“Scientific Research on Lifestyle Choices to Reduce Your Cancer Risk” (Nigel Brockton) [#40]

Brian McCloskey and Brad Power
January 18, 2023

“Every couple of years, we do a cancer risk factor awareness survey and about half of the people are unaware of most of these strong risk factors like alcohol, obesity, low physical activity, and diet.” – Nigel Brockton, PhD

“The immune system is important because then you're using a system against a system, rather than one tool against one target.” – Nigel Brockton, PhD

“There is a huge difference between what can be recommended at the population level (the predominant role of AICR) versus what can be assessed to be potentially beneficial at the individual level (clinical guidance and patient choice).” – Nigel Brockton, PhD

Meeting Summary

Advanced cancer patients are looking for every edge they can find to enhance their immune system and general health to fight their disease. In a diagnosis that can arrive "out of the blue", it is important to have agency and make a difference in things they can do, such as follow a healthy diet, reduce stress, get sleep, and exercise.
But what is the science that shows the potential impact of these and other lifestyle factors on patient outcomes?
A patient's medical team is usually focused on testing and treatment options with surgery, radiation, or drugs. Where should patients look to get advice on these other lifestyle factors?
How should a patient (and caregivers) think about the potential impact?
What should an active and engaged patient do?

As a cancer survivor (Ewing sarcoma) and Vice President of Research at the American Institute for Cancer Research’s (AICR), Nigel Brockton, PhD, is uniquely positioned to share the scientific evidence regarding diet, nutrition, body weight and physical activity as they relate to cancer risk and survivorship. The AICR was formed to try and distinguish evidence from opinion because patients were fatigued and confused by the changing messages about what was healthy. Dr. Brockton outlined the evidence about cancer risk generally and about prostate cancer specifically, and he explained the future direction of research on a global scale with AICR’s international colleagues.

What does the science show about the potential impact of lifestyle factors on cancer outcomes?

The AICR recommends in general that you should be at a healthy weight, be physically active, eat a diet rich in whole grains, vegetables, fruits and beans, limit consumption of fast and processed foods, limit consumption of red and processed meats, limit consumption of sugar sweetened drinks, limit alcohol consumption, and don't take supplements for cancer prevention. There are reasons to take supplements, but cancer prevention isn't one of them. In some

cancers, some of these supplements can interfere with the action of treatments. They can cut both ways.

If exercise were a pill, we'd give it to everyone. As long as you are capable of doing it, that is probably one of the strongest medicines, and it's based on evidence. Immune benefits seem to come more from high intensity workouts.

Specific cancers have specific recommendations. For example, in colorectal cancer there is strong evidence for five factors that decrease your risk: whole grains, foods containing fiber, dairy products, calcium supplements, and physical activity, and five that increase your risk: red meat, processed meat, alcoholic drinks, adult body fatness, and attained height.

In prostate cancer the only strong evidence is increased risk from adult body fatness, specifically for advanced prostate cancer. There is limited, suggestive evidence that dairy products, diets high in calcium, low plasma alpha-tocopherol concentrations (Vitamin E), and low plasma selenium concentrations increase cancer risk.

What should an active and engaged patient do?

You can substantially reduce your cancer risk by changing your behavior. About half of people are unaware of strong risk factors like alcohol, obesity, low physical activity, and diet, or that coffee is beneficial. People often think that it's genetics and pesticides and things, but they account for a fairly low proportion of cancers.

The cancer treatments that you receive could be bad for your cancer, but they are also bad for the rest of your body. The more you can do to maintain your resilience, the better off you are.

The call is for action, not perfection. The more of these recommendations you follow, the lower your cancer risk, and the better your outcomes. But any of these you address will be beneficial.

How should advanced cancer patients think about adopting lifestyle, nutrition, and exercise guidelines?

You can think about cancer like a bathtub which fills up with water (cancer risk). We're all born with a certain amount of water in our cancer bathtub. There's a leaky tap that adds water (cancer risk) over our lifetimes. Although we can never stop that leaky tap, we can reduce the flow by adopting healthy behaviors and avoiding unhealthy behaviors.

How do we know when our bathtub is getting full? We know through diagnostic tests.

It’s never too late to adopt healthy behaviors and slow the flow, and it's also never too early. It's pretty difficult to remove the water. We don't have evidence yet for the reversibility of cancer risk.

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What is the evidence for future cancer treatments, especially immunotherapies?

The future of cancer treatment, although it's been very disappointing so far in prostate cancer, is immunotherapy. The immune system is important because then you're using a system against a system, rather than one tool against one target. Prostate cancer tends to be a very immune cold tumor. The immune system doesn't respond to them. Males, particularly older males, tend to have poor immune systems. A lot of lifestyle factors have an impact on the immune system. If the immune system is already compromised, then immunotherapy is not going to be able to function. If you're giving immunotherapy as a last-ditch attempt, after you've wrecked somebody's immune system with chemotherapy, the immunotherapy has less of a chance. This is not sci-fi anymore because with melanoma they've shown some really good results with mRNA vaccines.

How should advanced cancer patients make decisions between treatments based on solid, evidence-based research and those that are based on solid scientific theories, but for which there is no randomized clinical trial evidence (and may not be for many years)?

There is a huge difference between what can be recommended at the population level (the predominant role of AICR) versus what can be assessed to be potentially beneficial at the individual level (clinical guidance and patient choice). Given the complexity of cancer treatment options and the unique context of each case, particularly in advanced disease, being your own advocate and engaging in collective advocacy is hugely valuable. Oncologists are well trained, but it is impossible for one person to assimilate the entire ever-expanding field. Tumor boards seek to exploit a group to optimize treatment approaches for individual cases, but you are the best advocate for optimal approaches for YOU!

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Meeting Notes

The information and opinions expressed on this website or platform, or during discussions and presentations (both verbal and written) are not intended as health care recommendations or medical advice by Cancer Patient Lab/Prostate Cancer Lab, its principals, presenters, participants, or representatives for any medical treatment, product, or course of action. You should always consult a doctor about your specific situation before pursuing any health care program, treatment, product or other course of action that might affect your health.

SUMMARY KEYWORDS

cancer, people, evidence, prostate cancer, recommendations, immune system, question, research, diet, exposures, colorectal cancer, factors, chemotherapy, risk factor, studies, exercise, risk, treatment, nigel, beneficial

SPEAKERS

Nigel Brockton, Rick Stanton, Amit Gattani, Brad Power, Brian McCloskey

Brad Power 00:03

Today we're going to have a session with Nigel Brockton talking about research on lifestyle, nutrition, and exercise, and how they can help in cancer treatment.

But before we do that, I want to read our standard disclaimer so that everyone knows that this is not medical advice and that if you say anything, or if you have your camera on, it all will be made public in a Zoom recording and a transcript.

Please note that the information and opinions shared on this website or platform or during this discussion or presentations are not intended as medical advice. It is important to consult with a healthcare professional about your specific situation before making any decisions related to your health. I like to point out that it's a ChatGPT version for those of you who know about ChatGPT, which took the legal words and made them a little simpler and clearer.

Nigel is going to start with a few slides, and then we'll open it up for discussion.

Nigel, if you could start by introducing yourself and the story you started telling me it would be perfect. There's someone named Wendy Fantl who is an ovarian cancer survivor and a scientist at Stanford. When we find people who are cancer survivors themselves, it really gives them a special perspective which is consistent with who we are and what we're up to.

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Scientific Research on

Lifestyle Choices to Reduce Your Cancer Risk

Prostate Cancer Lab
18 January 2023

Nigel Brockton, PhD.
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Nigel Brockton 02:09

I realized that there is a slight incongruity between my title and what I talk about because the blurb that we put together talks more about the post diagnosis space which I'm happy to talk about that, but what I'm going to go through in these slides is more about how we arrive at the evidence.

I'm Vice President of Research at the American Institute for Cancer Research. Brad was asking me how I got into this line of work before we went live. I was eight years old when I decided I wanted to be a marine biologist. I stuck with that single mindedly until I had a degree in marine biology. But on the way to getting a degree in marine biology at 18, I was diagnosed with Ewing Sarcoma in the soft tissue of my jaw. This was in 1989 when there was zero information about cancer. In fact, people wouldn't even say the word “cancer”. And it's quite amazing to see the societal change that I've lived through. Even between 1989 to 1992 when I had my recurrence, people had started to be able to say the word "cancer," but it wasn't common. I was working in a bar, or an English pub, and I was reading a book on chemotherapy. In those days, there were no layperson books. This was a book for doctors. Somebody asked me to put the book away because it had the word "cancer" on it. The fact that we now have these forums to have these kinds of discussions currently shows there's almost too much information.

One of the roles for AICR is to cut through to what we know. There's been some pretty massive changes. I had a recurrence, and I went through nine months of intensive treatment. I've been cancer free since I finished treatment in March of 1993. This will be 30 years next month. I get that look from oncologists when I tell them that I had an Ewing's and a recurrence that says, "What the hell are you doing here?” because there are very few recurrent Ewing sarcoma

survivors.

Disclosures

- No disclosures to report.

I have no disclosures to report.

The world’s leading authority on the links between

diet, weight, physical activity

and cancer prevention and survival

Who of you are familiar with the American Institute for Cancer Research before I popped on your radar? No? Good. That means I'm talking to a new audience and sharing our message.

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I've been following AICR since I started my PhD in 1997 when the first expert report was published. Certainly, from a research and clinical perspective, AICR WCF (World Cancer Fund) is seen as the global experts on diet, nutrition, physical activity and cancer prevention survival.

