“Exercise as a Countermeasure to Hormone Deprivation Therapy Side Effects and for Bone and Mental Health” (Kerri Winters-Stone) [#48]

Brian McCloskey and Brad Power
March 15, 2023

“Our vision for my research program is to use exercise as medicine for cancer.” – Kerri Winters-Stone

“There is potentially a 50% reduction in prostate cancer specific mortality and prostate cancer recurrence [from exercise]. It's more powerful than chemo. It's probably more powerful than a lot of the current treatments.” – Kerri Winters-Stone

Meeting Summary

Advanced cancer patients, especially patients on hormone therapy, want to learn more about how exercise can help treat their disease. Advanced prostate cancer and breast cancer patients on hormone deprivation therapy often suffer a decline in their muscle and bones. Their heart is a muscle, and declines in cardio health are a common side effect. Another side effect can be weight gain or weight loss. Prostate cancer patients often have metastases in their bones, which weakens them.

Exercise is an intervention patients can use to control or offset their cancer and the side effects of hormone therapy and other therapies. It is one of the best anti-cancer therapies, strengthening the heart, bones, and the immune system, and generally enabling resiliency in response to harsh treatments. For example, men with prostate cancer on androgen deprivation therapy need to preserve bone health through resistance training.

Dr. Kerri Winters-Stone is uniquely qualified to discuss muscle and bone toxicities and non-cancer threats to survival, such as falling, especially in relation to prostate cancer. She is an exercise scientist and professor and co-lead of Cancer Population Science in the Division of Oncological Sciences at Oregon Health and Science University. She is also co-director of the Knight Community Partnership Program and Co-program leader of the Cancer Prevention and Control Program for the OHSU Knight Cancer Institute, an NCI-designated comprehensive cancer center based in Portland, Oregon. As a scientist, Dr. Winters-Stone’s research focuses on the effects of cancer treatment on musculoskeletal health and cancer recurrence risk and the ability of exercise to improve health and longevity in cancer survivors. Her work has extended to consider the impact of cancer treatment on the health of intimate partners and relationships by innovating a partnered approach to resistance exercise that builds teamwork. More recently Dr. Winters-Stone received new NCI funding to determine the patterns and predictors of chemotherapy-induced neuropathy and mobility impairment during neurotoxic chemotherapy and several NCI supplements to integrate digital technology as a tool for continuous passive monitoring of symptoms, mobility and quality of life in aging cancer patients.

What are the complex health challenges that advanced cancer patients face?

People with cancer are often older and face problems from aging, as well as other conditions besides cancer. Cancer treatment side effects can either accelerate functional declines or add

new problems that accelerate functional decline. It changes body composition, causes extreme fatigue, and can result in slowness, weakness, and instability. Hormone therapy adversely affects bone health and strength. The condition of "frailty" leads to falls, combined with bone weakness, that can cause fractures, and those end up creating significant morbidity and mortality. Other side effects from cancer treatments include cardiovascular disease, diabetes, and loss of independence.

What are the benefits of exercise?

Dr. Winters-Stones’ research projects have established that an exercise program using bone loading is able to completely stop bone loss in the spine for men on androgen deprivation therapy. The broader benefits of exercise, such as resistance training, include the ability to do more activities without any assistance, cardiovascular and metabolism improvements, and reductions in circulating insulin levels and body fat.

What exercise program should you do?

You should work towards aerobic exercise three to five days a week, 30 to 60 minutes at a time; resistance training two to three days a week; and flexibility, stretching, and mobility every day. This isn't any different than the public health guidelines. But each one of those have different benefits and an ideal program would contain those different modalities, and these are the doses that are effective.

How should cancer patients with bone metastases exercise?

If you do exercises without weights and your form is correct, the risk is relatively low. As you start to increase weights, and if you do things incorrectly, the risk is going to increase. You should avoid highly dynamic, rapid loading kind of exercises, twisting exercises, hyperflexion hyperextension, or any extreme loading on the bone. You should be careful of exercises where the weights are away from the midline of your body.

