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Welcome to Yale Cancer Answers with doctors Howard Hochster, Anees Chagpar 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 it is a conversation about research myths in mainstream media with Dr. Perry Wilson. Dr. Wilson is an Associate Professor of Medicine at Yale School of Medicine and Dr. Gore is a Professor of Internal Medicine and Hematology and Director of Hematological Malignancies at Smilow Cancer Hospital.

Gore Myths, what is a myth?

Wilson So what I like to talk about a lot is how the popular media portrays medical research, so I'm a medical researcher myself, I think medical research is this amazing thing and high expression of the scientific method.

Gore That sounds like a myth to me.

Wilson Ha ha ha, in some cases it is. How the media conveys scientific research is filled with a lot of myths. So I am not talking about myths like people only use 10% of their brain, I mean those things out there. What I mean is how scientific research gets done and how the popular press tends to sensationalize the research that is out there.

Gore Could you give me an example?

Wilson There are so many examples.

Gore Let's start with one.

Wilson There are so many examples. So you know, we will see a study for instance, I have one that I liked where it was a large study in China about 600,000 people involved and what they found was that people who said they ate chili powder more often lived slightly longer and this was all over The New York Times and ABC News and basically you know, spicy food is the key to longevity is how that gets promoted.

Gore I'll go with that.

00:02:10 into MP3: https://ysmwebsites.azureedge.net/cancer/2017-YCA-1210-Podcast-Wilson_322902_5_v1.mp3
Wilson: Yeah, it would be nice, I like spicy food myself. When you dug into the actual study, you would find a number of things. Number one, you would find that in China, it turns out that spicy food is distributed very regionally, in particular rural people were more likely to eat more spicy food which is not fully accounted for. The other thing you would find out is that the effect size that they were talking about the amount that it would increase your life was incredibly small, so small in fact that you would have to take roughly 6000 people and put them on a spicy food diet to say one life over 100 years. So just incredibly, you know, of passing interest to those of us who enjoy spicy food, but not changing the world and I think the most disappointing part of that study was that the effect was only seen in people who don’t drink alcohol. Now, I don’t know if you are like me, but if I am having something spicy, you know, a little bit of beer on the side really helps.

Gore: I am not going to weigh in on that one.

Wilson: So we see that very often. You sort of take the headline from the study without diving a little deeper, in particularly studies that show very modest effects, it is rarely mentioned that those effects are so modest.

Gore: So who has responsibility for this, right, I mean the media is trying to sell their newspaper or their website, right, that is what they do for advertising whatever so they need to put stuff out there that is interesting to people and people seem to be interested in ways of improving their health. So I mean do you think the media has responsibility for doing the kind of deep dive. I mean I know all those people like Dr. Sanjay Gupta and stuff, I think they try to be pretty responsible right?

Wilson: Yeah, there are some great science journalists out there and to some extent the answer is yes, you know, journalism is journalism and obviously people want to generate clicks and website visits and things like that, but we would you know never expect our political journalists to not sort of dig a little bit deeper when a scandal breaks.

Gore: I did not know about that, it sounds like fake news?

Wilson: Ha ha. We would ask more of them and I think the good science journalists out there really do that. There are not many of them, not that there are not many good science journalists, but there are not many science journalists period. Because unfortunately, especially in print media we have seen less and less profits, they cut back on staff. So dedicated science journalists are rare thing, but to some extent you need those people, because they are ones who actually understand how to read a study and are not just going off the press release.

Gore: Right and what about scientific literacy among the lay community who is reading this. Do you think that you know you just talked a lot, you know rather simply which I appreciate, but talk about a sample size and small effect size and I certainly get what that means and I think many of listeners do too, but do you think the lay public can get beyond the headline even if the Sanjay Guptas in the world try to explain this, do we have enough scientific literacy to have this be part of our conversation?

00:05:21 into MP3: https://ysmwebsites.azureedge.net/cancer/2017-YCA-1210-Podcast-Wilson_322902_5_v1.mp3
Wilson  I have a lot of faith in the public.

Gore  I am not trying to put anyone down.

