



## **A Discussion on Gastrointestinal Cancers**

**Hosted by:** Steven Gore, MD

**Guest:** Charles Fuchs, MD, MPH, Director, Yale  
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Hospital

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*Welcome to Yale Cancer Answers with doctors Anees Gore, Susan Higgins and Steven Gore. I am Bruce Barber. Yale Cancer Answers is our way of providing you with the most up-to-date information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week Dr. Steven Gore welcomes Dr. Charles Fuchs. Dr. Gore is Director of Hematologic Malignancies and Dr. Fuchs is Director of the Yale Cancer Center and physician-in-chief at Smilow Cancer Hospital. Here is Dr. Steven Gore.*

Gore Charlie, thanks so much for joining me tonight.

Fuchs Steve, thank you for having me.

Gore You are a wonderful addition. Today we are not going to talk about that, but we are going to talk about your academic, clinical hat that you have worn all these years, which is in gastrointestinal malignancies. Is that right?

Fuchs That is exactly right. I have been doing GI or gastrointestinal malignancies now for 26 years. And so beyond my interest in leading the center, I want to continue that work because it is such a pressing need and I have had the privilege in getting involved in prevention, understanding biology and treatment of gastrointestinal cancers.

Gore How did you first get interested in that particular group of cancers, Charlie?

Fuchs It is interesting. For me, it was a matter of how it was contributing to the burden of cancer. I do not think people realize, but gastrointestinal cancer is a number of different cancers that afflict our population. We know about colon cancer, pancreatic cancer, cancer of the esophagus, stomach, liver, bile duct among other things. And what is incredible is if you look at the pie-chart of cancers in the US and you add up all the cancers that include gastrointestinal cancers, you are looking at 23% of all new cancer diagnosis in the US and 31% of cancer deaths this year. So, essentially almost 1 in 4 new cancers is a GI cancer. And when you look at that burden of disease and the pressing need for new methods of treatments in prevention, I saw that as an opportunity I wanted to take on.

Gore We know that a lot of these cancers, particularly the colorectal cancers, can be detected early and cured if people get the appropriate screening. Is that right?

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- Fuchs Absolutely. I think colon cancer is really the model of early detection, namely colonoscopies are a very effective way of finding these things either at the early cancer stage or even better yet at the polyp state because we know that colon cancers arise from polyps, and so what is amazing about that method in contrast to other early detection is not only do you find either the precancerous or early cancer lesion, but you can remove it. You are done, you get the test, it is gone and you are going to be cancer free. And so, it is such an effective means. Now, the problem is compliance, a substantial population of people do not get this type of testing. So, we need to push people to do it, at least engage in some method of early detection. Colonoscopy by far being the best, but also there is a test you can do on the stool to detect blood or other things in the stool, which can be a screening test, not as good colonoscopy but at least it is something.
- Gore Do you think the problem with screening colonoscopy in terms of uptake is patients not wanting it or do you think the primary problem is access, people who do not have insurance or do not have the right kind of primary care education?
- Fuchs I think it is a variety of things that you touch upon. Certainly, access to care is always a barrier when we look at effective implementation of good treatments and screening technologies, but the payers and the government have really tried to overcome that. That is, Medicare and Medicaid are supposed to cover colonoscopies. But I also think there is the barrier of perception. People do not want to do it. Understandably, it sounds like it is quite an ordeal and people would prefer to just avoid it. As well, I think that we as physicians, and I include myself, I think we need to do a better job of making that part of the conversation with our patients, which is you are 50 years old, we need to get your colonoscopy, which is the current guideline if you are somebody without a family history. Realizing that if you have a family history, and I am talking about just having one first-degree relative, a parent, a sibling or less likely a child with colon cancer, you should be starting 10 or 15 years earlier. So, it is between the ages of 35 and 40.
- Gore I am probably one of the few people who actually signed up for my colonoscopy at 50 years and 1 month and then I get to get my second one next year, I have not quite signed up but I feel great about it, honestly it is a nothing test with the current anesthesia, Propofol, you wake up and the guy tells that you are fine and that you are good for 10 years, and it is a great news.
- Fuchs Absolutely. And there are very few screening technologies that we have for any chronic ailment in the US where you can walk away from the test and know not only whether or not there was something found, but know that it was removed and you are done.