Any advice on supplements?

- Calcium: For women who are hormone deficient, e.g., postmenopausal, the recommendation is about 1500 milligrams of calcium a day. For men, it’s 1500 milligrams a day and you should break up your doses throughout the day, with no more than about 500 milligram per dose, e.g., at breakfast, lunch and dinner. Calcium citrate tends to be the most absorbable followed by calcium carbonate. Oyster shell calcium is not as good as Citric Cal or some other supplements that are on the market.
- Vitamin D: It depends on where you live. For those in Oregon, who don't get vitamin D in the wintertime, you might benefit from a supplement.

What do we need to do in the future?

Our goal is to make the patient’s quality of life as high as possible, for as long as possible. We know that exercise has the potential to control disease progression and to improve treatment side effects, but it is not yet part of standard care. Patients should have a warm handoff after treatment to an exercise program.

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Meeting Notes

SUMMARY KEYWORDS
exercise, adt, bone, trial, people, kerri, program, cancer, called, whole body vibration, men, bone loss, frailty, study, test, prostate cancer, improve, work, funded, guidelines

SPEAKERS
Amit Gattani, Mike Yancey, Jeff Krolick, Kevin Fordney, Brad Power, Brian McCloskey, Russ Hollyer, Rick Stanton, Kerri Winters

Brad Power

We're honored to have Kerri Winters-Stone with us today. I met Kerri through Cathy Skinner, who previously led a discussion with us on exercises for cancer patients.

Kerri Winters 00:16

Cathy Skinner connected us through Katie Schmitz (a professor and leader in exercise for cancer patients)..

Brad Power 00:22

All cancer patients should have an interest in exercise, especially those on hormone deprivation therapy. Exercise is an approach to keeping your muscles in shape generally, and for resilience, musculoskeletal strength, and just being generally healthy and having a strong immune system.

Kerri is not only an expert, but she is also involved in clinical trials, which means there's an opportunity to potentially participate in some of the things that she's got going. It's a "twofer." Kerri is at OHSU.

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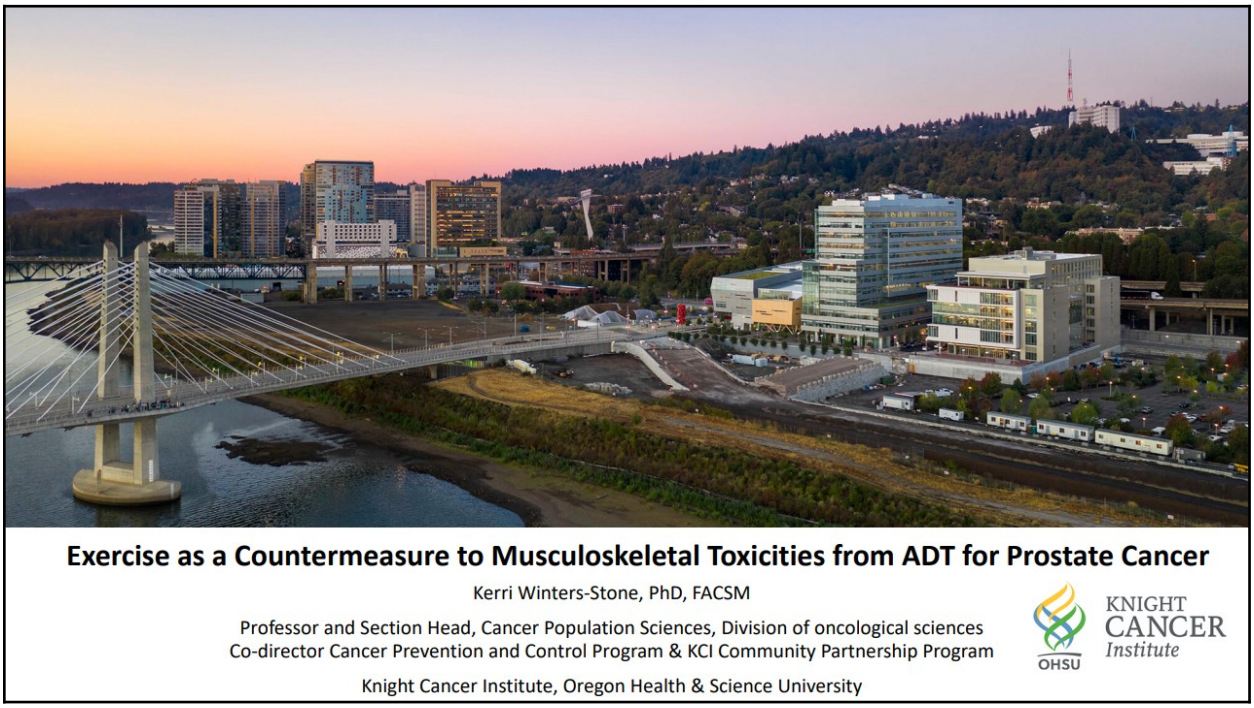

