

Yale CANCER
CENTER
answers

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Welcome to Yale Cancer Center Answers with Drs Ed Chu and Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center. Dr. Miller is a Medical Oncologist specializing in pain and palliative care and he also serves as the Director of the Connecticut Challenge Survivorship Clinic. If you would like to join the discussion you can contact the doctors directly at canceranswers@yale.edu or 1-888-234-4YCC. This evening, Ken Miller welcomes Dr. Susan Mayne. Dr. Mayne is Professor of Epidemiology and Public Health at the Yale School of Medicine and Director of Population Sciences at Yale Cancer Center and she is here to discuss cancer prevention and treatments.

- Miller Susan, let us start by talking about nutritional guidelines. What are the different guidelines that the American Cancer Society has, and other groups as well?
- Mayne The guidelines we should talk about today are based upon a recent report that was published last October. This was an attempt to look at all of the literature evidence on nutrition and cancer and synthesize that into a comprehensive review on what the data really says. What we tend to get is people's individual opinion, editorials and individual articles. This is the most comprehensive state of the science review of the literature on nutrition and cancer and was published as summary statements. It has been presented in many scientific meetings and I consider that now really state of the science in terms of nutrition and cancer. I would like to spend some time today talking about the recommendations that came from this new report.
- Miller Let's dive right into it. I am sure it sounds like there was a huge amount of material presented, but what are the important points that you want to share with the listeners?
- Mayne The first point we should talk about is one that has gotten new emphasis recently based upon what is happening worldwide. I must emphasize that this report was based upon worldwide data with the input of investigators working on nutrition and cancer from around the world. The first guideline that they emphasize is prevention of obesity and maintaining an ideal body weight; that did not used to be the primary emphasis when we looked at guidelines for nutrition in cancer. What we are now seeing is an epidemic of obesity in the United States and throughout the world. It is happening in developed countries and developing countries and what we are learning is that obesity is a very, very important risk factor for many cancers. So, the first guideline is really aimed at prevention of obesity as an important strategy for cancer prevention.
- Miller Obesity is associated with what cancers in particular?
- Mayne We have always known that obesity was related to some of the hormone-dependent cancers, and there has been a lot of scientific evidence linking obesity

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to things like postmenopausal breast cancer, colorectal cancers, etc. What we are now seeing, however, is a whole bunch of different cancers that we never knew were strongly linked to obesity, basically, because we did not have the problem of obesity that we have today. We are seeing cancers like non-Hodgkin lymphoma and cancers like esophageal adenocarcinoma that were not that common in the past, but have been increasing in incidence. One of the great concerns is that obesity is driving up many of these cancers, and while we have made some headway, at least in the US with regard to tobacco cessation which has lowered rates of many cancers like male lung cancer, we are losing those games because of what is happening nationally and internationally with obesity. We need to pay great attention to the prevention of obesity. That is the first guideline. The second guideline, which obviously links with that, is physical activity. After that we get into a whole bunch of different dietary strategies that are important in and of themselves, and important in terms of prevention of weight gain. The guideline for physical activity is basically to be physically active as part of your everyday life. This is a guideline we are hearing about throughout health promotion and disease prevention, not specific to cancer but certainly an important guideline for cancer prevention.

Miller What are some of the theories about how obesity causes, or is associated with, higher risk of cancer?

Mayne When people have excess body fat, it changes levels of many different hormones and many different growth factors. While the mechanisms are still being studied, what we are recognizing is that the entire hormonal milieu is different in people who are obese. The other thing that we are learning, that is one of my areas of interest, is that people who have high body mass and high body fat have lower levels of many nutrients in their blood, particularly the fat soluble nutrients, and many of those nutrients may be pretty important in cancer prevention. Basically what happens is that these nutrients get sequestered in the fat tissue where they are not available to the cells that really need them for cancer prevention purposes.

Miller Interesting, it is like a two-fold problem, one is that you do not have the things you need, and the other is you have too much of what is harmful.

Mayne That is correct and there is a lot of mechanistic data now trying to study what the actual mechanisms are that are involved here. It is a very robust, very strong scientific finding and it is very clear in animal models, as well as in human studies. We have known for 50 years that if you calorie-restrict animals, you can dramatically lower their risk of cancer. It is not surprising then that we are seeing an epidemic of cancer today in the environment that we live in, in regards to obesity.

