

Charles Ryan: Hello, everybody, and welcome to our first webinar hosted by the PCF, the Prostate Cancer Foundation. I'm Chuck Ryan, Charles Ryan. I am the president and CEO of the Prostate Cancer Foundation, and I'm really delighted to begin this process of discussions, live discussions that we're going to have on a monthly basis on many and diverse topics related to prostate cancer. I am delighted to introduce the PCF, for those of you who aren't familiar with us. We are the world's leading philanthropic organization dedicated to funding life-saving prostate cancer research. And our mission, quite simply, is to reduce the death and suffering from prostate cancer. We support work at about 2200 projects in 245 centers in 28 countries around the world. And we're delighted to have you with us tonight to talk about what I think is one of the most important issues in all of the care of men with prostate cancer, certainly in the patient journey, which is how to take care of yourself as others are trying to and working to take care of you and your prostate cancer.

So we're going to talk about physical health, and we're going to talk about mental health tonight, two very important topics. And I have two great, wonderful researchers and colleagues with me tonight, both of whom I've known for many, many years, and we'll get to that in just a moment. A little bit on the PCF is that we're really becoming... I want us to be known as the global public square of prostate cancer, a place where we can convene, where we can talk about research, where we can talk about science, where we can talk about wellness, where we can talk about the latest findings in the disease, and we most of all can help support patients in the end, at the day by bringing all of those together into this public square. So September is Prostate Cancer Awareness Month, and we have a number of projects underway that you can join. This is the Get Healthy with PCF for Prostate Cancer Awareness Month, and I urge you to visit pcf.org/pcam22 where you can get more details on how you can participate, and we'll have a little bit more on that in a moment.

So we're going to start with Stacey Kenfield tonight, and Stacey is an associate professor in the Department of Urology and is the Helen Diller Family professor of population science for urologic cancers at the University of California San Francisco. She's an expert on lifestyle factors such as exercise and nutrition and their impact on outcome in men who have been diagnosed with prostate cancer. She has many research interests, and I've been fortunate to be able to collaborate with her over the years on some of these around nutritional and lifestyle factors and how they may impact patients. And she and her colleagues were among the first in the world to publish the key findings on the benefits of exercise in patients with prostate cancer. And most importantly, perhaps, it all began when Dr. Stacey Kenfield was a Prostate Cancer Foundation young investigator. Stacey, it's great to see you. Thank you so much for joining us.

Stacey Kenfield: Thank you, Chuck, for having me.

Charles Ryan: So you are an epidemiologist, and I think you deal with data and assemble data in a slightly different way than what other scientists will do with prospective studies and things like that. And you have a really important series of messages for patients around nutrition. I thought we could first start out with talking about Prostate 8, and then I'd like to sort pull on those threads a little bit and talk about how you assembled that data and what it really means

for patients today. So let's have you just first introduce the idea of Prostate 8 so that folks can get used to that concept.

Stacey Kenfield: Okay. So the Prostate 8 is a set of eight recommendations that we recommend for men with prostate cancer. We have used these recommendations in a study called Prostate 8, which started around 2015 and was published in 2019 in European urology. So the Prostate 8 recommendations include building up to three or more hours per week of vigorous aerobic exercise, consuming one serving a day of olive oil-based dressing or nuts, consuming one serving a day of cruciferous vegetables... These are things like broccoli, cauliflower, kale, Brussels sprouts, consuming two or more servings per week of cooked tomatoes or tomato products... The lycopene and tomatoes is more bioavailable when it's cooked, so we recommend men eat this with some olive oil. And then consuming two or more servings per week of fish, and we recommend fish high in omega-3 fatty acids like salmon, mackerel, sardines, herring, trout. Avoiding all processed meat, so this includes things like hot dogs, bacon, sausage, luncheon meat. Not consuming a single vitamin or mineral supplement unless your doctor specifically prescribed it to you, and to avoid all tobacco products.

Charles Ryan: Great. So that's, I think, relatively easy to remember. I remember learning at some point along the way that the human brain can remember a list of seven without any problems. And so I always think about, I have to remember the seven things. And I'm always struggling for what the last one is, but it'll eventually come. I talk to my patients about this when they ask me about nutrition. I think it's a really nice sort of nicely packaged set of recommendations. Let's talk about each of them or some of the highlights of them and tell us how you came across these eight. What was the science that led to this becoming the list?