- Gore Now, pancreas cancer on the other hand, that is another story right?
- Fuchs It is. And what is really regrettable is it is one of the most difficult challenges we face in America today in medicine, and it is on the rise. This year for the first time, cancer of the pancreas became the third leading cause of cancer mortality. And in the next decade, if we do not change that trajectory, it will be the second leading cause of cancer mortality.
- Gore And is that because the incidence of pancreas cancer is increasing or?
- Fuchs It is. So, the frequency of diagnosis or incidence rate is on the rise for a variety of reasons, and unfortunately, it is really one of the great challenges of treatment. The problem with pancreatic cancer as you know, is there are very few warning signs, the symptoms are fairly nonspecific, it can include fatigue, sometimes abdominal discomfort, weight loss -- the things that people will often ascribe to other things and also even when you first develop symptoms, it is usually too far advanced. So, the problem is when an American is diagnosed with pancreatic cancer, 80% of the time it is beyond the opportunity of a curative operation.
- Gore I know that a large part of your work has really been around identifying those factors which contribute to these cancers and the environment and people's behaviors and potentially modifiable risk factors. So, could you tell us a little bit about that?
- Fuchs Yes. You asked me about when I got started, and I certainly got started like most oncologists with an eye of let us figure out the biology of these cancers and let us use that, that leverage, that knowledge to better treatments, and I look forward to getting to that point in this conversation, but the other aspect that I was actually interested in fairly early on is we got to figure out a way to prevent and some of it is through early detection, but some of that is through the phrase primary prevention because when we talk about early detection, we are not really talking about prevention, we are talking about finding it early. Primary prevention says what are the fundamental causes, either in diet or lifestyle and how do we modify those causes to reduce the burden of cancer. And colon cancer, which is really the area that I got started with in the prevention realm, has been a real lesson I think for us all. Namely, I took the interesting view of the following, which is if you look at the incidence or frequency of colon cancer diagnosis across the globe, you find out that in Western countries such as the US, the incidence rate is 40 times higher than places like sub-Saharan Africa.
- Gore 40 times?

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Fuchs Right. So, you might say, well that is because they just cannot diagnose colon cancer there, or maybe they do not get old enough to get colon cancer there. It is not that either because if you look at the incidence per age group, it is 40 times lower. And so, the last question you might ask is, well, it may be genetics. People who hail from that part of the world, their genetics cannot get colon cancer, but it is not that and I will tell you why. Because if you look at migration studies, people who leave those parts of the world, those underdeveloped parts of the world, such as sub Saharan Africa and move to the US, within one generation their family has the same rate of colon cancer as the rest of the US. So, it is something that we are doing in the US that is different and that is where I got motivated and so I got involved in these very large prospective cohort studies where for decades there are these cadres of several hundred thousand Americans such as the Nurses' Health Study, where basically they asked participants who are perfectly healthy, do us a favor, fill out these questionnaire, 16 pages long, every 2 years and tell us about everything you do.

Gore So that population of nurses becomes a cohort that you are following.

Fuchs In 1976, 121,700 female registered nurses completed a 16-page questionnaire about diet and lifestyle, medication use, family history, etc. We get all their medical records, we get blood on them, and if they get diagnosed with cancer, we get all their records and their cancer tumor box for analysis.

Gore And they fill this out every year?

Fuchs Every 2 years. And the diet questionnaire is 131 items and it actually has been validated vigorously and because of the nature of the questionnaire not only do we know for instance how much fried chicken they ate, but because of the nature of all the micro-nutrient data within these foods, I can tell how much folate they get or niacin they get. And it all is validated because if we do blood tests on them, the measure we get of the questionnaire matches their blood level.

Gore Although this questionnaire is from 1976, it way predates your involvement, right?