I'm not sure how many of you followed this back in February when they relaunched the Cancer Moonshot? I was frustrated. I'm totally supportive of the Moonshot, but I was frustrated when President Biden said, "We know cancer is a disease that we have few good ways to prevent." Part of what I'm going to present here is that we have lots of ways to prevent it.

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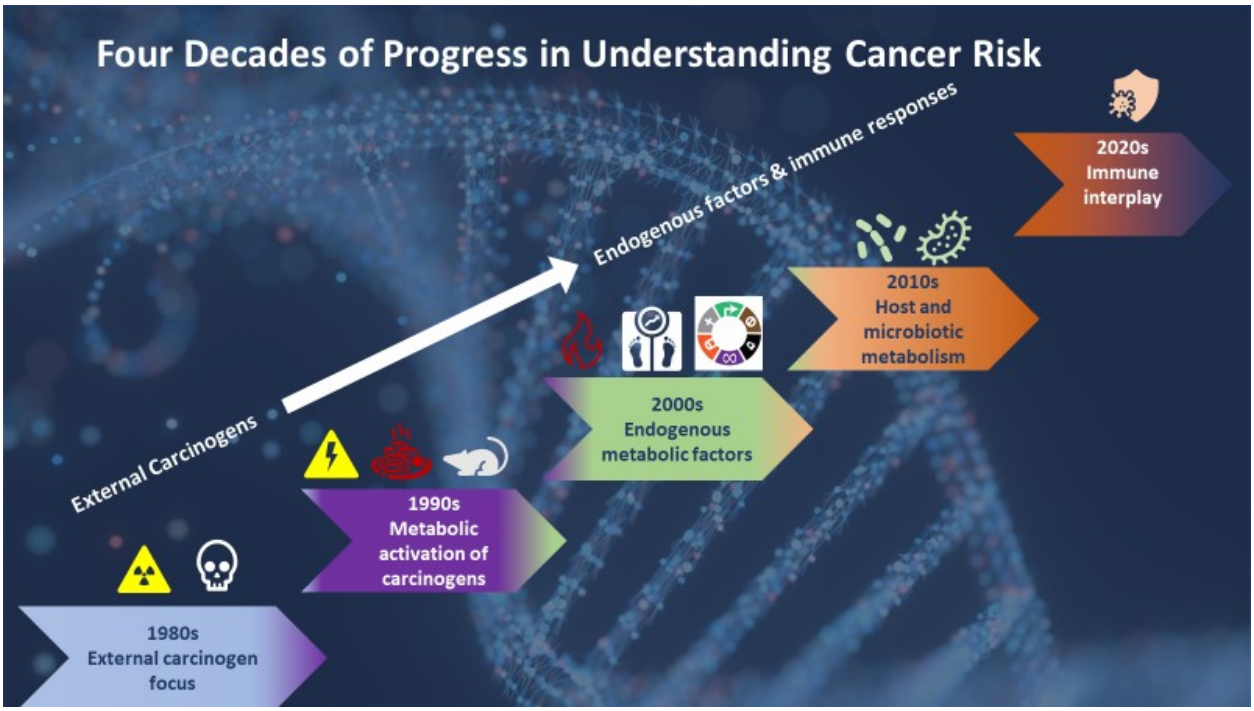

Here's a little bit of a history, or context, in terms of AICR. AICR was 40 years old in 2022. The way we think about cancer has changed dramatically over that period. When people were looking at the causes of cancer in the 1980s, it was all about external carcinogens. Even when people were talking about diet, it was, "What are the carcinogens in our diet?" Then when that research didn't really pan out, as expected, it was, "Well, maybe it's the enzymes and how we activate these carcinogens." There was some progress on that front, some mechanistic insights, but when we got into the 2000s, it was more about looking at metabolic factors and endogenous factors, obesity, and inflammation. Those became the causative factors that people were looking at. Now as they move into and through the 2010s, it was the host, and the microbiome and metabolism. Now, we really are in the era of immune responses and the interplay with tumors, which is a particular issue for prostate cancer.

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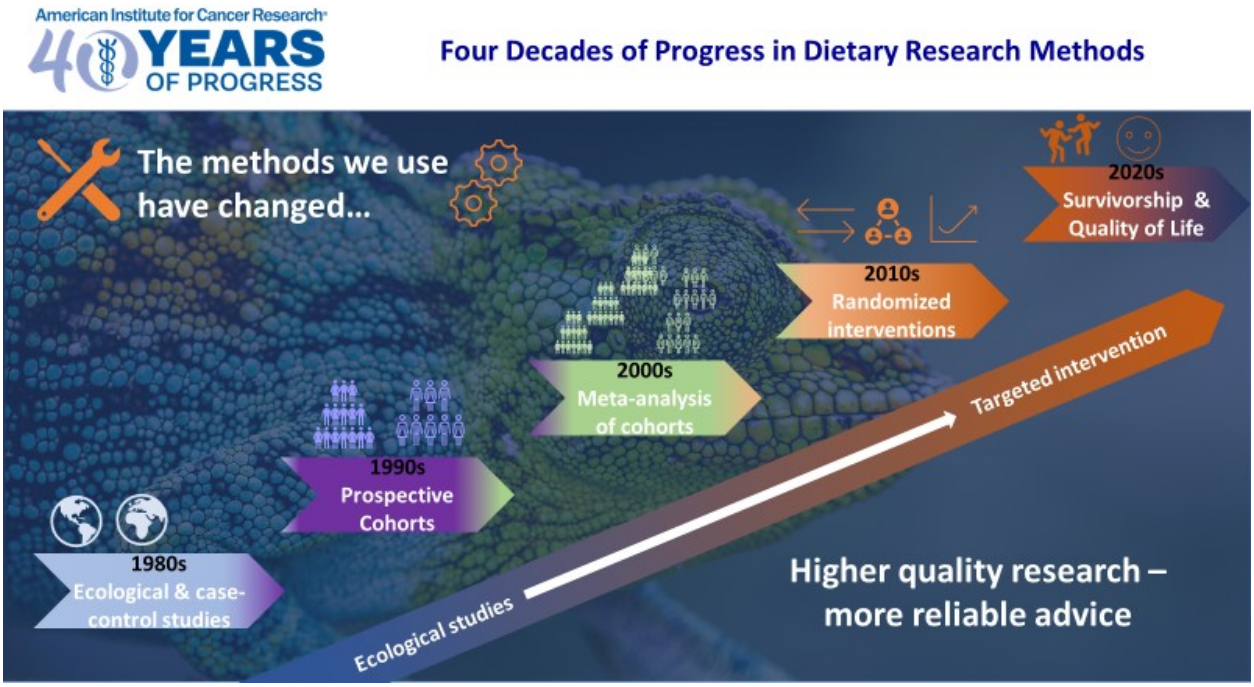
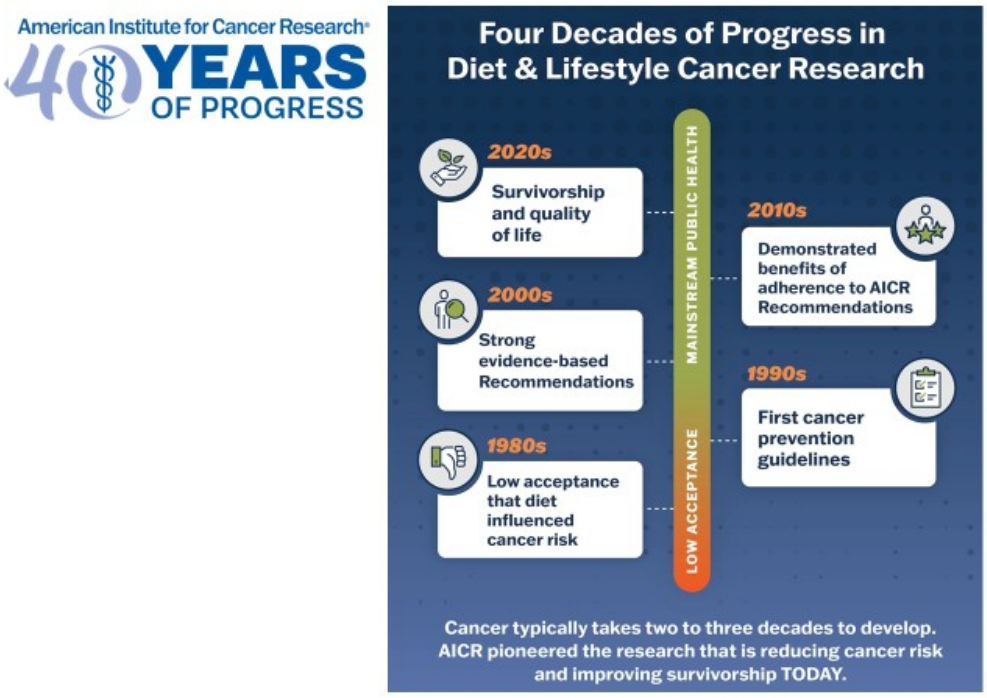


How we think about diet has changed. It was all about single nutrients and these magic bullets. I'm sure you've heard the beta carotene story. My mother was duly giving me beta carotene tablets when I was going through treatment. She was well-meaning, but that's what people thought it was to be anti-cancer. In lung cancer, the risk of lung cancer increased for smokers. Then it was about looking at the genes that regulate and metabolize these nutrients. Then as we got into the 2020s, it was really looking more at whole foods and dietary patterns, and the

big interest now concerns the time of eating. It's not just what you eat, but how and when you eat.