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- Miller In terms of physical activity reducing the risk of cancer, is that because of weight loss or is it even independent of that?
- Mayne That is an ongoing area of research right now. Certainly physical activities are important as a strategy to control body weight and to loose body weight for people who are overweight, but there is some scientific evidence coming out now suggesting that independent of weight loss there are some benefits for cancer prevention of physical activity. Being physically active has been shown to change the hormone levels to change many different factors, so even independent of weight loss, it may have some benefits for cancer prevention.
- Miller I find that being aware of this as an oncologist, I am talking more and more with patients about losing weight. One of the most common things that people say is, "I cannot." How do we advise these people?
- Mayne That is the million-dollar question, how do we get people to lose weight? If I knew the answer to that I am sure that I could win the Nobel Prize, but the issue is that it is a multifactorial approach. It is talking about healthy eating. It is about overall lifestyle modification. It is about physical activity and it is being aware of what people are eating. As I am sure you are aware there are many interventions occurring at a societal level to help people understand what they are eating. Things like calorie labeling on foods at restaurants and in fast food environments, things that are really important in order for consumers to make appropriate nutrition education. There are many societal changes that we can make to help improve education and help people understand about what they are eating to help them control calories and maintain body weight.
- Miller In terms of having an ideal bodyweight, physical activities and some of the other strategies, do they also impact the risk that someone has of having a recurrence of a cancer if they have already been diagnosed?
- Mayne It is a good question. Recently the American Cancer Society looked at that question in detail and what they were asking was the evidence of the role of diet, nutrition, physical activity in terms of prevention of recurrence for cancer survivors. Basically, the conclusion that the American Cancer Society review came up with was that the recommendations that we are using for primary prevention are the same recommendations that we should be using for secondary prevention, which is prevention of recurrence, prevention of second primary. So, the guidelines are essentially the same. What we are recommending in terms of dietary strategies, which we can talk about now, is that those particular strategies are the same whether you are trying to prevent the first cancer, or whether you are trying to prevent a second, third, or even higher cancer.

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- Miller What are some of those strategies?
- Mayne In terms of actual dietary guidelines, the first one that I think is really important is the one that is listed number one of the dietary strategies from this recent report. It is all about eating mostly foods of plant origin, and we are hearing this over and over and over again and it is basically the strategy that is an important approach to maintain body weight, and these are not nutrient dense foods. They are very low in calories and very rich in nutrients that our bodies need. They are not loaded with calories, but provide those nutrients and they are also linked with a lower risk of many different cancers. The review community looked in great detail, cancer by cancer, to see where the evidence is the strongest and what we see in terms of a plant food based diet. The consistent finding is that this is linked to a lower risk of many different cancers. That is an important strategy that we hope to communicate to the public; we really should be eating more plant-based foods.
- Miller For people who are about to cook dinner tonight, or planning their meals for the next week, what are some examples? What does that mean, plant based?
- Mayne More quantitatively people are probably familiar with the five-a-day program that has been out there for a long time. That was one public health message, a simple message to communicate that in order to have optimal health people should consume at least five servings of fruits and vegetables every day and inherent in that guideline is that you want variety. Some studies suggest that deep green leafy vegetables have particular benefits. Other studies suggest that certain citrus fruits may have benefits. So, we cannot say at this point in time that one particular class is the most important; instead, what we are recommending is a variety. The five-a-day program is one that most people are familiar with, but it recently has been replaced. They are starting to modify the five-a-day. The current recommendation is more is better, but in terms of quantitative guidelines the five-a-day makes sense to people and is certainly something that we should strive for. That guideline has been around now for many years, but what nutritional survey data shows is that a relatively small segment of the population is currently meeting the five-a-day guideline. An obvious way that people can impact upon their cancer risk, health promotion in their environment, is to consume fruits and vegetables 5 servings a day.
- Miller In terms of the American public, what is the average number of servings, it is not five is it?
- Mayne It is not five and it varies dramatically depending on certain demographic factors. It may not be surprising to you, but women are more likely to meet the guidelines than men. It also varies by SES factors, more affluent individuals who can afford fruits and vegetables are more likely to meet the guidelines than the low socioeconomic status segments of our population. I think that is why public

health professionals are trying to work in the inter-city in the low SCS population to increase the availability and affordability of fruits and vegetables. That is the segment of our population, in particular, where we are concerned about them not consuming the appropriate amount of fruits and vegetables.

Miller What are some of the others strategies?