Fuchs That is right. But it is all prospective and it is asked every 2 years, so I know what they ate in 2016. And it was established frankly to look at cardiovascular risk factors and from that we learned about perils of cholesterol and smoking and a variety of other things that put you at risk for cardiovascular disease, which has been a gold mine in prevention of heart attacks. So, when I got involved, they said you guys are sitting on the mother load for looking at prevention of cancer. And I am oncologist, I would love to learn how to do this and work with you. And so, I said colon cancer is the ideal,

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there is something going on here that we are doing, and what did we learn? We learned that frequent consumption of red meat increases your risk of colon cancer three fold. We found out that people who exercise regularly reduce their risk of colon cancer by 50%. We learned that obesity is a potent risk factor for colon cancer. We learned that vitamin D is a preventive agent for colon cancer. And so, when you add up the variety of things that we have looked at, we could explain roughly 80-85% of colon cancer. And here is the really interesting thing: We came up with a study, a companion study, of male health professions. So, fairly well-educated people in the field, and what we found is that if they do six simple things, they can reduce their risk of colon cancer by 85%.

Gore Well, we are going to want to know what those six things are that we can do to prevent colon cancer, and we are going to do that after the break. Right now we are going to take a short break for a medical minute. Please stay tuned to learn more information about gastrointestinal cancer with Dr. Charles Fuchs.

*Medical  
Minute*

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*There are over 13 million cancer survivors in the US and over 100,000 here in Connecticut. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life changing experience. Following treatment, the return to normal activities and relationships may be difficult and cancer survivors may face other long-term side effects of cancer including heart problems, osteoporosis, fertility issues, and an increased risk of second cancers. Resources for cancer survivors are available at federally designated comprehensive cancer centers such as the one at Yale Cancer Center and at Smilow Cancer Hospital to keep cancer survivors well and focussed on healthy living. More information is available at [YaleCancerCenter.org](http://YaleCancerCenter.org). You are listening to WNPR, Connecticut's public media source for news and ideas.*

Gore Welcome back to Yale Cancer Answers. This is Dr. Steven Gore, and I am joined tonight by my guest, Dr. Charles Fuchs. We are discussing the diagnosis and treatment of gastrointestinal cancers. Charlie, before the break you were saying that you have done this study in adult male health professionals and found that there were six modifiable causes or ways to reduce our risk of colon cancer.

Fuchs Correct. So, from the various studies that I mentioned that we had done looking at risk factors for colon cancer, we said okay, we have been studying individual items, now let  
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us look at a lifestyle, let us figure six things that we can advise people to do that are attainable, that are not too harsh in terms of the requirement. And so, those six things were, avoid being obese, exercising 2-3 times per week, not having more than one alcoholic beverage per day, so one a day is fine, and not more than one, not having red meat more than twice per week, not smoking and having a multivitamin that contains vitamin D. We did not think any of them unattainable, you can have your red meat – just not more than twice a week, exercise about twice a week, you can have a drink but not more than one a day, etc., and what we found is that if a man could do those things, he reduced his risk of getting colon cancer by 85%.

Gore So, did you actually test that?

Fuchs We did not actually do a trial per se, we just made them aware of it, and saw what happens among people who comply with it. Now, you and I are both physicians, so I will ask you the question because I know what proportion actually did it. Do you want to take a guess? What percent of these health professionals, well-trained health professionals did all six?

Gore Did all six? 20%.

Fuchs Three percent, and none of what I told you is unknown to health professionals or I think so difficult. Well, among those 3%, those brave souls, they eliminated their risk by 85%.

Gore Now when you studied all these factors, you said you accounted for 80% of the colon cancers. Does this make up for the 40-fold difference compared to sub Saharan African, this accounts for all of that?

Fuchs Exactly. I would not say necessarily all of it, but it speaks to the fact that much of that difference is our behavior. And it makes sense right, because if those people move to the US and within a generation take up our practices, they enjoy unfortunately the same high risk of colon cancer.

Gore Let me ask you this question, which is of interest to me. We know that in animals, we sometimes can change the risk of cancers in subsequent generations through various modifications and lifestyle that occur through what we call epigenetic changes. So, I am wondering in these people who have moved from Africa and who have an increased risk of colon cancer through the generations, is some of that going on that when they come to a Western diet, are there epigenetic modifications that change their cancer risk?