Back in the 80s, when the first lifestyle recommendations were released from AICR, there was quite a lot of pushback. We were seen as snake oil salesmen. There was nothing you could do personally to be effective in cancer prevention. Then we moved to strong evidence into the 2000s when the first expert report was in 1997. That summarized the evidence and made some conclusions, but really strong evidence occurred in the 2000s. Since the early 2010s, the research showed the benefits of adhering to the recommendations. Now the application of those recommendations and the evidence to support benefits in survivorship, both in quality of life and survivorship.

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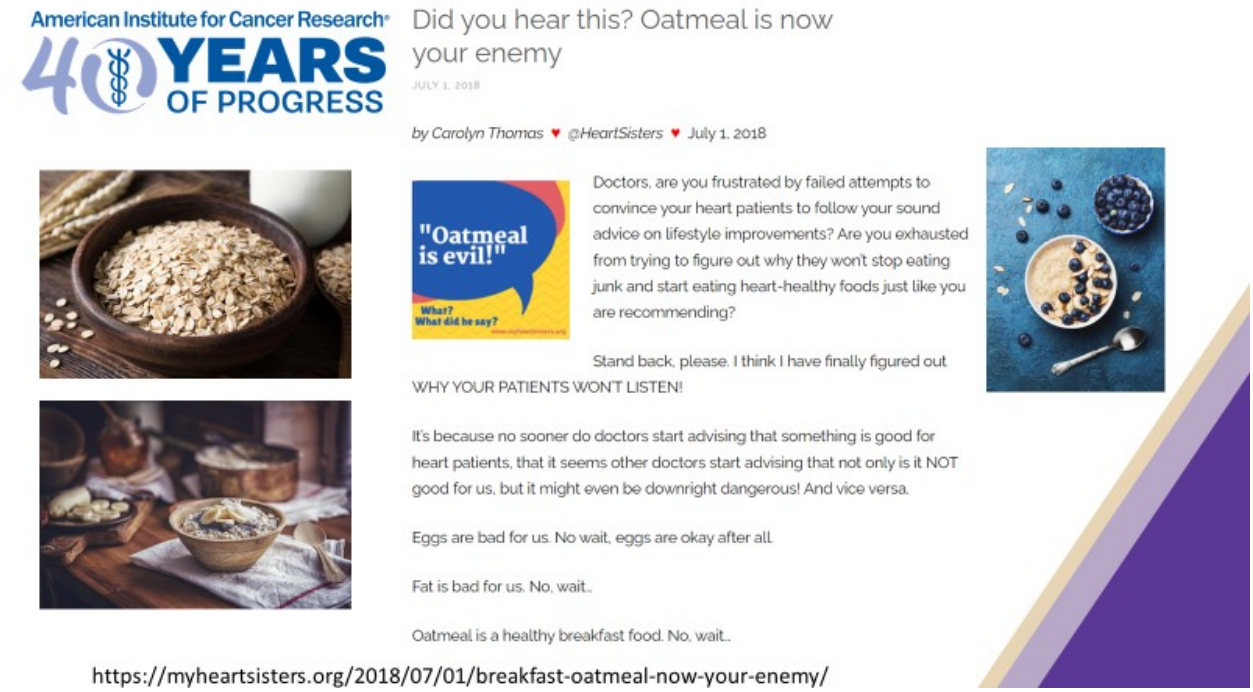

Basically, the reason that AICR was formed was to try and distinguish evidence from opinion because the consumer is fatigued and confused by the changing messages. This is just one example that I picked out. One week, oatmeal is bad for you, the next, it's good for you and what is the consumer meant to do.

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Distinguishing Evidence from Opinion

It was all about distinguishing evidence from opinion by summarizing all the evidence.

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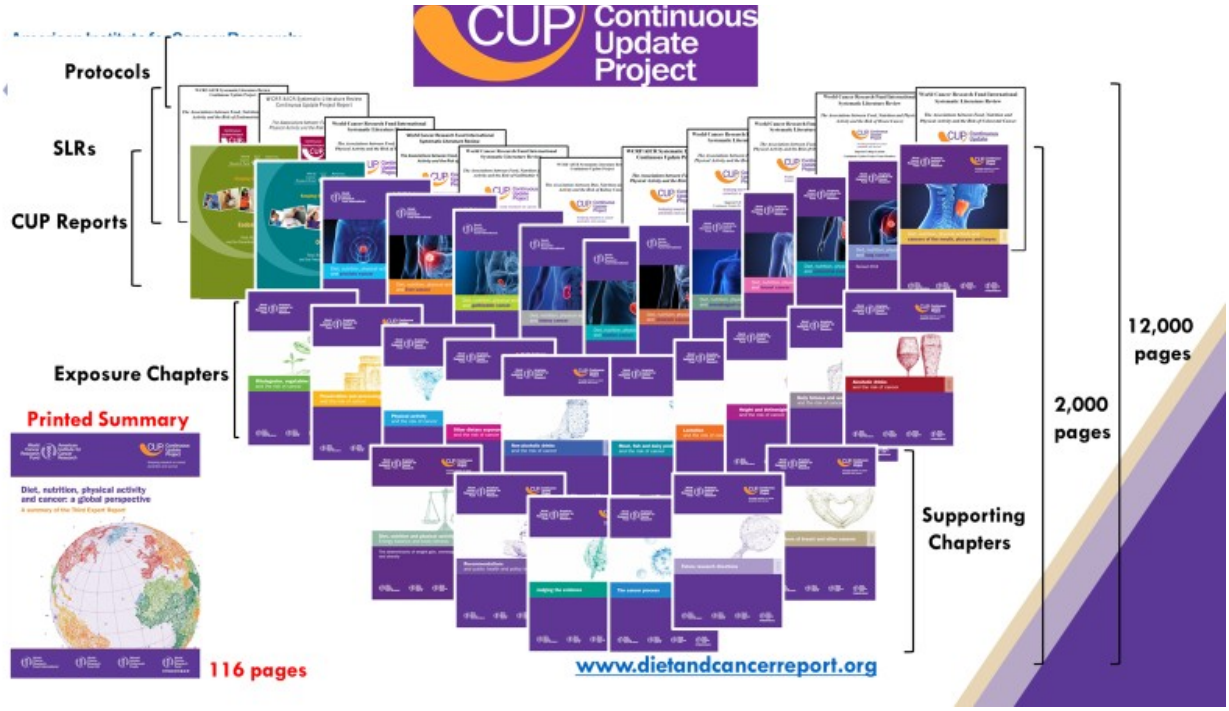

This is a very busy slide, but it's just to give you an idea of the printed summary of the expert report which is 116 pages. We used to have these reports that were 400 or 500 pages. There is a massive amount of information that is distilled down into usable recommendations. Everything starts with a protocol.

At the top here, these are the protocols that rather than just going in and analyzing the literature, and frankly looking for what you want to find, this is describing what you want to do before you start, then doing all the systematic literature review. The breast cancer report is 200 pages. The systematic review is where we take all of the evidence from around the world and meta-analyze it. That's a quantitative way to assess the evidence. If there are not enough studies, or they're not compatible enough, then they're just narratively summarized, and we take all of that together.

The highlights of this systematic literature review (SLR) go into the CUP reports, Continuous Update Project. All of this got updated in 2018. For the third expert report, there are exposure chapters. So, you can go through if you're interested in a particular exposure, and you can find it there. If exposures are not in the exposure chapters, they will be in the SLRs. All of this is available online and it is massive. In total, it's about 12,000 pages of information. I like to think of it as a funnel, where you have these DSLRs which are all the information in the gory details, the CUP reports, which take those highlights, and then the summary, which is what it says it summarizes all that information across all of the cancers. And then we have our recommendations.

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In 1997, in the first expert report, the evidence was pretty embryonic at that stage. In the next 10 years there was a lot more research, a lot higher quality research and a much better process was put into very uniformly assessing the evidence. Then that process was used in the third expert report in 2018. At the point of the 2018 report being published, internally, we had a meeting beforehand, and we presented the recommendations. People were a bit disappointed that they weren't that different from before. Well, that's good because that shows we've been on the right track and that the things that we're talking about are effective. Especially now it'd be fairly easy to criticize the quality of the research in 1997. But we came up with pretty good conclusions that have stood the test of time. We had better evidence in 2007. We had slight changes to the recommendations but nothing major. So we really know the factors that are in a lot of cancers, not all, that can reduce and contribute to reducing risk.