Wilson  No of course not not after reading the studies. I think with a couple of sort of simple tricks we can vastly increase the scientific literacy, so one thing I tell my patients and I am sure like you I have patients that come in after having looked on Google, you know about a disease or treatment they come in all the time. A couple of simple rules of thumb I tell my patients is number 1 is that no single study is enough and much of the science news – the medical news that comes out, is about a single study that is just the nature of the news cycle, something gets published and we are going to talk about it. Those single studies we should not go off of, please read the article, be interested, kind of keep it in the back of your head on chili powder, I am going to keep an eye on it.

Gore  Talk to your doctor about it.

Wilson  Talk to your doctor about it absolutely, but one study is never enough. The second thing is this concept that I like to get into people's head which is how many people do you need to treat with this drug to benefit one person. That has a technical name, it is called the number needed to treat, but if a patient just asks that question to their doctor, you know how many people need to be treated with this drug to benefit one person, they will be very surprised by the answer more often than not.

Gore  You think most doctors can answer that question?

Wilson  Most doctors should have the ability to answer that question with a quick internet search of the relevant studies.

Gore  Okay.

Wilson  If they don’t, they should learn. I think it is a critical part of medical education is to know how to read the medical literature and we are seeing more and more of that in medical schools and I am encouraged by that, but if patients look, they can even go to certain websites, there is a great website called thennt.com, the number needed to treat and that site just lists medical studies and tells you how many people need to be treated with this drug to benefit one person and you will see numbers that will shock, you will see numbers like 200, 1000, 5000 and when you realize that you have to give a drug to 100 people to prevent one person from dying, you ask a whole new interesting series of questions, now it does not mean the drug does not work or that the drug is not good in fact if the drug is relatively harmless or it has very little side effects and is not crazy expensive, then that might be a totally reasonable proposition to treat the 100 people to save 1 life, but you can imagine situations obviously where that is not reasonable and that is a key to really having an informed discussion with your doctor about taking the medication.

00:07:58 into MP3: https://ysmwebsites.azureedge.net/cancer/2017-YCA-1210-Podcast-Wilson_322902_5_v1.mp3
Gore Yeah, but you know, let me just push back a little bit. From my perspective, what patients are interested in is not so much how many patients are needed to be treated to see a statistical effect, but what are my chances of benefitting from this thing, me, right, it is all about me, which is appropriate, right. So how do you invert that?

Wilson Very simply. If 100 patients need to be treated for want to see an effect, the chance that it will benefit you is 1% and again, we might say that is crazy, but if it is a once a day kind of vitamin or something and it is preventing death, well then yeah may be I will take, I will that 1% chance that I am the one in 100 people, but what it will also do is force you to have a conversation you’re your doctor about your individual risk, right because those studies present the data from a whole population - the average benefits of people you know 1% of the time, but you might be significantly higher, particularly if your risk of that outcome is much higher. If your risk of death is much higher, well may be that vitamin is much more effective in you.

Gore You know, it is really interesting. Last night, I happened to be out for dinner with a couple of friends, one is a lawyer and one is an engineer, they are both very intelligent people and we were at a sort of health food oriented kind of place that happened to have like an emporium upstairs and I was just amazed at the number of supplements. I mean, I guess that I should not have been surprised that they were just rows and rows of supplements and when I brought this up at dinner and one of my friends was saying how he really, you know, wants to start taking B complex, so why? He started to listing these things that he thought to be a couple of things and I said you seem to eat a pretty healthy diet, I am not sure you are not deficient in any B vitamins and we had a very reasonable conversation about it, but I could tell that he was not interested in hearing that, right. He wanted to believe the B vitamins were going to do whatever it was he wanted and I find that true with a lot of very educated people there is this belief system, I am not putting them to be down about it, about untested supplements in particular, what’s your experience or thoughts about that.

Wilson Absolutely.

Gore Turmeric powder, milk thistle.

Wilson I am a kidney doctor.