- Fuchs Absolutely, and let me tell you what you are saying is really music to my ears that you are interested in it. Because when I first got started, really the available resource was the questionnaire data which was a gold mine as I said. But you and I obviously as oncologists want to understand cancer biology. And so, the other aspect of the study that we convinced the participants to do was when you were diagnosed with colon cancer or any other cancer, have the hospital send us the tumor for analysis in a molecular laboratory. And so, we are at now, what do these things do in terms of biology, be it epigenetic changes in the DNA, certain mutations, certain changes in some biochemical features of the blood or the cell that actually is creating cancer. And what we are finding is, you can actually understand these things and how they are driving the molecular basis of cancer. There really is a relationship. So, people who are obese, who are sedentary, they get biochemical changes in their circulation and there is clearly a footprint, essentially a fingerprint of changes in the cancer, and it speaks to the fact that energy balance pathways as they are often referred to because you are sedentary, because you are obese are activated in a way that promotes cancer.
- Gore Well then, I think you are going to motivate me for the next 24 to 48 hours to get back on the scale and re-up my Weight Watchers tracking, but whether that motivation lasts through next Sunday, we will see.
- Fuchs I will keep you on it.
- Gore I will have to report back, we will have you back next year and I will weigh-in for everybody. So, thanks Charlie, that is really fascinating information and it gets so clear that basic elements of lifestyle in our society including smoking and obesity impact the public health so greatly and yet as I can say as a motivator physician who likes to be thinner and who does exercise regularly and as you quote from your motivated health professionals in your previous experience, it is not so easy. You could say, well get to a healthy weight or healthy body mass index, and for some of us that is just not easy.
- Fuchs It is not. But we have to stay on it because we are obliged to use these studies and improve the lives of people at risk. And I will tell you one other anecdote, which is the people who actually are most interested in these data are not healthy people, because as you rightly pointed out even physicians do not do it. The people who are most motivated are people recently diagnosed with cancer. And what we know from studies is that 75% of newly diagnosed cancer patients believe that there is a diet, lifestyle or supplement that will modify their likelihood of cure. You know that because you hear it in clinic too. And there are studies that show it. And the sad truth is that even though patients believe it, there have not been rigorous studies to test that. Because all the studies I just quoted to you are studies of healthy people looking at the risk of

developing colon cancer. But the more relevant question for a patient is, if you have now been diagnosed with colon cancer, does diet or lifestyle matter now? We actually embarked 10 years ago on the same studies except instead of asking healthy people, we have now been asking thousands of newly diagnosed cancer patients to fill out these same questionnaires and see whether their diet or lifestyle changes the success of cure for the cancer, and I can tell you today that we are actually starting to get information and much like the risk data – exercise, avoiding obesity, healthy diets improve the success of treatment for cancer patients.

Gore That is fascinating. You know that it has been my experience with patients that this great interest in nutritional supplements and so on means that many patients want to be able to go to the GNC Store or go online and get some berry from Tahiti or something that somehow we are keeping a secret, the medical staff which is keeping a secret and be able to spend a lot of money on and I am not trying to make fun on anybody, this is to people who are really doing research and wanting to help themselves, but if it really means losing 30 pounds, that might be a different story. Not that they might not want to, but it is one thing to take pills that they perceive as safe and another thing to really modify lifestyle, this is not trivial.

Fuchs Absolutely. Those supplements are a 20-billion-dollar industry. It is purely anecdotal and what I tell patients newly diagnosed with cancer is that from most cancers and most studies if you would exercise 2-3 times a week, which if you look at studies of cancers patients, is not long distances in the gym, it is walking. We did a study of colon cancer patients, and individuals who walked regularly significantly improved their likelihood of cure.

Gore And of course, here at Yale, we have Melinda Irwin's really wonderful work looking at the influence of exercise on breast cancer survivorship.