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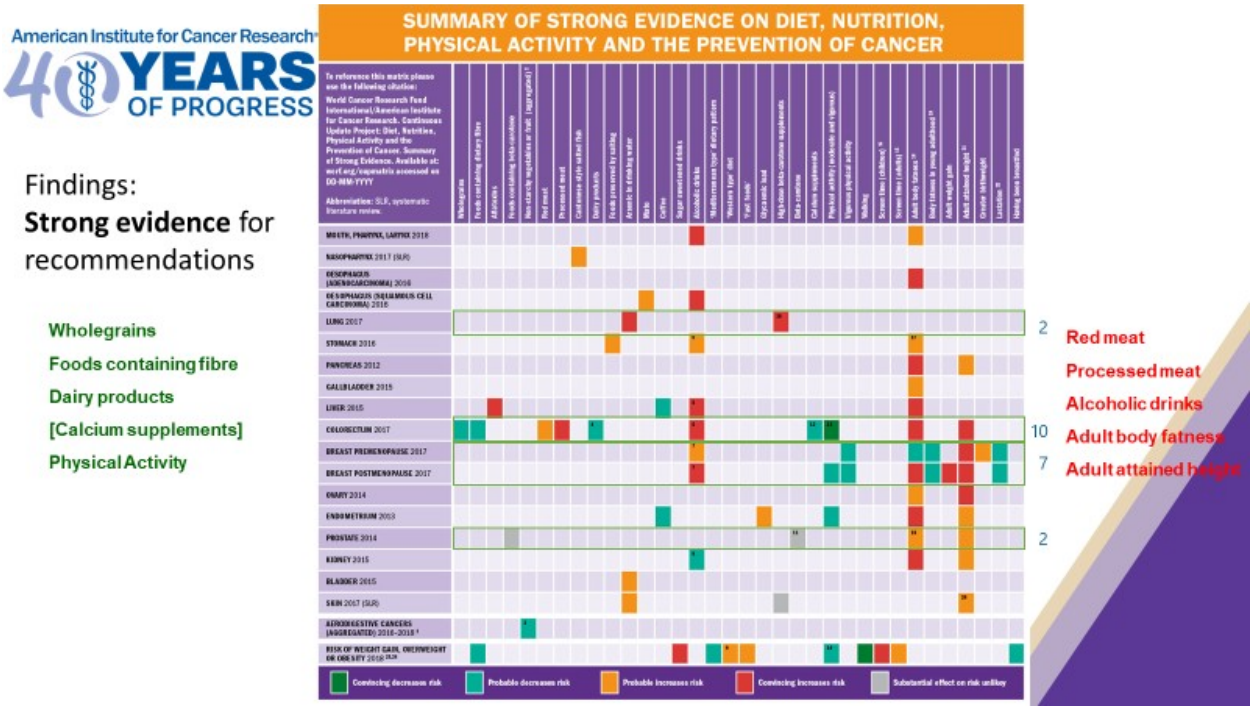
What do we actually know? This is, for the moment, focusing on all cancers.



This is a strong evidence matrix. I like to use the two examples here of colorectal cancer where we have 10 factors that we know change your risk. Five over here that decrease your risk of colorectal cancer, five over here that increase your risk of colorectal cancer. Adults attaining height is a risk factor across many cancers, but there's not much you can do about it. Adult body

fatness is another one. With the obesity epidemic it is increasingly important. There's a lot you can do to reduce your risk of colorectal cancer.

For prostate cancer, we have foods that contain beta carotene, but it says that substantial effect on risk is unlikely. There are concerns in lung cancer. There's a lot of research done on prostate cancer and beta carotene is not a risk factor. This is actually a strong evidence conclusion. For prostate cancer, we only have adult body fatness, and that is specifically for advanced prostate cancer. Because of the issues of overdiagnosis with PSA testing, there was a bit of a wash of the epidemiologic evidence. Advanced prostate cancer was defined as either fatal, which is obviously post hoc, or higher stage.

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2014 DIET, NUTRITION, PHYSICAL ACTIVITY AND PROSTATE CANCER

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing		
	Probable		Body fatness (advanced prostate cancer)[1,2] Adult attained height[3]
LIMITED EVIDENCE	Limited – suggestive		Dairy products Diets high in calcium Low plasma alpha-tocopherol concentrations Low plasma selenium concentrations
	Limited – no conclusion	Cereals (grains) and their products, dietary fibre, potatoes, non-starchy vegetables, fruits, pulses (legumes), processed meat, red meat, poultry, fish, eggs, total fat, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, plant oils, sugar (sucrose), sugary foods and drinks, coffee, tea, alcoholic drinks, carbohydrate, protein, vitamin A, retinol, alpha carotene, lycopene, folate, thiamin, riboflavin, niacin, vitamin C, vitamin D, vitamin E supplements, gamma-tocopherol, multivitamins, selenium supplements, iron, phosphorus, calcium supplements, zinc, physical activity, energy expenditure, vegetarian diets, Seventh-day Adventist diets, individual dietary patterns, body fatness (non-advanced prostate cancer), birth weight, energy intake	
STRONG EVIDENCE	Substantial effect on risk unlikely	Beta-carotene[4,5]	

In terms of prostate cancer risk, there is limited suggestive evidence that dairy products, diets high in calcium, and that's probably how the dairy products are operating. Diets low in plasma, alpha tocopherol B or C, we don't recommend supplementing with these. It's just if there are diets that are specifically low, and then there's limited suggestion. There are all these limited, or no conclusion findings despite there being a lot of research on this. It's not strong enough to make any recommendations. And the two things that we do know increased risk are body fatness and adult attained height.

Amit Gattani 18:16

Can you talk about what attained height means here?

Nigel Brockton 18:22

Taller people tend to be at higher risk of cancer. That's seen pretty much across all cancers and is believed to be due to genetic factors. Taller people have more growth of cells. Cancer is basically the growth of cells. It may be a marker of nutritional stages. It's not something we can do anything about. We wouldn't want to stunt people's growth. But if you were trying to assess

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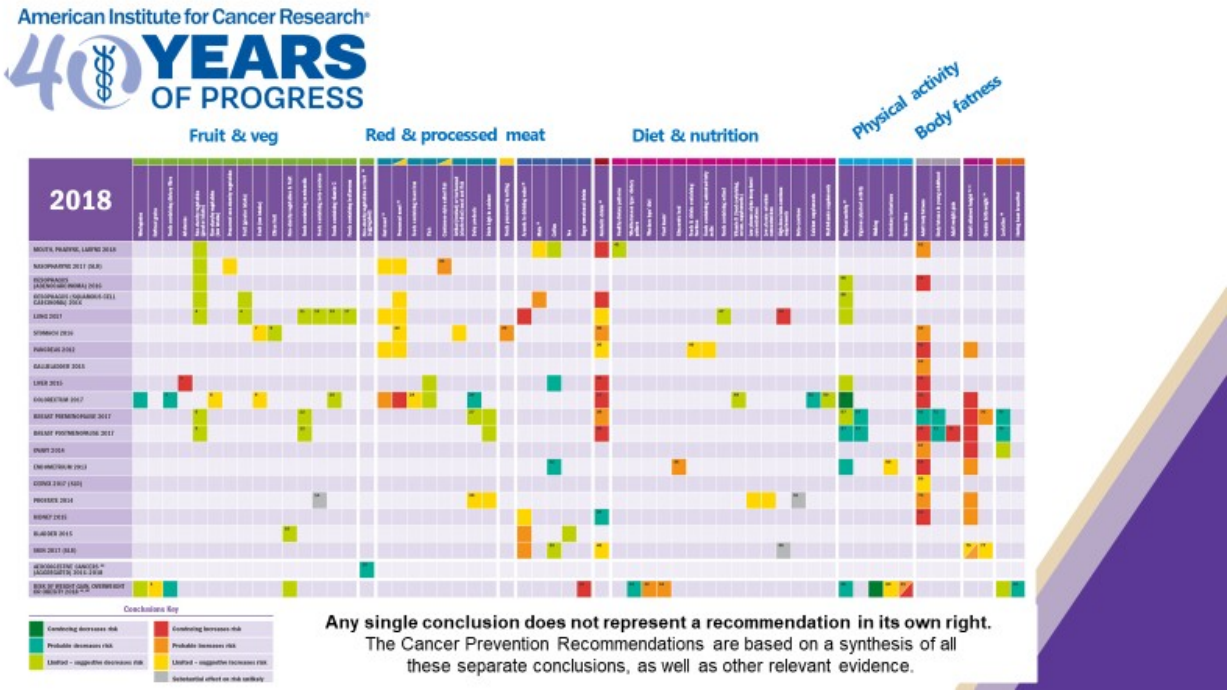
your risk of cancer based on your lifestyle and your anthropometry, height would be in there as a factor.

Nigel Brockton 19:22



These things are all probabilities. This is looking at not just strong evidence, but also the probable and limited evidence. You have dairy and calcium in here, low plasma concentrations, all the things that were in that last matrix. The exposures are on the top and the cancers down. We have a lot of information, but there are a lot of gaps here. For some of it, there’s just not enough evidence or it just hasn't been looked at.

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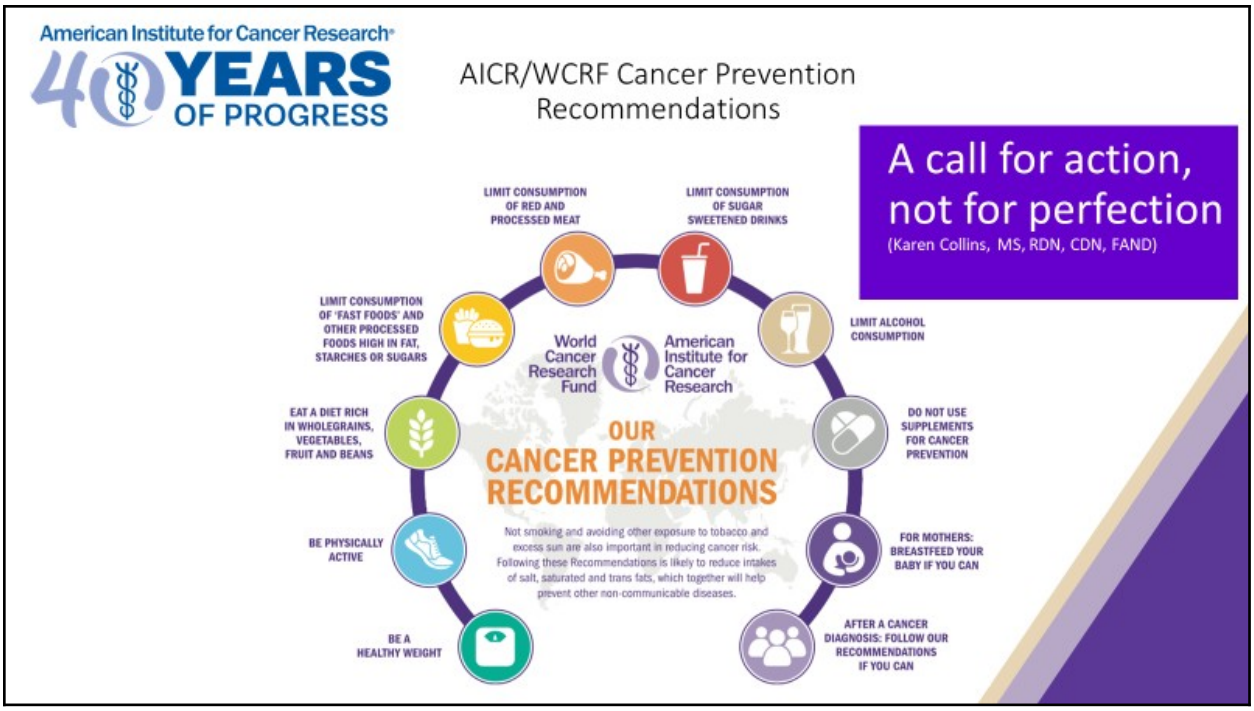