Mayne The second guideline is kind of the converse of the plant-based food guideline. It is to limit the intake of red and processed meats. This guideline was issued many years ago. The American Cancer Society was the first one to come out and really say, limit your red meat intake. It has now been endorsed and continued as an important strategy for cancer prevention. It is not to say that people cannot eat red meat, they can, but it is all about moderation. There is increasing evidence, particularly for colorectal cancers, that people who consume more red meat have a higher risk. You can modify that risk by eating more plant-based foods; you can consume it in moderation and consume it infrequently. We are not telling people they cannot eat red meat or processed meat, but just watch how much you are consuming, try to moderate that consumption and balance it with more plant-based foods.

Miller Any other strategies?

Mayne The next guideline they talk about is alcoholic drinks, and interestingly we know that when people consume excess alcohol, it raises the risk of many cancers. There is new evidence, growing evidence, over the last decade that even moderate drinking can raise the risk of breast cancer. From a cancer prevention point of view the guideline is really to limit alcoholic drinks. However, we do recognize that moderate drinking has been associated with a lower risk of cardiovascular disease, so there is some gray area in that moderate drinking may increase the risk of breast cancer, but may lower the risk of heart disease. In that particular situation, we would recommend that individuals talk to their physicians about their risk for heart disease and the risk for breast cancer to get advised about how much drinking may be appropriate. Either way, higher levels of drinking, and that is more than 2 drinks a day for women and more than 3 drinks a day for men, are strongly and consistently related to a higher risk of certain cancers. That is the specific guideline to limit alcoholic drinks.

Miller What I am hearing, which I find exciting, is that people can modify their risk. There is something that everyone can do, and for parents in particular, we can start to modify our children's risk and their behaviors.

Mayne The emphasis on early life is becoming increasingly important. We are recognizing that many dietary habits are set in childhood and the environment that our children are in today, in terms of nutritional quality and what they are eating,

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is really problematic. As a society, that is something we are trying to address right now.

Miller We would like to remind you to e-mail your questions to us and Dr. Susan Mayne at canceranswers@yale.edu. We are going to take a short break for a medical minute. Please stay tuned to learn more information about cancer prevention with Dr. Susan Mayne from the Yale Cancer Center.

Breast cancer is the second most common cancer in women. About 3000 women in Connecticut will be diagnosed with breast cancer this year but earlier detection, noninvasive treatments, and new therapies are providing more options for breast cancer patients and more women are able to live with breast cancer than ever before. Beginning at age 40, every woman should schedule an annual mammogram and you should start even sooner if you have risk factors associated with breast cancer. Screening, early detection, and a healthy lifestyle are the most important factors in defeating breast cancer. Clinical trials are currently underway at federally- designated comprehensive cancer centers such as Yale to make new make treatments not yet approved by the Food and Drug Administration available to patients. This has been a medical minute, and you will find more information at www.yalecancercenter.org. You are listening to the WNPR Health Forum from Connecticut Public Radio.

Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller and I am here with Dr. Susan Mayne who is a Professor of Epidemiology and Public Health at the Yale School of Medicine. Susan, there is always a lot of information in the press about supplements. Tell us about some of the supplements that people take and if they tell their doctors about it.

Mayne The most widely used nutritional supplements in the United States are multivitamins and multiminerals supplements. Those are number 1 followed by a variety of different single nutrient supplements, the most common of which are things like calcium, vitamin E and vitamin C. Those are all pretty commonly used supplements. It is interesting if you look at who takes nutritional supplements in the United States, there are some very interesting patterns. The people who are most likely to take nutritional supplements are women, primarily older women, and interestingly the people who are most likely to take supplements are people who have the best diets to begin with. If you are thinking about supplementation as a remedy for having a poor diet, that is not what is happening in the United States. The people who have the poorest diets are the least likely to take nutritional supplements. That is a little bit of background on nutritional supplements. In the setting of cancer, we know that many cancer survivors and many people who have been recently diagnosed with cancer are turning to nutritional supplements and herbal and botanical supplements. Much of this is encompassed under what we might call complimentary or alternative

medicine; complimentary medicine to traditional cancer treatment. The problem here is that there is evidence that some of these nutritional supplements might interfere with the efficacy of cancer treatment. The current guideline is for cancer survivors to avoid nutritional supplements because there are many unknown effects on how it might interfere with the traditional cancer treatments. The guideline is why take a risk and take something that might make that therapy that we know works, less effective.