Stacey Kenfield: Sure. So at the time we came up with this list, we looked back at the literature, and the way that you discover something like this is to do a study called an observational study. So what we did was, and I did many of these papers, where we look at people that are followed over time. So for example, a lot of this data comes from the health professionals follow-up study based at Harvard. This was a cohort that was started in 1986, and 51,000 people that identified as male health professionals. And every two years, they consented to receive a questionnaire, via mail at the time, where they answered a bunch of questions about their lifestyle habits. So this included their exercise practices, their dietary intake for various foods, their smoking status, as well as their medication use, their supplement use, and any health conditions they had in the past two years.

And so we have been able to accumulate these data across now 36 years of the study. And at the beginning, we had very few men who reported a prostate cancer diagnosis. We mainly looked at whether factors such as these were associated with risk of developing lethal cancer, prostate cancer, in a cohort of healthy men. So that's where we started this research process. Over time, over these 36 years, many men were diagnosed with prostate cancer, and we were very interested in asking the question, after a prostate cancer diagnosis, is there anything that you can do to prevent dying of prostate cancer, to lower your risk of dying of prostate cancer?

And so we were able to look at the data collected from these men after they reported a prostate cancer diagnosis. We have many now time points of data where they reported their exercise every two years after their diagnosis and can look and see what the association is between that exercise level and the risk of an adverse prostate cancer outcome. In this cohort study, because the data were collected for such a long time and we collected data prior to a prostate cancer diagnosis, we're able to adjust for their pre-diagnosis physical activity level, for example, so that these results are really independent of what they were doing prior to their diagnosis.

Charles Ryan: So you really... These recommendations, just to reiterate what you said, come from behaviors that men had after their time of diagnosis, and following these recommendations, more or less, is associated with a decreased risk of dying of prostate cancer or lethal prostate cancer. So these are things that men... You may have not been a healthy eater your life or maybe you've never exercised, but if you were diagnosed with prostate cancer yesterday, adopting these behaviors is something that could positively impact your survival.

Stacey Kenfield: Yes.

Charles Ryan: And so that's, I think, a key point to it. This is not about preventing prostate cancer, although maybe these behaviors do, right? But this is about after the diagnosis.

Stacey Kenfield: Right. Right.

Charles Ryan: And approximately how many men did you have in that data set? Were you able to look at those who unfortunately did die of prostate cancer versus those who did not?

Stacey Kenfield: Yeah. I think the data set is about three to 5,000 men. It's growing every year. So in our current analyses, we have about 4,500 men with prostate cancer that are part of the data set.

Charles Ryan: So it's a live data set, if you will. So you're still analyzing this. And perhaps these recommendations could change over time if the patterns change, do you think?

Stacey Kenfield: Yes. So these recommendations were part of a study that was done now many years ago. And there are a number of factors that have been discovered since we created this list. So I can name two. One is whole milk. It has been looked at now in multiple studies, and the data are consistently showing that whole milk intake after a prostate cancer diagnosis is associated with an increased risk of prostate cancer progression or a prostate cancer-specific mortality. And it's probably likely that this whole milk, it is high in saturated fat and there is association there between saturated fat and adverse prostate cancer outcomes after diagnosis. Another factor is alcohol. So there are limited data at this point, but we did publish a study coming out of the health professional's follow-up study that showed that modest levels of alcohol intake after diagnosis, so this is really one drink three to five days a week, seems to be beneficial for men with prostate cancer.

Charles Ryan: Okay. Beneficial. And then is there any, at any point, where you can cut off and say alcohol... This is, I think, a challenge in epidemiology. What is the cutoff point between where alcohol goes from being beneficial, perhaps, to being adverse or for being dangerous?

Stacey Kenfield: Right. So, I mean, it looks like there is a U-shaped curve. So it looks like the most benefit that you get is when you're a very modest drinker, at this level of one drink three to five times a week.

Charles Ryan: Great. Great.

Stacey Kenfield: So it's less than what the recommendations are, which say men should have two or less fewer drinks per day.

Charles Ryan: Okay. And with regards to whole milk, you say specifically whole milk, not dairy products.