Gore We just had a Coenzyme Q, sorry, go ahead.
Wilson: I know, there is a lot of this, we just had a negative study for turmeric powder. So people fall into Google holes all the time and the technical term for this is confirmation bias where you Google B vitamin health benefits and you are going to find an awful lot, so you can get this really self-reinforcing area, you are correct, it is really hard to disabuse people with some of these notions. The best thing to do is often just to suggest other methods of search, ‘hey have you checked out this website and if you are interested I can give you some very authoritative websites that look at things like this, but have you have checked out this, you know, they have some great information.’ Let people discover the alternative information themselves rather than you know, sort of beating them over the head with it. Now, there are some cases where, a lot of doctors are ‘eh, you know you want to take a B vitamin, it’s not going to hurt you know,’ I am a nephrologist, I am a kidney doctor, we say vitamins give you expensive pee and they just kind of get peed out.

Gore: I tried that one too.

Wilson: And you know, what is the harm and probably it is not a little harm to your pocket but that is okay. In some cases, though people are foregoing you know what we would call more conventional therapy and you know you can think of some high profile cases like Steve Jobs, where.

Gore: He did not get treated for his pancreas cancer.

Wilson: Exactly, and in those situations I think as medical professionals you actually do have a bit more of a role to ensure that if they are taking the vitamins that is fine, but let’s not forget to take your other medication as well.

Gore: Yeah while you know I have to say that I was a little humbled a year or two ago when a patient of mine who may have or may not have had a particular kind of low grade leukemia that I treat, you know declined my recommendation or tried it one day, and he had a real big list of these things including milk thistle and all those other stuff, I cannot tell you what milk thistle and for whatever reason, his counts got better, now may be really had a transient viral thing or whatever, but he is a believer and I cannot disabuse him because well you know he is better.

Gore: It can be very hard to tell. Fortunately, we do have an apparatus to test these things. We have things called randomized trials where we can evaluate whether drugs work and whether supplements work. The supplement companies are not terribly interested in doing this because I do not think they stand to gain very much by doing a trial, it either turns out to be negative and there is some evidence against them and they are already getting people to buy them, so unfortunately we do not see as much of that as we should.

Gore: Right and it is not easy to get such studies funded all the time either if you are an academic wanting do them.
Wilson Absolutely, grant funding is an issue.

Gore It is expensive to do these trials.

Wilson It can be incredibly expensive. The average clinical trial of a new therapeutic, this is if you are trying to get FDA approval, I think the most recent estimate 50 million dollars, a little bit more, despite our Yale salaries, right? But nevertheless there are ways to do these studies, especially supplements do not need FDA approval that are much cheaper.

Gore Very well, this is really fascinating topic and we are going to want to continue more about this, but right now, we need to take a short break for a medical minute and for me to take all my supplements. Please stay tuned to learn more information on media myths.

Medical Minute
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The American Cancer Society estimates that over 15000 people will be diagnosed with colorectal cancer in Connecticut this year. When detected early, colorectal cancer is easily treated and highly curable and as a result, it is recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Tumor gene analysis has helped to improve management of colorectal cancer by identifying the patients most likely to benefit from chemotherapy and newer targeted agents resulting in more patient-specific treatment. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital. More information is available at 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. Perry Wilson from the Yale School of Medicine and we are talking about myths about medicines, supplements, and other health issues in the media and how people respond to them. Perry, one thing that I am not sure how it fits into the myth thing, but one of the frequent complains you hear from colleagues, friends, and patients is the frequently changing recommendations, dietary recommendations often based on this new clinical study versus that old clinical study, so coffee causes pancreatic cancer, coffee prevents pancreatic cancer, something is good for your blood pressure, something is bad for your blood pressure, you should take this for your cholesterol, no you should do this diet instead, there is a lot of exhaustion around, then of course people are screwing around, but you know, what do you think about that?

Wilson This is a major issue for patients, especially when the media is reporting kind of breathlessly about the newest study in coffee, oh it seems to just get a lot of attention, I think because it is a such delicious good thing.
Gore: You do not think Starbucks is paying for that?

