excellence or SPORE to address critical barriers to treatment of head and neck squamous cell carcinoma due to resistance to immune DNA damaging and targeted therapy.

00;14;55;24 - 00;15;34;14 WNPR More information is available at Yale Cancer Center dot org. You're listening to Connecticut Public Radio.

Dr. Winer Welcome back to the second half of Yale Cancer Answers. We're talking tonight about cancer prevention. Both about risk factors and about what we can do to modify those risk factors and reduce an individual's risk of developing cancer. Before we get to another behavioral intervention, and that is exercise, I want to talk for just a minute or two about drugs.

00;15;35;02 - 00;16;07;25 Dr. Winer And there was a time when we were very focused on medical interventions, specifically medicines that could reduce cancer risk. And there were a number of different clinical trials. And I feel to some extent that that has fallen a little bit out of favor, not that we're not still pursuing some of these investigations, but that people are less interested in giving drugs.

00;16;07;25 - 00;16;36;18 Dr. Winer And Melinda I'm interested in your thoughts on that and why that may be the case.

Dr. Irwin Yeah, that's a great question. So I immediately thought of two sort of drugs, one endocrine therapy for women who don't have, say, breast cancer but might be at higher risk. So taking Tamoxifen, you know, in research that

was done looking at that a decade or so ago showed very, very little uptake or interest.

00;16;36;18 - 00;17;01;23 Dr. Irwin I think it was like less than 1% of women interested in taking that. You might know way more about this than I do, but so that I don't think there's as much research focused on that area. However, what we do know is of strong interest to people is anti-obesity medications. And so this obviously could have an association with cancer risk or prognosis.

00;17;01;23 - 00;17;27;24 Dr. Irwin There's been studies, observational studies showing those who've taken anti-obesity medications have maybe lowered their cancer risk. But when we go back to talking about sort of cancer prevention, I also think about obesity prevention. And while it is important for us to focus on those who have obesity or those who have cancer, when we think about obesity, 60% of the population does not have obesity.

00;17;27;24 - 00;17;53;13 Dr. Irwin And the medications are helping the 40% that do. But what are we doing as a society in making sure those 60% that don't have obesity don't develop it, too, then take a medication? And so that's where my research focusing on exercise and healthy eating on an individual, but more so on a population and a society level. What can we do to prevent obesity, to prevent cancer?

00;17;53;26 - 00;18;18;21 Dr. Irwin I think those are really important questions that can't be answered, with some of these medicines.

Dr. Winer Yeah, well, and I think the other issue with medicines and we'll get to the weight loss medicines in in just a second, I'll make a comment about that. But I think with many other medicines and this was certainly true with Tamoxifen, which was clearly shown to reduce a woman's risk of developing an invasive cancer.

00;18;18;29 - 00;18;41;24 Dr. Winer But as you said, almost no one chose to take it. And it's because when your risk is ultimately pretty low, you know, most of the women in the study over the course of five years had a risk that was well under 5% in those five years. And people don't really want to take a drug that is going to have side effects.

00;18;42;24 - 00;19;15;04 Dr. Winer The healthier you are, the less you want to do that. And with the obesity drugs, where there's been much more interest, of course, there is a two, four or a three-four, meaning there are added benefits. So you lose weight, you feel better and it helps with other problems. So people aren't just taking it to prevent cancer.

Dr. Irwin And you know what a follow-up, which is all over the news in social media right now is hormone replacement therapy, which is the opposite of Tamoxifen.

00;19;15;13 - 00;19;57;09 Dr. Irwin And so why are so many women wanting to take hormone replacement therapy now? You know, after the landmark study

in 2002 from the Women's Health Initiative showing that it increases CVD and breast cancer overnight, you know, providers stop prescribing this, but now it's coming back and we know why side effects are powerful. If women have, and you know why? menopausal related side effects, those, you know, dictate their day in the medication they're going to take much like A.B.C. medications, if they have struggled with weight for a decade or two or their whole life, they don't want to anymore.

00;19;57;09 - 00;20;28;12 Dr. Irwin And so those are when medications are of interest to people.

Dr. Winer Absolutely. And you know, of course, most people value survival, living a long life above everything else. But of course, we all make choices and most of us don't want to be miserable taking a medicine or miserable because of some other problem that we can fix with the medicine just to live an extra month or two or three.

00;20;28;12 - 00;20;56;26 Dr. Winer And so it's all this balance of length of life versus quality of life. So let's talk about one of my favorite topics since I'm a believer, and that is exercise. You've been interested in this for years, and I'll just share with the audience that if I remember correctly, you were a competitor, a gymnast.

Dr. Irwin Yeah, I was a couple of decades ago. From age 4 to 21.

Dr. Winer Yeah. So do you think that's part of what got you interested in exercise?

Dr. Irwin For sure, yeah. I mean, I'm still reaping the benefits of those early years that I was physically active and training every day. So obviously, I'm not training at close to that level. I'm lucky if I can make the physical activity, recommend an amount each week, which is about two and a half hours per week of a minor intensity activity.

00;21;27;27 - 00;22;00;22 Dr. Irwin But I think being active in your childhood, much like the opposite. We were talking in the earlier segment about weight loss. You gain weight through child and into adulthood, but if you exercise in childhood, it can continue into adulthood. And so this behavior, of course, I love exercising and I love doing research related to exercise, because unlike a medication that really usually impacts one pathway, exercise affects multiple pathways, multiple disease outcomes and health outcomes.