Kerri Winters 02:11

Thanks for the invitation. I was excited to talk to all of you and to learn about your group and what you're aiming to do, and how I can potentially be helpful. Brad said prepare a couple of slides. Well, you say that to an academic, it's like I'll take my slide deck of 45 down to 10. I will walk you through who I am and my research program. I would love to get a little bit more in depth, but I know that this isn't quite the forum for that quite yet.

As Brad mentioned, a lot of my work is focused more broadly on exercise oncology. But I'd say probably 50% of the work that I've done since moving into this field has been in prostate cancer and specifically on using exercise as a countermeasure to ADT (androgen deprivation therapy). Hopefully, I'll be able to provide you with some helpful information today.

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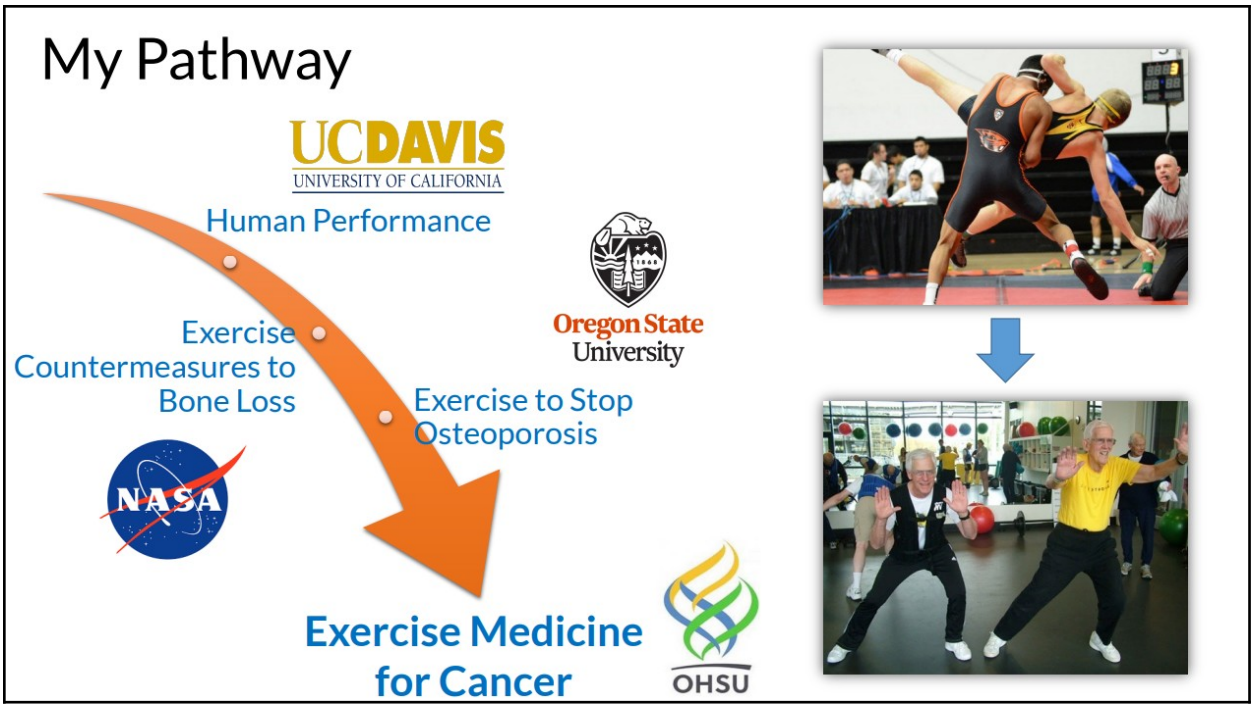