These are our recommendations: be a healthy weight, be physically active, eat a diet rich in whole grains, vegetables, fruits and beans, limit consumption of fast and processed foods, limit consumption of red and processed meats, limit consumption of sugar sweetened drinks, limit alcohol consumption, and don't use supplements for cancer prevention. For mothers, breastfeed your baby, if you can, and after cancer diagnosis, follow the recommendations if you can. We don't have specific survivorship recommendations, but all of these are likely to have a beneficial effect. Of course, breastfeeding is not too relevant to prostate cancer, but all of these are likely to have a beneficial impact on survival, reduction of risk and other chronic diseases. Not smoking and avoiding exposure to excess sun. Follow recommendations if you can and have that discussion with your healthcare provider. In terms of supplements, there are reasons to take supplements; it's just that cancer prevention isn't one of them. We don't have strong evidence in the survivorship setting yet. I like this comment by nutrition advisor Karen Collins, to call for action not perfection. What we see is the more of these recommendations people meet, the lower their cancer risk and the better their outcomes. But any of these you could address will be beneficial.

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Received: 4 October 2021 | Revised: 20 September 2022 | Accepted: 23 September 2022

DOI: 10.1002/ijc.34321

SPECIAL REPORT

IJC INTERNATIONAL JOURNAL of CANCER

Postdiagnosis dietary factors, supplement use and breast cancer prognosis: Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis

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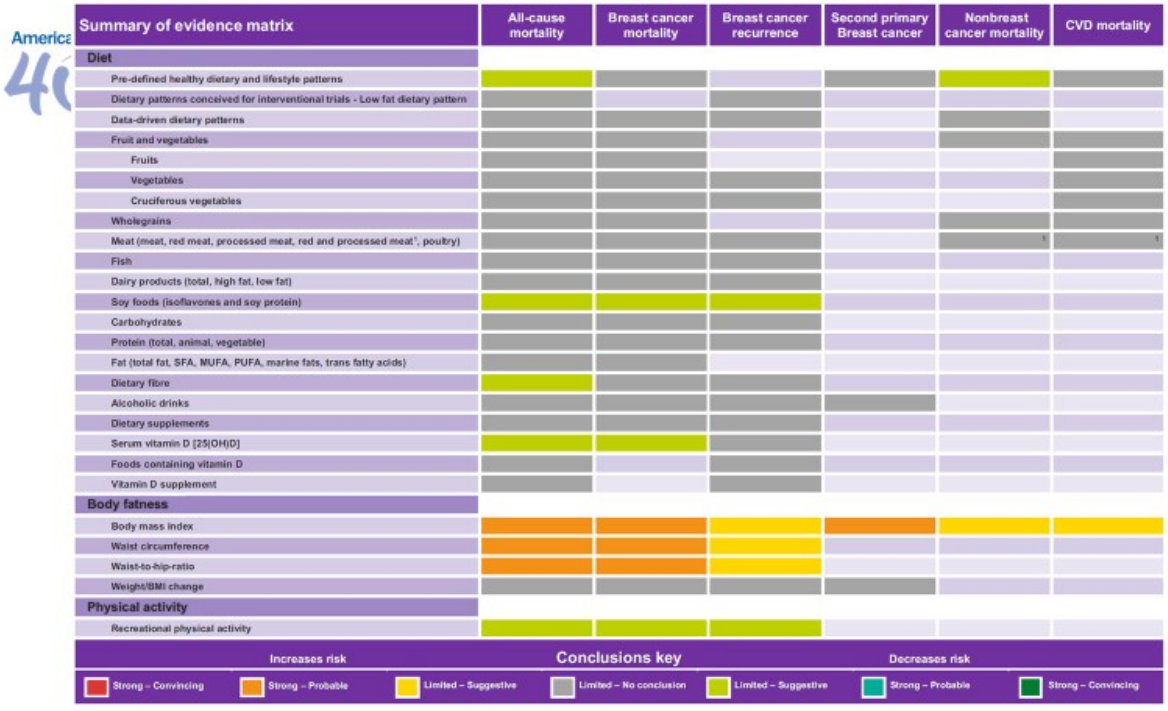
This is the breast cancer analysis in survivorship that we just published in October. We've just done colorectal cancer. The next one is childhood cancer or childhood leukemia, and then we're doing prostate cancer. There will be this kind of synthesis.



Summary of evidence matrix	All-cause mortality	Breast cancer mortality	Breast cancer recurrence	Second primary Breast cancer	Nonbreast cancer mortality	CVD mortality
Diet						
Pre-defined healthy dietary and lifestyle patterns						
Dietary patterns conceived for interventional trials - Low fat dietary pattern						
Data-driven dietary patterns						
Fruit and vegetables						
Fruits						
Vegetables						
Cruciferous vegetables						
Wholegrains						
Meat (meat, red meat, processed meat, red and processed meat[1], poultry)					[1]	[1]
Fish						
Dairy products (total, high fat, low fat)						
Soy foods (isoflavones and soy protein)						
Carbohydrates						
Protein (total, animal, vegetable)						
Fat (total fat, SFA, MUFA, PUFA, marine fats, trans fatty acids)						
Dietary fibre						
Alcoholic drinks						
Dietary supplements						
Serum vitamin D [25(OH)D]						
Foods containing vitamin D						
Vitamin D supplement						
Body fatness						
Body mass index						
Waist circumference						
Waist-to-hip-ratio						
Weight/BMI change						
Physical activity						
Recreational physical activity						

Conclusions key

Increases risk: Strong – Convincing; Strong – Probable; Limited – Suggestive; Limited – No conclusion

Decreases risk: Limited – Suggestive; Strong – Probable; Strong – Convincing

This is looking at these different outcomes along the charts are all cause mortality, breast cancer mortality, breast cancer recurrence, second primary, non-breast cancer mortality and cardiovascular mortality. Looking at all of these outcomes, with all of the exposures that

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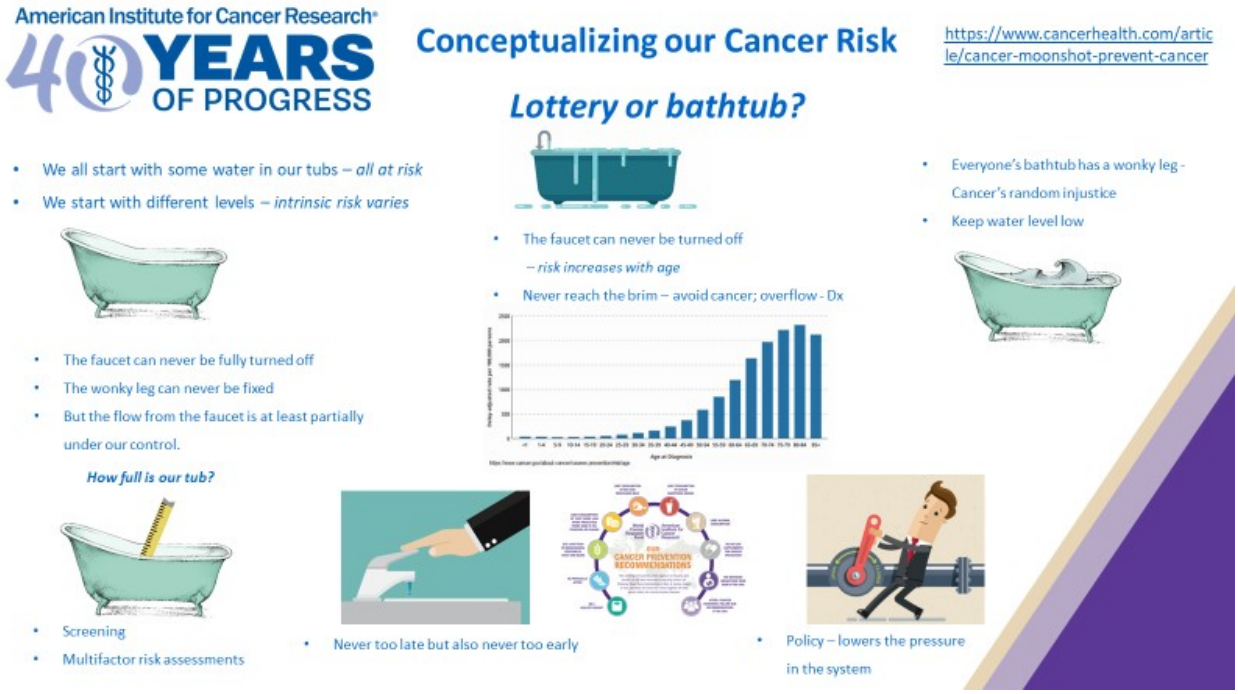
summarize lifestyle, as you can see a lot of gaps in here. But body mass, body fatness, basically using BMI as the surrogate is where the strongest evidence is for breast and there are a lot of parallels between breast and prostate cancer. Watch this space in terms of us to come up with something that is analogous to this in prostate cancer.