00;22;01;10 - 00;22;42;14 Dr. Winer So we all have some hunches about exercise and cancer, and maybe you can tell us where we're still in the hunch phase and where we've actually proven that exercise makes a real difference.

Dr. Irwin Yeah, so it used to be and hopefully this is changing because of one major study that just came out. But it used to be that clinicians, scientists, others thought that any study that showed exercise was related to a favorable health outcome wasn't really exercise that was a proxy of something else.

00;22;42;15 - 00;23;10;08 Dr. Irwin Maybe that person happened to be eating healthy, lower BMI, higher socioeconomic status, but it wasn't exercise. But there was a new trial, the challenge trial in patients with colon cancer that randomized patients to exercise a three-year exercise program that was primarily walking a minor intense activity or to the usual care group. And they found a significant improvement in survival.

00;23;10;13 - 00;23;50;06 Dr. Irwin And in fact, a 37% lower risk of mortality in at eight years in these patients with colon cancer. Those in the exercise group had a 90% survival rate compared to an 83% survival rate in the control group. So a seven percentage point difference from exercise only in the exercise was basically brisk walking.

Dr, Winer As an oncologist who takes care of patients, I can tell you that a 7% improvement is often what we see with a variety of different drugs when we give them to prevent cancer.

00;23;50;06 - 00;24;16;07 Dr. Winer There are some that work a little bit better. There are a lot that we give routinely that don't even have a 7% benefit.

Dr. Irwin And this trial was methodologically strong. It was a randomized controlled trial was balanced at baseline in that the participants patients in the intervention of the control group were similar at baseline. And so in following them, the only thing that was added was exercise to the one group.

00;24;16;07 - 00;24;48;04 Unknown So that's what explains the survival benefit. Unlike observational studies where there are other confounding or residual factors. So this is really an important finding and I hope it shifts the narrative among providers, people, whomever that exercise can really matter. So it has to shift the conversation to how can we make it easier, How can we change our environment to make it easier for people to exercise where the default is being active?

00;24;48;08 - 00;25;21;03 Dr. Irwin You go to Amsterdam. What is the default there? People bike, they don't drive, they bike, they might smoke while they're biking, but they're still biking.

Dr. Winer No, this is true. And although this study wasn't conducted in the United States, it was conducted in Canada and Australia.

Dr. Irwin So in two of our favorite countries (laughs)

Dr. Winer Exactly and patient populations that are not so fundamentally different than the standard U.S. population.

00;25;21;04 - 00;25;43;13 Dr. Irwin And also important to note is these were patients diagnosed with stage two and three colon cancer. So it wasn't limited to an early stage cancer, but that among those with stage two and three exercise really improved their survival.

Dr. Winer Talk to us a little bit about breast cancer and exercise. That topic comes up over and over again. I talk to my patients about it.

00;25;44;19 - 00;26;22;05 Dr. Winer I, I think it's a very interesting area.

Dr. Irwin Yes. So I've been fortunate to do research for the last 20 years or so with exercise in patients without breast cancer, but at high risk and then those with breast cancer. And most of my research when I first came to Yale was among those who had completed treatment. And so looking at sort of how to improve that phase after treatment ended, how exercise might improve long term side effects and prevent recurrence and mortality.

00;26;22;17 - 00;27;10;10 Dr. Irwin I've now shifted in the last five or so years to look at how exercise might benefit patients. While they're receiving treatment. In particular, chemotherapy and exercise could improve adherence to chemotherapy. It could improve the efficacy of chemotherapy doing its job. It could improve other related sort of side effects of chemo that could then in turn improve outcomes. So we're really trying to tease this apart in the role of exercise during treatment, and we're really excited to do this one study right now among women with neoadjuvant chemo, chemo before surgery, and it's women with triple negative breast cancer to see if exercise can improve the pathologic complete response.

00;27;10;10 - 00;27;34;24 Dr. Irwin We have evidence of that from a previous study, but we're going to focus in on triple negative breast cancer to see if through improving immune markers, inflammatory markers, metabolic markers — can you actually have no evidence of breast cancer when they go for surgery after neoadjuvant chemo? So we're really excited about that trial.

Dr. Winer 00;27;34;24 - 00;28;12;12 Well, this has been really a great conversation. I think that what our conversation is illustrated is that our thinking about cancer in cancer prevention is really getting broader than it used to be. And the whole idea that people have more control of their risk of getting cancer and potentially how they do through changes in diet and exercise, I think is important. On the other hand, if so many people say, I've eaten well my whole life, I've exercised every day, how did I get cancer?

00;28;12;12 - 00;28;39;25 Unknown And no matter what, there is always some risk, certainly. And we also have to be careful not to make people feel badly if for some reason they haven't been able to do these things.

Dr. Irwin Absolutely. We have to look at this on a population and a societal and an environmental level.

WNPR (radio voice) Dr. Melinda Irwin is the Susan Dwight Bliss, professor of epidemiology and Associate dean of research at the Yale School of Public Health. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. We hope you'll join us next time to learn more about the fight against cancer funding for Yale Cancer. Answers is provided by Smilow Cancer Hospital.