I’ll start by giving you a little bit of an idea of who I am and how I got into exercise oncology. I started out at UC Davis. I heard someone was from the SAC area. I started out in California, and I am a human performance major. This is a field that may be unfamiliar to some people. But it's the more sophisticated version of physical education. It was really where we moved the field toward using exercise to study how to make people stronger and faster and more competitive and harnessing those adaptations that happen from exercise training and using it to actually help either prevent disease in the first place, or to help manage disease when somebody has it either by controlling disease or managing the side effects. I did my PhD at Oregon State University down in Corvallis in human performance. At that time, I moved from working with athletes to working with women to use exercise as a way to prevent osteoporosis. My work was funded by NASA because they were looking for ways to use some of the research that was being applied to prevent bone loss when people go up into zero gravity to actually benefit the general public. Some of my work was funded through that mechanism. We were really trying to figure out the training principles and the ways that we can manipulate exercise to preserve bone due to deconditioning, or due to aging and hormone changes. In my work at OSU, we actually used athletes as a model. We tried to characterize the bone strength across different types of athletes and figure out what is it about the athletes who have really high bone density and their training regimens that we could harness in a way that we could use it as a either preventive strategy or a treatment strategy to address bone health in people back in one-G environments. That is the principle of the work that I do which is around this kind of training concept called specificity. How do we take some specific principles around exercise training around different exercise modalities and then manipulate that in a way that can treat human health? When I came to OHSU, I used a lot of that work to start addressing problems that people were incurring because of their treatment for cancer. That started with some work in prostate cancer where we were using these bone loading programs that we developed to see whether or not they could be effective at preventing bone loss that was associated with hormone therapy for prostate cancer.

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To give you an idea of kind of how my journey evolved into exercise oncology and at OHSU, I am a professor here in the Division of Oncological Sciences. I oversee a division called Cancer Population Sciences. I also co-lead the cancer prevention and control program for the Knight Cancer Institute. That's a scientific portfolio of work in cancer prevention and control. We have a very strong cancer survivorship program of which I oversee and am a part of, and I also co-direct a program called the Knight Community Partnership Program, which is a granting program funded by the Knight that was actually a result of a huge philanthropic effort, in partnership with Phil Knight from Nike, to raise funds for the cancer center and a portion of those were allocated to go back to the community. We run a granting program to put funds back into the community to address cancer related issues about which they're concerned.