Coming back to the probability, this is my last slide before we can have a discussion. I am not sure if anyone's aware of the cancer lottery analogy. I've used it for many years. Cancer is like the lottery that you don't want to win. We're all born with at least one cancer lottery ticket. If you have a predisposition, then you may be born with many. It doesn't mean you're going to get cancer. But for each of the unhealthy lifestyle factors that you adopt, you're basically buying cancer lottery tickets. I've used that analogy for years. Because it's negative, people think winning the lottery is good and obviously winning the cancer lottery is bad. I was trying to think of a way to communicate cancer risk and I thought of it as an old fashioned clawfoot bathtub with a wobbly leg. We're all born with a certain amount of water in our cancer bathtub. There's a leaky tap that we just accumulate that leads to cancer over our lifetimes. Although we can never stop that leaky tap, we can lower the flow by adopting healthy behaviors and avoiding unhealthy behaviors. How do we know when our bathtub is getting full? We know through screening for various cancers, that it's getting full by our 50s. What can we do about it? The first is it’s never too late. But it's also never too early. The reason for the wonky leg is that if you have water in your bathtub that we're all born with, any kind of perturbation can cause that water to overflow. This is an analogous situation to cancer, which is cancer breaking out from its local environment to cause chaos. Policy has a role in this in terms of lowering the pressure in the system to stop the amount of water coming in. It's all probabilities. People say, "My grandfather smoked his whole life and lived through 100." Not many do. But yes, there is a probability of that. But we know the vast probability is that people that live unhealthy lifestyles have shorter lives with more disease. But equally, people who live these perfect lives can be struck down by cancer, or disease early in their life. So it is a probability. And the best solution we have right now is to follow the recommendations that I've just shown you that are based on strong evidence.

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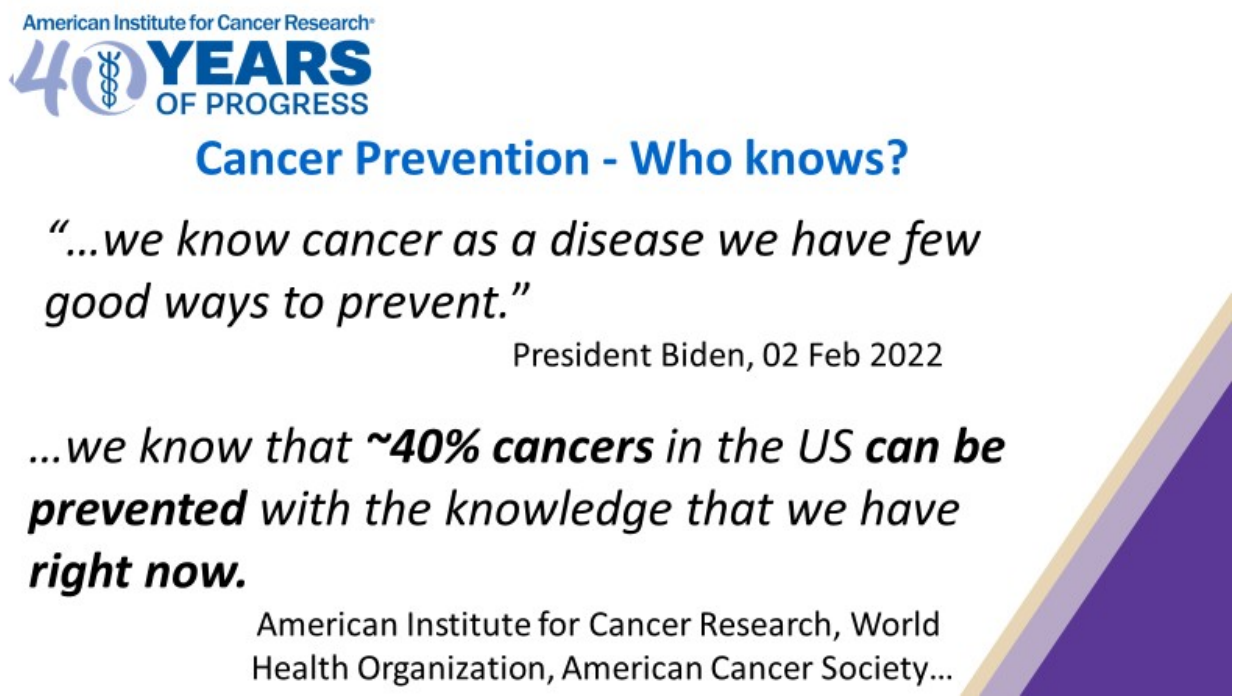
Rick Stanton 27:02

So the water can never go down?

Nigel Brockton 27:14

Colorectal cancer is probably the example where when you have a colonoscopy, and they take out those polyps, that could be analogous to removing some water. But it's pretty difficult to remove the water. I mean, what we've seen in cardiovascular disease is that if you stop smoking, I think within 10 years, you have the same cardiovascular risk as a nonsmoker. We don't have that kind of evidence for the reversibility of cancer risk. It's not to say that it doesn't exist. But we don't have that evidence yet. Considering the laboratory setting and the cancer risk associated with obesity, if obese mice lose weight, lots of things improve. But the cancer risk doesn't necessarily improve in that situation. The tumor formation doesn't do so. That is an area that research is really needed to look at because there hasn't been that much work done on people changing their behaviors. We know about these static exposures. But in terms of changing behaviors, that's really where the research needs to be done. Good question.



As President Biden said, there are few good ways to prevent cancer, but we know that about 40% of cancers can be prevented with the knowledge that we have right now if everyone did it, and that's not to say that if an individual changed their behavior, then they weren't necessarily going to get cancer. It's maybe unrealistic to expect everyone to adopt these things, but that is the goal. We know we can substantially reduce cancer risk by changing people's exposures and part of that starts with awareness. Every couple of years, we do a cancer risk factor awareness survey and about half of the people are unaware of most of these strong risk factors like alcohol, obesity, low physical activity, and diet. People often think that it's genetics and pesticides and things that account for a fairly low proportion of cancers.

“Scientific Research on Lifestyle Choices to Reduce Your Cancer Risk” (Nigel Brockton) [#40]

Nigel Brockton 30:07

It differs by each of the risk factors. But for instance, less than half of the population believe or understand that alcohol is a risk factor for cancer, and it's a risk factor for six types of cancer. Obesity awareness has gone up. I think it's just over half of the population that are aware that it's a risk factor for cancer. It's very high for smoking, pretty much everyone knows that smoking is a risk factor for cancer. In 2019, 45% of the population understood that we're aware that alcohol was a risk factor for cancer, 43% for red meat, that's the highest it had ever been. Only 38% of people realize that diets low in fiber are a risk factor for cancer. Only 10% know about coffee being a beneficial factor. People know that sunlight is bad for you, 82% of people realize that. Only 39% of people knew that insufficient physical activity was a risk factor for cancer. Being the organization that we are, we have an engaged audience and know all this stuff. They say, "Why do you keep telling us this' '? Then we have other people, the 40-50% that say, "Really, obesity is a risk factor for cancer, alcohol is a risk factor for cancer?" There are two very different worlds out there. You're obviously a very knowledgeable audience, but there's a lot of people out there that have no idea.

When you look at the recommendations, when we launched the third expert report and the recommendations, someone in the audience said, "If there's one recommendation for weight and one recommendation for activity, but five recommendations that cover diet, is that because diet is five times more important"? No, but it's at least five times more complex. If you just said someone eats a healthy diet, some people would think a Snickers bar is healthy because it's got nuts in it. You really have to try and frame it with some structure like, “Eat lots of vegetables, don't eat processed foods, and limit red meat.” We don't say never eat red meat, never eat sugar, and never drink sugar sweetened beverages because we do want the recommendations

to be accessible, realistic, and attainable. Because if you said you should never do these things, people would probably just say, "Well, I'm not doing that. I'll ignore them all."

Amit Gattani 34:16

I have a couple of questions. I assume you are looking at data that is internationally available as well. For example, The China Study is considered one of the bigger studies related to nutrition and effect on health. There's a lot of work probably happening internationally. That's question number one.

Second, you said in the 2020s you guys are looking at the timing of eating. We haven't talked about fasting, long fasting, intermittent fasting and those kinds of things. If you could comment on that as well.

Nigel Brockton 34:55

First, the data is global. In fact, we just changed the name of the program to Global Cancer Update Program. The China study is a very famous study, but the quality of the data is not as strong as it could be. There are some things that we would agree with the Chinese study, certainly the vegetables recommendations. But there are some things that are in the China study that are advocated by Colin Campbell and his followers that are not supported by evidence. Just a caveat there.

What was your second question again?

Amit Gattani 35:47

Related to fasting, since the timing of eating is something that you guys are looking at?

Nigel Brockton 35:52

Yes, we are looking at it. It is something that comes under dietary patterns analysis because it's not just what you're eating, it’s when you're eating it. The evidence isn't really strong at the moment. There is in breast cancer. There are some encouraging results looking at the overnight fast. 14 hours is the kind of sweet spot that seems for breast cancer survivorship. I haven't seen any studies in prostate cancer. I'm sure they are probably out there. I think that is an area, but I think actually I saw a negative study on the ketogenic diet and prostate cancer. But fasting, that overnight, intermittent fasting does seem to be beneficial in breast cancer. I can't comment on prostate cancer, but it's certainly an area that's relatively easy to do compared to some of these other more extreme interventions. I think that sort of evidence is going to be coming in.