Stacey Kenfield: We did look at full-fat dairy products and low-fat dairy products. The association is less strong for full-fat. I think it's because people have trouble... This is a food frequency question [inaudible 00:11:40], and I think people can better report their whole milk intake than these other foods that are on the questionnaire. And so I think the relationship is just stronger because the actual item on the food frequency questionnaire is probably easier to report.

Charles Ryan: Got it. And then a couple of other questions. Should we weight these all equally? Are they eight equally powerful forces on survival? Or I would think that tobacco might be more important than any one of these other ones. Or how do you tell people to rank them?

Stacey Kenfield: Sure. So looking at them individually, yes, they are not the same. I think, if one were to choose what to focus on, the relationship between tobacco use and prostate cancer death is strong. It's very consistent across studies. Current smokers in a study published in JAMA had a 60% increased risk of prostate cancer death if they were a smoker at diagnosis. And so if you are a current smoker, we would urge you to try and take steps to quit. The other association that is quite strong is between exercise and prostate cancer death. Vigorous exercise... The intensity of exercise seems to be important. Although, if you are doing moderate intensity exercise...

So these are things like brisk walking or swimming at a moderate pace or biking, but you still able to say a few words without having to pause for breath. So vigorous activity is when your heart rate is up, you're breaking into a sweat, you can't say more than a few words without pausing for breath. But I think people who are doing less than vigorous activities still see a benefit. The benefit is the most strong if you're doing this level of vigorous activity. And in our paper, we reported that this level of three or more hours a week was associated with a 61%

reduction in risk of prostate cancer death. And then going to the other factors, there is a range of benefit between 15 to 50% for these different dietary factors.

Charles Ryan: What do you mean by that? What do those numbers mean, 15 to 50%?

Stacey Kenfield: Yeah. So if you are... For example, cruciferous vegetables, there's limited data, but it does show that if you are eating one serving a day of cruciferous vegetables, which is half a cup of cooked cruciferous vegetables, the association was about a 55% reduction in risk of lethal prostate cancer.

Charles Ryan: Okay. That's a lot.

Stacey Kenfield: So that one was quite large. Others like cooked tomatoes or fish are more in the range of a 20% reduction in risk of prostate cancer, with every two serving per week increase in those items.

Charles Ryan: So if you're only able to do... Apart from smoking, with regards to the food, if you're only able to do one thing, it should be cruciferous vegetables every day.

Stacey Kenfield: And reduce risk of processed meat. [inaudible 00:14:38]

Charles Ryan: And so is the cruciferous vegetable story, is that about the fiber? Or is it about some ingredient in the cruciferous vegetable? And by the way, this would be cauliflower, broccoli, spinach, kale, these kinds of things, which are high in fiber.

Stacey Kenfield: Yeah, so there are compounds in these vegetables that detoxify carcinogens, and that is the secret sauce, essentially, of the cruciferous vegetable.

Charles Ryan: All right. So this is great. And just a couple other questions on this, then I want to talk a little bit, take a little bit of a deeper dive into exercise. I get a lot of questions about the vitamins. People say, well, wait a minute, I thought vitamins were good. And there are a lot of people out there who they're diagnosed with prostate cancer, one of the first things they might do is they might look up various different vitamins or supplements that they could or should be taking. And there's a lot of literature out there, a lot of advertising on these types of things. So set us straight on what number seven's all about.

Stacey Kenfield: Okay. So current data suggests that supplements do not help you prevent cancer or prevent cancer growth. So if you take anything away, that is the summary of supplements.

Charles Ryan: Okay.

Stacey Kenfield: However, there are caveats. So one caveat is that many men and women have low vitamin D levels, and even if they're eating a bunch of foods that have some level of vitamin

D, it's probably not enough. So we tell people to go to their doctor and have their vitamin D level measured and then work with your doctor to figure out what dose of supplement you need to actually be at an adequate level of vitamin D. So for that, we definitely recommend most people needing to take a supplement just to get to the adequate level they need.

Of course, some people are deficient in certain nutrients based on their cancer treatment or problems digesting different types of foods. And so if that's your case, you may need to take a supplement to get to those adequate nutrient levels. You definitely also need to consider having enough calcium in addition to vitamin D and exercise for bone health. And so if you're not getting up to your level of calcium that you need, we do recommend you getting about 1000 to 1200 milligrams a day of calcium. And you can get this easily from food. But if you are not able to, then we recommend taking a supplement to get to that level that you need.