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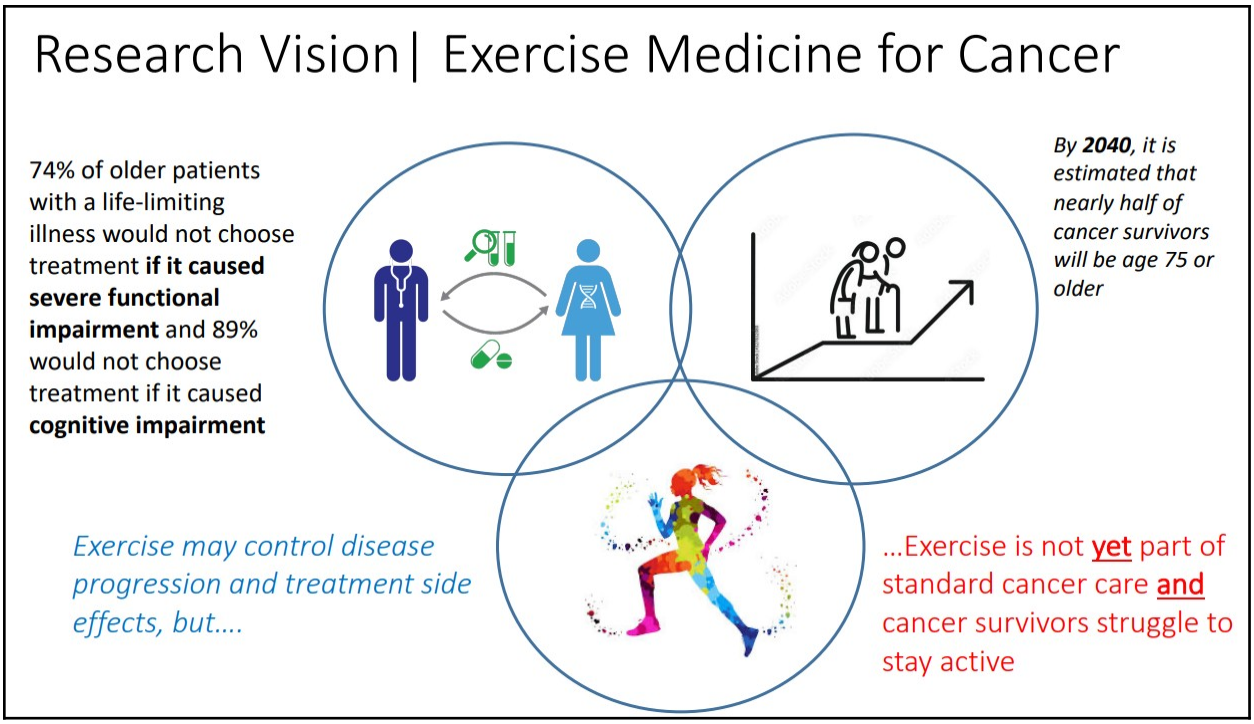
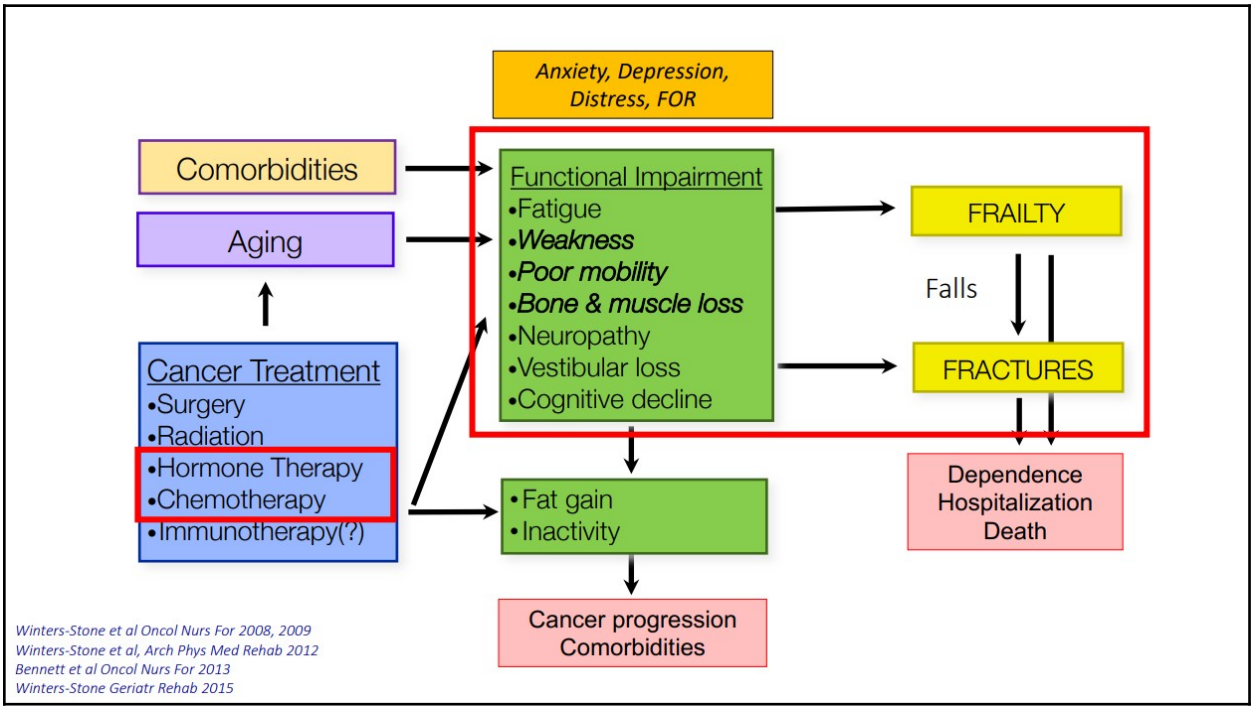