Miller Can you give us an example of where it might interfere?

Mayne One of the classes of nutrients that there has been quite a bit concern with are the antioxidant nutrients. This is because of the way that radiation therapy kills cancers cells and the way that many chemotherapeutic drugs work may involve oxidative stress. If the patient's are taking high doses of antioxidant supplements, it may actually interfere with the precise mechanism of the action of how some of these cancer therapies work. Another example is some of the chemotherapeutic drugs that work through a mechanism called anti-folates, the antagonized folate. If the patient is taking a high dose of folate supplements at the same time that they are having chemotherapy, they are undermining the efficacy of the treatment.

Miller So we are encouraging people to avoid supplements when they are receiving therapy, and certainly to talk to their medical team about it.

Mayne Yeah, that certainly would be what I would recommend. That is in the setting of cancer survivors. The other thing I would like to mention is supplements in the setting of cancer prevention; primary prevention in the general population. As part of this recent scientific review of all the literature, the committees that looked at the literature looked at a number of different studies evaluating whether or not nutrient supplements had value for cancer prevention; primary prevention and secondary prevention. The conclusion is that there is no overwhelming evidence of the efficacy of any nutrient supplement at this point for cancer prevention. The guideline that was issued from the American Institute for Cancer Research, the World Cancer Research Fund, is that people should aim to meet their nutritional needs through diet alone. In fact, what we are learning is that this kind of over-reliance on supplementation can be really problematic. People are concerned about meeting, let's say, folate requirements, so they consume Total cereal which has 100% of the recommend dietary allowance for folate. They also take multivitamins so they are now at 200% of the recommended dietary allowance. Many people are consuming things like vitamin fortified waters and things like that and then putting that on top of a normal diet, and before you know it, people are consuming 5 times the recommended dietary allowance of these nutrients. If there were not any adverse effects, I would not really be concerned, but we are entering a situation in our population where people are really over the limit in

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terms of what the recommendations are. We really have to be aware of that. Micronutrient deficiency is not as common in the United States as it is in many other parts of the World. In fact, I am just as concerned about micronutrient excess and what that is doing in terms of chronic disease.

Miller Let me ask you about that. You are saying that some of the micronutrients at too high a dose may be harmful?

Mayne That is what the scientific evidence seems to be showing again and again when we do clinical trials and intervention studies with nutritional supplements. An emerging theme is that if you supplement a population that has low status to begin with, there are sometimes benefits. As an example, one of our most successful cancer prevention trials involving nutritional supplements was done in China in a region where there was profound micronutrient deficiencies. In that particular study, cancer mortality was significantly reduced with nutrient supplement, but you cannot take that finding and put it into the United States. We are in a very different setting and what we are seeing in many US studies is that people who started with adequate, to really good nutritional status for certain micronutrients, if you give them additional micronutrients above and beyond, there are increases in cancer risk for several different nutrients. This has been shown for beta-carotene. It is now being suggested for folate and may be true of selenium and certain other nutrients. I am concerned that just because a little bit may be good for you, a lot is not necessarily better.

Miller Let me ask you about vitamin D. I have been hearing a lot lately about vitamin D in cancer prevention, what can you tell us about that?

Mayne Vitamin D in cancer prevention is probably one of the most controversial and one of the most exciting areas of research at this point in time. What we know is that there is research that suggests that people who have lower blood levels of vitamin D are at increased risk of certain cancers. Vitamin D is very difficult to measure in terms of exposure because you get it from diet and you get it from sun exposure. We measure it as blood levels. We have this finding that people who have lower blood levels of vitamin D have a high risk of certain cancers; in particular colorectal cancer. Many people will use that information and say, "Well shouldn't we all go out and take vitamin D supplements then?" The problem with that approach is that we are not sure why the level is low. We know the blood levels of vitamin D are influenced by many things such as slight sun exposure and race, which is because African-Americans are less efficient in producing vitamin D in response to sun exposures, so African-Americans in particular are at greater risk of having low vitamin D levels in their blood. The other group is people who are obese. That is because of, again, this relationship that higher body fat sequesters vitamin D which is a fat soluble nutrient and so levels in the blood decline. Essentially what vitamin D is, is a marker for sun

exposure, much of which may be coming through physical activity. It is a marker for obesity status and it is a marker for race. The fact that it may be related to cancer may be completely unrelated to the vitamin D, it may be due to these other risk factors. What we really need are carefully controlled clinical studies to see if vitamin D supplementation reduces the risk of cancer.