Wilson: That we all love. I have not seen Starbucks directly financing any of this research. Dietary research is, you know, I do not mean to be overtly critical here, but it is in its own circle of hell in my opinion. So, much of dietary research relies on something called the food frequency questionnaire and basically, what you do is you give a patient these 100 questions, how often do you eat meat, how often do you eat smoked meat, how often do you eat soft cheese, how often do you eat hard cheese, on and on and on. This is a huge amount of data for each patient and now you can take all that and put it in a computer and you can dice that anyway you want. You can look at each individual question, you know, soft cheese as it relates to lung cancer or you can say, well soft cheese has lactulose, so let's combine all the things that have lactose in it and relate that to lung cancer or you can say what total calories in and you can cut this data in a million different ways, that is very dangerous, because the more times you can test the hypothesis, the more likely you are to get it wrong which is why I think we see all these back and forth about dietary research. You know, people say the coffee effect and a lot of research, I like to point out, you know, some people will have their coffee black, some people have a double tall mocha frappucino with extra sugar and I highly doubt that those have the same effects. In addition, coffee, just black coffee has hundreds of different chemicals in it, right, so we have no idea what is going on there. The coffee effect may as easily be the biscotti effect, because we are just picking up patterns of behavior.

Gore: The oatmeal effect may be.

Wilson: The oatmeal effect, right, or the working effect, right. So people who work more or have more intense jobs may drink more coffee.

Gore: They have more stress.

Wilson: They have more stress as well, so there is a lot of these things playing and unfortunately, these observational studies just never capture all of that, so I hesitate a lot when any new diet fad comes out and promotes long-lasting health benefits. To the credit of some of the societies out there that make recommendations, they tend to slow walk these things a little bit. It took a longtime for the American Heart Association to sort of evaluate how much salt is appropriate in the diet and they are still evaluating, but they do not change with every single study. The news media would like us to believe that, oh now eggs are good for you, now eggs are bad for you.

Gore: Okay, that was a big one, eggs and cholesterol, right?

Wilson: Yeah, there are some broad trends that I think are very true, so I think the shift away from you know fat as a danger and more towards simple carbohydrates as a danger seems to be supported by more and more evidence, but again, we have to be very careful, we have to be slow, we need a lot of studies saying the same thing. Any given study, even you know in the venerable New York Times, you got to take with a grain of salt, but not more than 2500 mg a day.

19:16 into MP3: https://ysmwebsites.azureedge.net/cancer/2017-YCA-1210-Podcast-Wilson_322902_5_v1.mp3
When I had this in my life, just an internist that I used in Baltimore, when I lived there, who is a great guy, had me taking fish oil because there was heart disease in my family and stuff and I had a little bit of not a cholesterol problem, but subtype of cholesterol problem and then the fish oil data kind of turned out to be not as convincing to say the least and I threw away a big bottle of fish oil capsules, which is fine because it is kind of yuck anyway.

Gore

Wilson

Right. We also have to explain the patients that science is supposed to change, we are supposed to kind of keep testing things and reevaluating things and so I would be very worried if we would be treating the same condition with the same medicine for 100 years, that is sort of a bad sign for not making progress there. So I do not think patients should just distrust the medical profession when we say you know what we got some new data and we thought this drug worked but the better data suggests it does not. There are some really dramatic examples of that. There was a drug called flecainide which was used to suppress abnormal heart rhythms and 20 years ago or so, it was known that after people have a heart attack, these abnormal heart rhythms precede death, and the thought was ‘ah, you know they are going to have these abnormal rhythms and then they die.’ This drug suppressed those abnormal rhythms and it did it beautifully, worked very well. So for some period of time, we were treating patients with this. Then the longer-term studies showed that the use of that drug was associated with a three-fold higher risk of death and so we do not use that any more. Now, this was not the medical profession being bought out by big pharma, this is how research works. You have initially studies that look at an important outcome like the rate of abnormal heart rhythms and then you have a longer term more comprehensive studies that look at a really important outcome like death and we should expect things to change. I gave you a notable example where it really went wrong.

Gore

And then, there was Vioxx, right?