Our vision for my research program is to use exercise as medicine for cancer. I work in a cancer center that is very strong, and very focused on precision medicine and on developing therapeutic approaches for cancer. One thing that we have to keep in mind is that even with therapeutic advances, aging is a part of cancer. As those therapeutic strategies are being developed, people like me also have their eyes on how they are altering the trajectory of someone's aging, what other additional problems may they be incurring that actually create additional health problems. A large proportion of people with cancer, as you guys know, are older and a lot of people are concerned about their quality of life. If treatments are going to compromise their quality of life, then that makes it difficult in terms of decision-making. Some people would just avoid treatment altogether if it significantly affects their quality of life. We know that exercise has the potential to control disease progression, and it has the potential to improve treatment side effects, but it is not yet part of standard care. A lot of people struggle to become active enough to know what to do to feel like they're exercising safely. This is part of my vision, to develop a strong enough evidence base and contribute to the evidence so that exercise does become part of standard care for people with cancer. That's really the ultimate goal of the work that I'm doing.

From Dr. Winter-Stone’s bio:

> Dr. Winters-Stone has been funded by the National Cancer Institute, National Heart Blood and Lung Institute, the American Cancer Society, and the Susan G. Komen for the Cure, Livestrong, and Movember Foundations. This work has supported over 14 controlled clinical exercise trials that have trained over 2000 cancer survivors in different exercise modalities including resistance, aerobic, flexibility and tai ji quan training. She has also co-led the update of the American College of Sports Medicine Exercise Guidelines for Cancer Survivors, released in October 2019. The long-term goal of Dr. Winters-Stone’s research is to develop prescriptive exercise programs for cancer survivors that meets their needs and preferences, optimizes their health outcomes, and

provides the support and encouragement they need to stay active so that they can live better and longer with cancer. After developing new virtual approaches to the delivery of exercise training during the COVID-19 pandemic, she is now exploring how supervised group exercise can reach the most underserved patients living in rural and poor regions of the U.S.