Charles Ryan: Now, you started out by saying there is no data to show that the supplements actually benefit patients, but that's different from explicitly recommending against it, in which case... And the other components of the Prostate 8 are factors that are associated with an adverse outcome. Processed meat, it's associated with the higher risk of death. So why are supplements on there? Is there evidence of adverse effect?

Stacey Kenfield: Sure. So I published some data back in 2015 looking at selenium supplementation and lethal prostate cancer, that high dose selenium supplementation of 140 micrograms per day. And what we observed was a 2.6-fold increased risk of prostate cancer death among people taking high dose selenium supplements. There aren't a lot of data on high dose other types of supplements, but there are no data suggesting these are beneficial.

Charles Ryan:

Got it.

And so just to err on the side of caution, we're telling people there's no data. You're taking these at your own risk. Supplements just don't always mean benefit.

Charles Ryan: Right.

Stacey Kenfield: In some cases they do mean harm.

Charles Ryan: And in fact, there was a prospective study with selenium and vitamin E conducted many, many years ago to see if it reduced the risk of prostate cancer. And I believe it was the selenium arm where there was actually an increased risk of prostate cancer. And in the vitamin E arm, I might have that backwards, there was an increased risk of diabetes. So 10,000 or so patients, they weren't patients, they didn't have prostate cancer, enrolled in the study, they actually found some harm for some of those supplements. So I think it's a really important contribution to the Prostate 8, and I'm glad you're able to clarify that for the listeners. So in the last few minutes we have, let's talk about exercise. And it's something that a lot of people are studying, you in particular. We've collaborated. We had a clinical trial we helped design on that.

And tell us... Let's just take a little deeper dive on what men should do around exercise and what part of it is beneficial.

Stacey Kenfield: Sure. So currently, the US Physical Activity guidelines suggest that adults and older adults should be doing at least 150 minutes of moderate intensity aerobic exercise per week. If you're already doing 150 minutes, they say go up to 300 minutes of moderate intensity aerobic exercise. Now you can... So there's a range. So you can do 150 minutes of moderate aerobic exercise, 75 minutes of vigorous, or a combination. But the recommendations are really to spread this out over the week. Don't try to do this all in one day.

Charles Ryan:

Yeah.

And if you aren't doing this level of exercise, start gradually, work with... Ideally work with a health professional if you're inactive. Don't just start on your own. Start at a low level and then gradually increase the frequency and duration of the exercise over time.

Charles Ryan: And you've spent a lot of time in the past few years designing and are implementing a very large prospective study of exercise in a prostate cancer population. Tell us a little bit about what the patients are going through in that clinical trial.

Stacey Kenfield: Sure. So the study is called GAP4. It's funded by Movember. It's a high intensity interval training exercise program focused on both aerobic and resistance exercise for men with metastatic prostate cancer. It has recently evolved to allow men to do this exercise at home, but it started as supervised exercise three times a week at an exercise facility. And we're hoping to show in this phase three clinical trial that exercise for men with metastatic prostate cancer will reduce risk of overall death and then prolong survival, essentially, and also reduce disease progression. And so we're hoping to show that with this amount of exercise, which includes two days of resistance training, three days of aerobic exercise, over the course of two years... So the program is a two-year program. It starts out supervised or monitored and then moves to a self-managed program within the second year of the program. And we're hoping to show across 12 sites in the US and abroad, so it's open in seven different countries right now, that exercise is beneficial for this advanced prostate cancer group.

Charles Ryan: And there's a lot of data, of course, as you know, showing different biochemical changes that happen with exercise, ranging from things like DNA repair, where your cells are more able to recover from damage, following exercise, to certainly the metabolic effects. And I think one of the tie-ins with the conversation that we're going to have with Dr. Roth in a few minutes with exercise is of course that prostate cancer is a unique disease, especially for men with advanced disease where they undergo hormonal therapy. And the truth of the matter is hormonal therapy is one of the most effective systemic therapies we have in any cancer. But it is unique as a cancer therapy because not only are we treating the cancer, we're altering the physiology, we're altering the body composition of the patient. And so much of what you've talked about, whether it's nutrition and exercise, are things that a gentleman can do that are within his power, and that's I think another key part of it, within his power to mitigate the side

effects of the treatment and then the toxic effects of the treatment on the heart and other parts of the body.