Wilson

Oh that is another great example more information came out. Now, Vioxx in contrast does seem to - some of that information that we should have had initially may not have come out when it should have and that is a major problem this way.

Gore

Let us talk about that. So people may not remember that the Vioxx was an arthritis drug or anti-inflammatory, right?

Wilson

That is correct, yeah.

Gore

And it was supposed to be safer or better than things like Advil.

Wilson

Yeah may be less risk of gastrointestinal bleeding which was a rare complication of some of these other drugs.

Gore

Yes right, so can you remind us what the problem was?
Wilson  Well the data showed that sure enough it was very effective in terms of pain control and people had a lot of benefit in terms of their arthritis symptoms, but the longer term data showed that it increased the risk of heart attacks and other blood clotting problems and had that longterm data come out with long-term follow up, you know careful surveillance as we do of a lot drugs that would be one thing, but the lawsuit is a legend that the maker of Vioxx which is Merck, I believe, was actually aware of some of those complications beforehand, I am not a lawyer, you know, so I do not want to get into that too much, but that is we would call a failure of the system, but the existence of occasional failures like that does not necessarily you know should not discount the whole process because by and large medical research is methodical, slow, and accurate, reporting on medical research is not.

Gore  So why do you think people and the public, you know there are so many people who kind of believe that the cure to cancer is known and somehow physicians do not want to tell people that they are not willing to test the special berries or whatever. Why is this mistrust?

Wilson  I think some of the mistrust is rooted in history, you know there are some notable ethical failures in the history of medical research, think of the Tuskegee experiments where you know deliberately infecting people with syphilis and not treating syphilis, things like that did happen in the past. There are a variety of ethical and legal obligations. We have now conducting human research that we do not have then, which is very important, so there is that kind of backdrop. The other thing is that people really want there to be a cure of cancer, cancer is scary, and we all know someone who has had cancer and most of us probably know someone who has died of cancer and just knowing that it is out there is frightening and it is very reassuring to think that there is a cure. What I tell people when they tell me "Oh you guys know what the cure to cancer is" is - especially as a struggling assistant professor at Yale, you know, if I had the cure to cancer, they could not pay me enough to, you know, shout it from the rooftop and be the most famous physician scientist in the history of mankind, it is just that type of conspiracy is a little too difficult for me to swallow.

Gore  Yeah that is interesting, you know, yesterday I was offering a clinical trial to a patient where I really thought it was probably her best option at this time and I of course discussed other options and she had a cousin with her, you know, nice person, and I am very careful while going through the consent form with the patient when I have time to do so, because I think our consent forms tend to be very difficult for most people to read even though this was supposed to be at a lay level, they are very hard and there’s so much information there from lawyers that I look this kind of look at paragraph four, you can take the whole thing home and read it. So I went through the add in, you know, of course it talks about, you know, one of the investigators has a conflict of interest that he is this closest because he consults for the pharma company that makes it and the cousin said, although she was not discouraging the patient from going on, it was like "we know, it is all about the money," and you know, "they should be paying you to be on this to be a guinea pig." I was very disturbed that was her response, but I also kind of got it, you know.
Wilson: I get it, I get it. It is in the pharmaceutical industries, you know, multihundred billion dollar industry, pharmaceutical companies are profitable, they charge a lot for their medications, they do have a vested interest in a positive result. The nice thing is that we have this governmental institution which is called the FDA which is going to pour through their data and make sure that they did not cook the books at all, that is the public's voice in this process and to date, the FDA has been an incredible advocate for public health and public safety, in fact to the point where some people complain that they are not approving drugs fast enough. So you know, fortunately, we have a watchdog group there and I think that is very important that we explain that to patients.

Gore: Do you think that physicians who participate in these studies have some complicity, you know kind of look the other way or allow statements we made, how often do you think that happens?

Wilson: A lot of statements to be made about a drug that turns out not to be true or?

Gore: Well, how the data may be interpreted, how complicity when there has been, you know, we are the authors of these articles, right, even though the pharma company is sponsoring it?