Fuchs It is a common thread, and so we have looked at a few other things for instance in colon cancer patients. There have been studies saying that in addition to taking their prescribed treatment, that if they take an aspirin a day, it improves the likelihood of cure for colon cancer patients. Not all vitamins probably matter, but there is evidence that vitamin D can improve the success rate of treatment in colon cancer, and we just recently completed a clinical trial of adding vitamin D to standard colon cancer therapy. So, we want to study these things and let me emphasize, in contrast to the anecdotes that we are frustrated with, we want to study these things with the same rigor as we would with a new drug or a biological phenomenon so that at the end of the day, we give people the right answers.

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Gore And vitamin D is good for your bones on top of it, right? As long as you do not take too much of it.

Fuchs Exactly. That is right.

Gore Unfortunately some of your patients come in with advanced cancer I am sure and that is what people dread. Our listenership is very worried about what to do when they have cancer. Are things moving forward in terms of treatment for advanced cancers?

Fuchs Absolutely. And I will tell you having now practiced GI oncology, gastrointestinal cancer treatment for 25 years, I actually think this a very exciting time. For instance, in colon cancer, we have essentially tripled the survival of patients diagnosed with metastatic or advanced colon cancer in just the past decade.

Gore What does that tripled mean? Does that mean people are living three times longer, does that mean three times as many people are being cured?

Fuchs Well the cure rate unfortunately is still low in terms of eradicating the cancer, but yes people are living three times longer with metastatic cancer. Now, it is not sufficient and we want to get to the point of curing people. But it is a meaningful difference. I can tell you as somebody who has worked with patients and families, it is a very different outlook when people can live their lives much longer and successfully with these cancers. We've got to do better. But I think the evolution has been treatments now that are based on a sound understanding of the biology of colon cancer. Because for too long in the solid tumor world and not in the hematologic or blood-based cancers that you and your colleagues have been successful in, but I think in my world, it has been sort of taking a drug off the shelf and trying it, and we really learned from people like yourself, Steve, that like leukemia, if you really understand what is driving it biologically, you get better treatments and so we have figured it out that that is what we needed to do and so the treatments that we have been testing and developing now are really based on that understanding and so they are much more effective. When we get into clinical trial, the likelihood of success of testing new drugs is much higher because there is really a sound basis for testing it and the drugs are really making meaningful differences, and so I think now with the advent of precision medicine where we now at Yale are routinely sequencing tumors so that we can best inform the best treatment for that patient's colon and we are starting to advance other novel treatments like immune-based approaches, new small molecules that target the individual genes, I think it is a very different and exciting landscape for the treatment of patients with colon cancer, and I would say we are doing the same now in patients with

esophagus and stomach cancer where we have a variety of new drugs. Immune-based therapies is an exciting and novel idea, but we have a lot more work to do, but I am very optimistic about the future for patients with these cancers.

Gore           What can patients do to make sure that their tumors are being studied appropriately in a way that can help their oncologists chose the right therapies? Or is this not something quite ready for primetime?

Fuchs           I think for a patient who is diagnosed with a newly diagnosed metastatic colon cancer, they should be routinely having their tumor analyzed for mutations in the DNA of the tumor. It informs treatment today. The data are available now and we can make better treatment decisions with that information. So, I think you need to have that conversation with your oncologists. This is something we should be routinely doing for all patients because it really can make a difference today. I am not talking pie in the sky. Treatment decisions can be made more logical and more effective with that information.

Gore           And if that was not done right out of the gate as long as there is some tissue stored, which most pathology labs have, that can usually be done post-hoc right?

Fuchs           Absolutely, it is not too late. For patients or family members that might be hearing this now, if it has not been done yet, that is fine, sit down with your doc and make a plan to take the tissue that we stored away and get it analyzed.

*Dr. Charles Fuchs is Director of the Yale Cancer Center and Physician-In-Chief at Smilow Cancer Hospital. If you have questions, the address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu) and past editions of the program are available in audio and written form at [YaleCancerCenter.org](http://YaleCancerCenter.org). I am Bruce Barber reminding you to tune in each week to learn more about the fight against cancer. You are on WNPR, Connecticut's public media source for news and ideas.*