Brad Power 37:13

I've got a question on personalization. There are two major thrusts of this group: one is power to the patients, that patients should have more say in the system which is dominated by institutions. The second is trying to accelerate personalization. I was very frustrated when I got my chemo. For example, there was no advice about what I should do from a lifestyle or dietary perspective and nothing about genomic biomarkers that would guide my chemo. Subsequently, I got microbiome analysis thinking that might give me some guidance on things I should do. There's metabolomics, transcriptomics, and genomics. What do you see in the frontier of personalization as it relates to the typical cancer treatments like chemotherapy, immunotherapy,

and radiation? Are there things that are associated with those treatments in cancer? Are there any other personalizations based on any kind of omics analysis?

Nigel Brockton 38:28

In the cancer survivorship setting, there are various rearrangements that are seen in the genome of prostate cancer. Patients with TMPRSS-ERG... I'm not a prostate cancer expert. I've published a little bit in it. Prostate cancer doesn't have the benefit of the subtypes, for instance, that drive breast cancer treatment. The personalization, as you indicated, is down to the individual. We don't have strong clinical guidelines. I'm not an oncologist. But my observation is that if someone is diagnosed, there's now the watchful waiting, which is probably better than the radical surgeries up front. And then treatment. I'm assuming that you're all advanced and that it is all bone metastases?

Rick Stanton 40:15

No.

Brad Power 40:17

Not all but most. 70 or 80% have bone metastases.

Nigel Brockton 40:24

Most of that research has really come from what's worked in breast cancer. We don't have really good, targeted therapies. Where this is going, although it's been very disappointing so far in prostate cancer, I believe is immunotherapies. But prostate cancer tends to be a very immune cold tumor. The immune system doesn't respond to them. I was thinking about this on the way in. There are sex differences between the immune system in terms of males and females. Males, particularly older males, tend to have poor immune systems. I wonder how much of the immune coldness of prostate cancers is due to being in typically older males. But I'm seeing lots of younger looking males in front of me, certainly, I don't consider myself old. A lot of these lifestyle factors have an impact on the immune system. I think all of these immunotherapies are not magic. They need the immune system to be doing its job. If the immune system is already compromised, then they're not going to be able to function. I also wonder about the sequencing of chemotherapy and immunotherapy because chemotherapy is terribly bad for the immune system. If you're then giving immunotherapy as a sort of last-ditch attempt, after you've wrecked somebody's immune system with chemotherapy, and I am not dissing chemotherapy, I am here because of chemotherapy. But it is a blunt instrument. My own feeling, and this is not sci-fi anymore because with melanoma they've shown some really good results with the mRNA vaccines, therapeutic vaccines. That is a way I believe we will see massive progress because of mRNA vaccines. You can pretty much 3d print them just if you know the sequence that you're trying to target. But again, you still need an immune system to put those into use and these lifestyle factors all influence the immune system. That's where I think things are going. Right now, in terms of personalization and the way the system is set up, you have to be your own advocate and look at these things that have strong evidence.

One of the things that we struggle with is we have this process to assess the evidence, and the bar is very high because we don't want to say that there's strong evidence for something if there's not, and if it can do any harm. We have a lot when we just did the colorectal cancer analyses. There was a lot of evidence there. But almost nothing that we could make strong

conclusions about because you can always look at flaws in the evidence and say, "they haven't accounted for comorbidities" or whatever the factor is that reduces your confidence in that conclusion. We're in an information landscape where people are making all sorts of outrageous claims about things. Never mind no evidence, no research, just a product and a claim. We stick by, if you like this conservative approach, and it's arguably overly conservative. But then, knowing that these factors can have a benefit, and there is a low risk of harm. That's why we take the approach that we do. Let me get down to these questions in the chat, or do you want to do those, Brad? Rick, why don't you give voice to the questions you put in the chat, please?

Rick Stanton 45:49

We all have metastatic prostate cancer. We're beyond the risk phase so we can't lower the water. But it seems like we can stop the water from getting fuller. But we already have a lot. We already won the lottery. Fortunately, from what I can discern relative to us, is maybe a hope that's a little more aggressive than your conservatism, which would be okay. I'm going to address my diet to slow down the water. What can I do? I can't undo everything that's been done in the past, but I can work on my weight, my diet, my waist circumference, and my intermittent fasting. That's about all I can do. Is there anything else?

Nigel Brockton 46:56

I can't even say there's strong evidence in this survivorship setting, but those are things that we believe are beneficial. That is why we have an overall recommendation to follow the cancer prevention recommendations. Not only will it impact your prostate cancer progression but all those other factors. I could have had heart failure because of the chemotherapy that I received in my late teens and early 20s. If I hadn't been physically active all my life, I would not be here. The treatments that you receive could be good for the cancer or bad for the cancer, but they're also bad for the rest of your body. The more you can do to maintain your resilience, the better off you are. I'm seeing this note about starving the cancer. Your ability to actually do that is negligible because the cancer cells do have a greater affinity and demand for glucose, but it's difficult to do. There are certain clinical situations where that is feasible, but they are a few. The fasting acts on a more metabolic level. but trying to starve out your cancer is not going to work. Are you on active treatment, Rick?

Rick Stanton 49:10

Yes. Pluvicto and I just started Abiraterone again this morning.

Nigel Brockton 49:20

Those are bone targeting?

Brad Power 49:23

Abiraterone is a hormone therapy and the Pluvicto is a radiation targeting PSMA.

Nigel Brockton 49:36

We've seen in other cancers that some of these supplements can interfere with the action of the treatments. The way I look at it is you can't have it both ways. If these supplements are powerful

medicine, then they can do harm, and if they're not powerful medicine, then what are they actually doing?

Rick Stanton 50:08

I believe they're anti-inflammatory. That is the concept for most of them.

Nigel Brockton 50:15

Resveratrol was certainly originally looked at because it was related to telomere length. Turmeric shows some evidence. It has some anti-inflammatory impact. But there isn't strong evidence for any of these. I suspect that I might be managing expectations. There are pros and cons to all of these things.

Brad Power 51:07

Can you say more about exercise? You've referenced it a couple of times. Exercise enhances your immune system. You could be in the gym lifting weights, or you could be running and working on cardio. It could be a little bit every day, or a variety of routines.

Nigel Brockton 51:28

It's often said that if exercise was a pill, we'd give it to everyone. As long as you are capable of doing it, that is probably one of the strongest medicines, and it's evidence based. We don't have great evidence yet because of the problems in the way this research is done. It's really difficult to eliminate reverse causality. It looks like people are doing better because they're exercising, but is it because people are exercising because they're doing better? But I would say the overwhelming evidence is that it's beneficial. In breast cancer, we got strong evidence for quality of life and those were all based on randomized trials. That's one of the few settings where we had those randomized trials, and lots of them. It was massively beneficial for quality of life. In terms of the immune system, Ricky Simpson, at the University of Arizona, has done lots of work showing that every bout of exercise increases the release of immune cells, and they're using this in bone marrow transplants now to try to increase the number of cells that can be harvested. Yes, physical activity if you're able to do it. I've had this discussion with an oncologist in Calgary and he considers me an extraordinary responder, those people that really shouldn't be around. I've been physically active even through my treatment. I used to hibernate for three days after chemo, but then would be back to riding my bike. It's physical activity. It doesn't have to be exercise, but just being physically active, avoiding sedentary behavior. They make you sit in a chair when I was three days in patient infusions for chemo. Just going through cancer and sitting in waiting rooms, you have a fair amount of sedentary time, but I think breaking that up being active is huge.

Brian McCloskey 54:14

I have two questions. Brad alluded to this, but there are a lot of different types of activities. Is there any evidence that would suggest, for example, more vigorous activity is more beneficial? We talked to somebody recently who had indicated he had research that if you burn 1000 calories in a workout, which is a lot, that it can be meaningful in helping to keep your cancer in check, or maybe even improving your condition. That's the first question.

The second question is: with all of the devices we now have to track activity generating a whole bunch of real-world evidence, how is that getting integrated into our research?

Nigel Brockton 55:11

I'll answer the second one first. The frustrating thing is that all that Garmin data and Fitbit data that is not being used as widely as I hope it should be. Just even looking at COVID. I ride and I do indoor rowing. I have a lot of friends who have had COVID and then experience significant deficits in their fitness and performance. But because they track their behaviors, they're motivated, they're trying to train back up to it. A lot of people will just think that's their new normal. There's going to be a step down in the population level physical activity. The linkage between cancer and that kind of data, they're all individual studies. It would be great if someone could do a registry linkage with people who are using those devices because there are huge data resources there. There are privacy issues that get in the way of it. People would have to opt in. There would be a skewing towards those people who are more active certainly at the moment. Mobile phones give us pretty good data. Most people carry their mobile phones on them. There's a whole potential there for that kind of movement data, but we're not there yet unfortunately.

Brian McCloskey 57:20

What about the other question, the first question in terms of intensity?