The largest vitamin D supplementation trial was one of the arms of the women's health initiative where calcium and vitamin D were given. In that clinical trial there was no benefit in terms of risk reduction for cancer. At this point, it is premature to advise people to take vitamin D supplements because of this finding; this link between low blood levels of vitamin D and cancer. Perhaps an even more kind of perverse interpretation of this is a recent campaign that was been put out by the tanning bed industry and they are basically saying, "If you want to increase your vitamin D status, come into the tanning parlors and expose yourself to UV radiation and raise your vitamin D status." We certainly know that tanning parlors dramatically increase the risk of skin cancers, in particular melanoma, which is a lethal form of skin cancer. We do not recommend tanning parlors as a mechanism to increase your vitamin D status. The common sense public health recommendation is go out and take a walk, be physically active, get a little bit of sun exposure, control your body weight and your vitamin D status will improve.

Miller We have talked before about your interest in research on biomarkers. Aside from a blood test, how else are you able to measure someone's nutritional status?

Mayne Biomarkers are critical. For example, with vitamin D, we would have no information on vitamin D and cancer if we did not have a biomarker of vitamin D status which is a blood measure. Biomarkers are critical to research in nutrition and cancer, but as you appropriately point out, it is hard to get blood samples from people. People do not want to do that if they do not have to, and there are newer technologies being used in the field of nutrition science that are aimed at being able to evaluate nutritional status through noninvasive methodology. Some of my own research is looking at using light and optical sensing devices to measure nutrient levels in skin to get a better hold on nutritional status without having to rely on either blood measures or asking people what they are eating. There has been a lot of research looking at self-reported diet in cancer and many of the recommendations that I mentioned to you today come from that. It is hard for people to report what they are eating; it is hard to be accurate in terms of estimating portion sizes. Cancers are a disease that takes a long time to develop. People do not remember or recall what they ate in the past. We can measure it objectively with biomarkers that can improve the quality of the scientific evidence that we are generating on nutrition in cancer.

Miller There is a partnership between the National Cancer Institute and Yale in terms of studying diet and cancer risks, what is that study all about?

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Mayne It is a training program to train the next generation of investigators to do research on nutrition in cancer. The reason that we set up this program in partnership with the National Cancer Institute is that we are learning that in order to do the best studies on diet and cancer, we need large population samples. We are finding out that there is so much heterogeneity for different types of cancers. For example, the risk factors, including diet, for postmenopausal breast cancer are different than those factors for premenopausal breast cancer. Similarly, even the type of breast cancer, whether it is a hormone receptor positive tumor or not, can be important in trying to identify risk factors. Our research is using large sample sizes in partnership with the National Cancer Institute who are conducting very large cohort studies. For example, one of the cohort studies that some of our trainees are working on include something like 90,000 individuals. We are studying large numbers of people with very good measures of diet and biomarkers if at all available, to try to better understand the role of diet in all these different types of cancers and subgroups of different types of cancers.

Miller Cancer takes a long time to develop and many factors contribute to risk. Of those factors, do you think nutrition rates as one of the most important, or is it just a co-contributor?

Mayne The top three in terms of we call population attributable risk, what is causing cancer, what is preventable, and what is modifiable, the biggies are tobacco exposure, body mass index and obesity, which is determined by both diet and physical activity. Those are really the big ones. Smoking, diet and physical activity, operating through obesity, are the most important modifiable risk factors of cancer. There is evidence in terms of those three alone, that we could probably prevent two-thirds of all cancers if people followed appropriate guidelines in terms of tobacco control, diet and physical activity. Beyond those there are additional factors that we recommend, such as avoiding too much sun exposure. We touched a little bit upon that in terms of vitamin D, and a little bit of sun exposure is fine, but it is excessive sun exposure that we know is clearly an important risk factor for skin cancer. That is another modifiable behavior that we can embark upon to reduce the risk of cancer.

Miller I want to thank you. It has been a really fascinating half hour, and on behalf of the Yale Cancer Center, I want to wish you all a safe and healthy week.

Mayne Thank you Ken.

If you have questions, comments or would like to subscribe to our Podcast, go to www.yalecancercenter.org where you will also find transcripts of past broadcasts in written form. Next week, you will meet Christine Frisbee the author of Day By Day.