We know, of course, that diabetes is a risk, for example, of androgen deprivation therapy. So even if exercise does not prove to slow down prostate cancer, the disease, it's certainly going to still help some of the other mitigating factors that the other, I should say, toxic effects that happened from the treatment. And what we're going to talk about in a minute with Dr. Roth is side effects of depression and other emotional distresses that can occur during the course of androgen deprivation therapy. So if patients want to hear, individuals want to hear more about the study and how they might want to be able to get involved, they can go to look up pcf.org or go onto clinicaltrials.gov would be a place, and they could look up... The trial's called, you called it GAP4.

Stacey Kenfield: Yeah.

Charles Ryan: That's an acronym for Global Action Plan 4, and it's Movember, with an M, which is the sponsor of the study.

Stacey Kenfield: Yeah. We have a website. It's called GAP4.movember.com.

Charles Ryan: Okay.

Stacey Kenfield: If you're ahead and learning more.

Charles Ryan: All right. So great. So open in many countries, in the US and many other countries around the world. So any other, in the last couple of minutes that we have, Stacey, thoughts you have on the direction that we're going to go with regards to our understanding of how these metabolic and nutritional and lifestyle factors are going to drive men with prostate cancer? I mean, are we... Speak a little bit more about the challenge of developing prospective data, of proof of some of these things. I think that's one of the challenges.

Stacey Kenfield: Yeah. I think we have sort of moved from looking at singular factors to looking at scores. I wanted to just mention that we have a new paper that was published last month in the British Journal of Cancer looking at various scores. We looked back at our 2015 score that we developed for men, healthy men looking at lethal prostate cancer. We just published this score looking at these factors after diagnosis and risk of dying of prostate cancer and showed that a one-point increase in this six factor score reduced prostate cancer death by about 19%. And so, again, data suggests that adopting these behaviors after you're diagnosed is actually protective for prostate cancer death. I think, also, another area of research that needs to be done is looking at this in a diverse racial/ethnic populations. I just actually found out today that I got an RO3 to look at a plant-based diet and these scores in the multi-ethnic cohort study. So at least-

Charles Ryan:

For those who aren't familiar, an RO3 is an NIH grant. Congratulations.

Thanks. So I think this type of research is absolutely necessary because a lot of these studies are done in mostly white populations, and we need to understand if there's differences by race and ethnicity and learn more than we do know and see if the data are still consistent across diverse populations.

Charles Ryan: That's a hugely important issue, and it's going to be a topic of a future webinar as well. It's really part of my emerging stump speech, if you will, around PCF, is that we need to be addressing some of these disparity issues because they undercut our basic knowledge of the disease and how we can recommend therapy approaches and lifestyle approaches for patients. So I want to thank you for your time, and any parting comments you have with regards to the future of your work or how individuals might be able to access some of it? You've mentioned a number of academic papers, but you've got some other things out there that men can access that might be a little bit more accessible for them, I should say.

Stacey Kenfield: Sure. So if you are interested in some of the work we've done, some of the open research studies, we do have one that's open right now for men prior to having prostate cancer surgery, providing diet and exercise programs for these men. If you have any interest in that, please contact me. My email is stacey.kenfield@ucsf.edu. We also have a whole page of information for prostate cancer survivors on these topics. And if you just Google UCSF urology lifestyle, you will find it.

Charles Ryan: Very good. Well, I suspect you're going to be perhaps inundated with some emails and questions, which I think there's nobody better on the planet to answer them than you. And I want to thank you for your time and thank you for all that you've done to help actually patients with prostate cancer, that goes without saying, but you've also been a huge help to clinicians like myself. Because we get asked these questions all the time, and for us to have sort of epidemiologically validated findings that we can recommend to our patients, I think is really, really useful. And I've recommended the Prostate 8 to many people and referred them to your videos on Euro Today and things like that. So, again, thank you so much for your time, Stacey, we'll look forward to catching up with you in the future.

Stacey Kenfield: Thank you, Chuck.