Nigel Brockton 57:27

It depends on the purpose. If weight loss is a goal, then probably a mix is best. If somebody is completely sedentary, then the first advice is usually walking or some sort of low and slow type of exercise. The immune benefits seem to come more from the high intensity hit type workouts. This idea about aerobic exercise lowering the immune system is probably false. It comes from research that was really from mass participation events, where it was talking about people who get more infections after a marathon etc. It's probably more the fact that they're mixing with lots of people rather than the aerobic exercise itself. I think all exercises help unless you're overdoing it. Because the immune system is part of an energetic process, if you are overtraining in some way you could reduce your immune system, but it's wise to get active with high intensity. At least some high intensity seems to be more beneficial. The role of weight training has been studied, but I'd say the results are less compelling. There was a lot of research on aerobic exercise, or activity. Then we thought what if we added strength. It's only relatively recently that the high intensity studies. 15 or 20 years ago, people did not think that cancer patients should be exercising, and their oncologists were very protective of their patients. This is true in their dietary advice as well. Historically cancer patients had very toxic treatments and got sick and skinny. But that was before we had 70% of the population overweight and obese. For some cancers that have a cachexic effect, wasting away is still an ever present danger. But for breast and probably for most prostate cancer patients, the bigger problem seems to be weight gain.

Nigel Brockton 1:01:13

There's a question about exome sequencing. I used to do a bunch of work in head and neck cancer. In 2012, we were writing this big programmatic grant to try and do what had been done in breast cancer over 20 years in five years. We were identifying those targets then screening drugs to try and target those particular features in tumors. We were at a conference where

everyone was trying to do this. It was 2012. In 2016, we didn't get funded to do it. And as hard as that was at the time, we went to the conference in 2016 and it was basically the whole field of head and neck cancer saying, "That didn't work." because you can find these changes, you can target them, and you get the odd, extraordinary responder. There are lots of these personalized oncogenomic programs around the country, or around the world. But typically, if you are just going after one target, cancer finds a way around it. You may get a really nice response straight off the bat, but then the redundancies of these things just don’t happen. That's why the immune system is so important because then you're using a system against a system rather than one tool against one target. The exception to that is lung cancer, where there has been great success. But again, they're relatively short lived. But in lung cancer where survival was so short, you're doubling somebody's survival, but that may only be taking them from three months to six months, or maybe six months to a year. But the problem universally with those targeted approaches is resistance tends to develop.

Amit Gattani 1:03:46

My understanding is very little funding goes into controlled experiments and trials related to diet and lifestyle studies. Does AICR actually drive and fund studies in this area?

Nigel Brockton 1:03:55

We fund research. Obviously, we've got a few prostate cancer grants, one of them is looking at the role of coffee in trying to reduce progression on people on active surveillance. But yes, these are expensive studies, and the size of the effects tends to be fairly modest. You need a lot of people. These are not areas where pharma has been typically very interested. I know I keep going on about the immune system, but I do believe that in the near future, the role of lifestyle in assisting the immunotherapies is going to put these kinds of exposures front and center. There is a relatively small community of people and a relatively small funding envelope for this kind of research.

“Scientific Research on Lifestyle Choices to Reduce Your Cancer Risk” (Nigel Brockton) [#40]

Post Meeting Email Discussion

Jan 18, 2023 at 2:00 PM Nigel Brockton <n.brockton@aicr.org> wrote:

> Dear Brad,
> Thank you for the opportunity to present today. You mentioned that it’s a different conversation when a cancer survivor is presenting…and, likewise, it is different for me when presenting to survivors. For survivors, these are not abstract concepts. They are the lived reality with direct and immediate relevance. It is also frustrating that research has not yet caught up to where patients/survivors need it to be. I wish I could offer more certainty. But it is important to put the current research honestly in context. Our current knowledge is limited and incomplete…but that does not mean that there is nothing that we can do. The evidence-based strategies may be less “eye catching” than the more speculative ones…but they are the approaches that are supported by the strongest evidence.

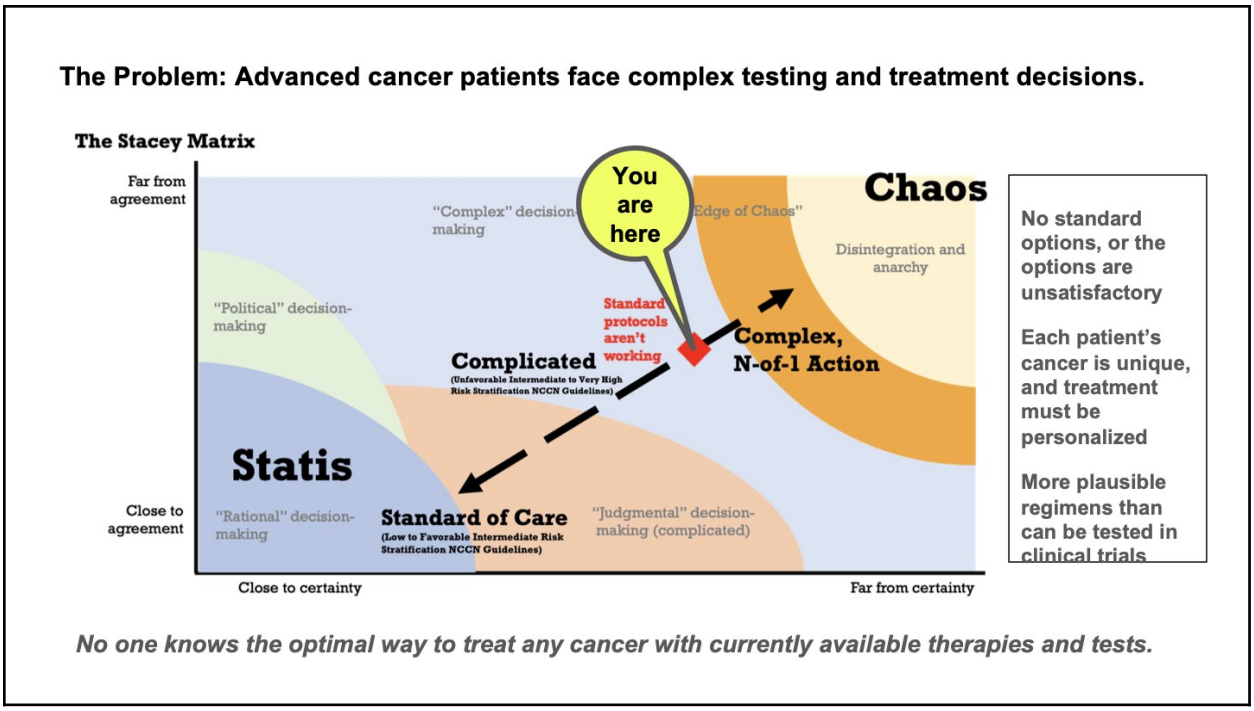
Jan 18, 2023 at 6:24 PM Brad Power <bradfordpower@gmail.com> wrote:

I have a close nutritionist PhD friend off of whom I always bounce the new ideas I hear about. She steers me to the evidence. Particularly with diets there are many charlatans, and we need to rely on solid evidence.
My pet peeve is that there isn't more personalized guidance, as we discussed.
It's a systemic failure that there isn't more personalized guidance.

I had a debrief with Brian and Rick after our meeting, and we picked up on Pete's point that there is a gray zone between solid evidence and pure conjecture that patients will want to explore because things may help and probably won't hurt.

This is similar to our mission to help advanced cancer patients at the border of the zone of chaos in the Stacey Matrix:

“Scientific Research on Lifestyle Choices to Reduce Your Cancer Risk” (Nigel Brockton) [#40]



We want to be early adopters of the borderline treatments that have some scientific theoretical basis but aren't yet proven.
We can't wait for proper evidence to be established at the end of a couple of decades of a validated clinical trial because we need to deal with our disease today.
We also believe in accumulating N-of-1 observational experience and uncovering patterns that may indicate efficacy for those who will follow.

Jan 18, 2023, 7:52 PM PWE Kane <pete@researchtothepeople.org> wrote:
"borderline treatments that have some scientific theoretical basis but aren't yet proven" - YES to this. I would say there are plenty of evidence based things that can be implemented as well, but come from a different area of medicine. For example in Vanessa's case, Dr. Jahanbani and Dr. Castro Identified a pathway they wanted to block and there was evidence in the literature that an HIV drug could achieve what they needed. They proposed the HIV drug in combination with several others as a leading next option. Unfortunately this was never able to be put into practice, but creativity was nonetheless inspiring.

Jan 19, 2023 at 1:25 AM Nigel Brockton <n.brockton@aicr.org> wrote:
Thank you all for the discussion and perspective. I absolutely agree that there is a huge difference between what can be recommended at the population level (the predominant role of AICR) versus what can be assessed to be potentially beneficial at the individual level (clinical guidance and patient choice). I also greatly appreciate the very thoughtful and deliberate approach that you all take to gathering information and the Stacey matrix is a great visual to summarize the boundary zone in which you find yourselves. The personalized oncogenomics programs have had some conspicuous successes…and those successes are transformative for those individuals. And I certainly wouldn’t discourage that approach. I do think we are on

the cusp of a more broadly effective strategy through immunotherapies (and there is no reason why combinatorial approaches could not be used – since those have been the primary strategy for cytotoxic therapies for decades).

The targeted therapy era has provided a rich armamentarium of agents that correspond to various genomic and cellular features that may crop up in many different cancers…and the accessibility of methods to identify candidates for these therapies has also increased dramatically. From an AICR-centric perspective, the interaction of these agents with lifestyle factors is more parallel (i.e. supporting overall health) rather than interactive/synergistic as is plausible with immune-focused therapies. Although lifestyle factors can improve efficacy of some cytotoxic therapies too.

Given the complexity of cancer treatment options and the unique context of each case, particularly in advanced disease, being your own advocate (or engaging in the collective advocacy that you demonstrate) is hugely valuable. Oncologists are well trained but it is impossible for one person to assimilate the entire ever-expanding field. Tumor boards seek to exploit the “group think” to optimize treatment approaches for individual cases…but you are likely still the strongest advocates for optimal approaches for YOU!