Wilson: Yeah in some cases, often times yeah, personally I would say that my research funding comes from the NIH so yes, but I think that once a study is published and a physician is out there discussing the results, yeah I think there is a human tendency to put the best line on that, because none of us are going to sign up to do a clinical trial or run a clinical trial that we do not believe in to some extent right.

Gore: There is an impetus to be right, to look good right?

Wilson: You know, if someone came to me and said, you know, I want to do a trial of slapping people on the head to see if it cures cancer and I will give you all this money, I would still say no, you know I do not think that is going to work and so.

Gore: That might work for kidney failure?

Wilson: Yeah well for kidney failure, that is a different story. So I think there is that and unfortunately, we do have this disclosure requirements so that physicians when they speak have to say if they have received funding from drug companies. I often encourage patients, you know, one sort of my rules of thumb, when they are googling is if you on a website that is advertising the thing they are talking about is not the best website for you and that holds true whether it is a supplement or whether it is a pharmaceutical product, you know the pharmaceutical websites going to have a lot of information and most of it is going to be factually accurate because they are legally bound to be factually accurate, but clearly you know there is a lot of pretty pictures and smiling faces in the background, so you want some independent people to discuss the results of any trial.

Gore: The elderly couple sitting in bathtubs on Big Sur looking at the water?

28:32 into MP3: https://ysmwebsites.azureedge.net/cancer/2017-YCA-1210-Podcast-Wilson_322902_5_v1.mp3
Wilson  Exactly, right and then the list of side effects, you know, 500 things deep in small print next to them.

Gore  I did not know, that whole bath tub thing looks pretty good to me.

Wilson  Well, I would take it if I had any free time.

Gore  Fortunately, we keep you too busy.

Gore  What about abject fraud, is there really ever fraud in research?

Wilson  That is a great question. There are undoubtedly is because there are known cases of fraud. The question how prevalent it is a different question. In some surveys that have asked, you know, when you ask people directly have you committed research fraud, believe or not the answer is often no, but when you ask research associates and study coordinators - do you believe that fraud has even been conducted, the numbers are higher, you know the yes response to that question is sometimes is as high as 20% in some surveys. I do not think that is the rate of abject fraud. It is hard to commit a fraud, so I will give you my favorite example because this touches on the media. So in 2001, there was a randomized control trial in Korea and they took women who were undergo in-vitro fertilization trying to get pregnant and they randomized them to usual care which is just whatever happens in in-vitro fertilization and the other group was prayer, and it was not the women praying for themselves, they sent pictures of the women to prayer groups in the United States and had the prayer groups in the United States kind of pray at these pictures, they did not know the women's name, they could not contact them. The rate of successful pregnancy was about 30% in the controlled group which is decent actually for in-vitro fertilization, 60% in the prayer group, which is amazing, you know, if there was a drug that did that it would be a blockbuster and you know, prayer is cheap, so this kind of headlined in The New York Times, study names prayer in pregnancy, the senior author in the study was a guy named Rogerio Lobo, the then chief of OB-GYN at Columbia University which is my alma mater from med school, but you know there is something a little strange here and then shortly after the study was published, it all fell apart. The interesting story is that the study never happened, it was completely fabricated, the women, the in-vitro fertilization clinic were never found nor were the prayer groups in the United States. The guy who wrote the study was a guy named Daniel Werth and he was later prosecuted, check fraud, he had been collecting his deceased father's social security checks for about 10 years. He went by the alias and this is the best alias I have ever heard, John Wayne Truelove. He did not have an MD, he had a JD, so why he is writing the medical paper is unclear and as you look back you see all of these red flags. This is a great example of how peer review can sometimes go wrong. So peer review we think as this beautiful thing where we have an independent arbiter who says the study is good or not but if you just going to lie, you know I would like at that study and say well it is a randomized trial, that is the highest evidence, that is good enough, so we do need to be skeptical, especially about claims that are particularly fantastic.

Dr. Perry Wilson is an Assistant Professor of Medicine at Yale School of Medicine. 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. I am Bruce Barber reminding you to tune in each week to learn more about the fight against the cancer. You are on WNPR, Connecticut's public media source for news and ideas.