This is the model that I work from as a scientist, and I'll walk you through it ever so briefly. In addition to the changes that people are facing from aging, as well as other conditions besides cancer, we know cancer treatment on top of those conditions either accelerates functional declines or adds new problems that accelerate functional declines and that ultimately could result in additional health problems besides cancer. So I'm very focused on musculoskeletal health. I am concerned about the impact of cancer treatment on accelerating a condition we call "frailty" that leads to falls combined with bone loss that can cause fractures, and those end up creating significant morbidity and mortality. Of course, I'm also concerned about the effect of disease and treatment and how they may accelerate cancer progression. I'm becoming increasingly interested also in mental health and making sure that what we can do, if it has the potential to improve mental health, that we're able to look at that. This is the model that we work through. Like I mentioned, I'm pretty focused on musculoskeletal outcomes. I'm interested in disrupting this pathway through exercise and making sure that quality of life is high, as high as possible, for as long as possible.

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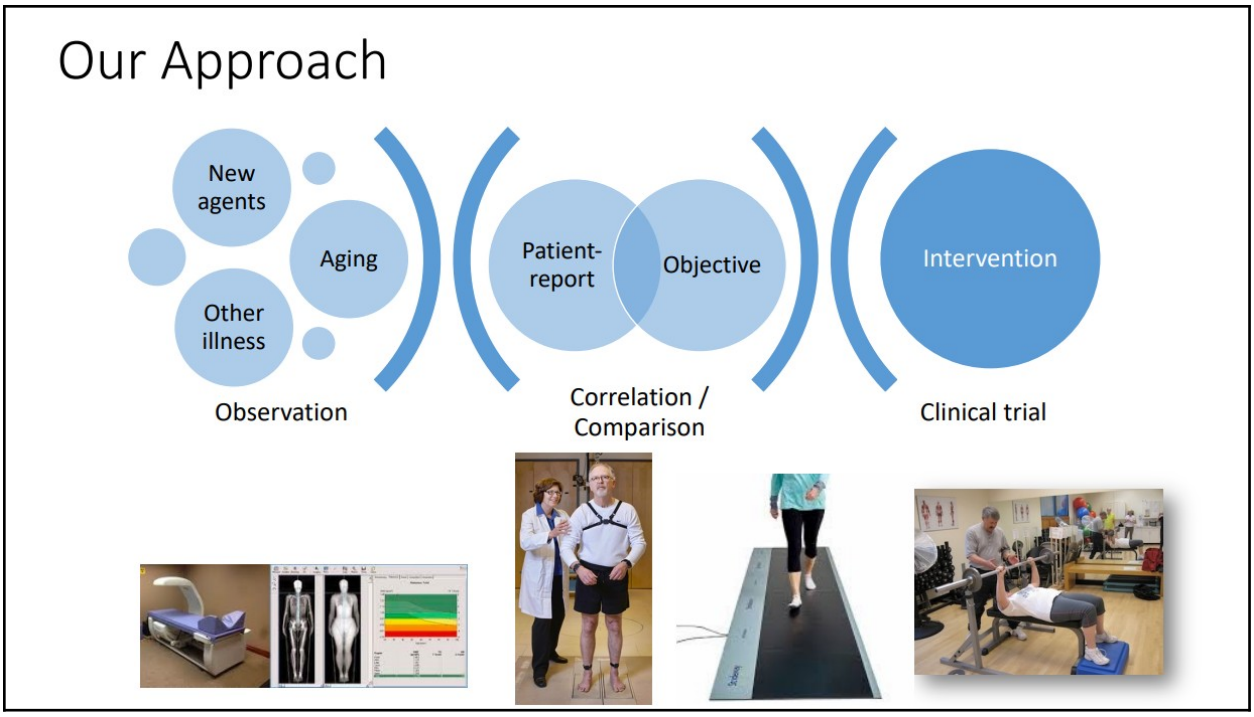

The approach that I use is the pathway that takes us to a clinical trial. We do some observation studies, we identify the problem, we develop an intervention, and we run a clinical trial. A lot of what I do, besides just clinical trials, is also focused on trying to understand the problems enough so that I know what the right intervention is. Back to this concept of specificity. If I'm trying to prevent falls, or I'm trying to improve bone health, I don't necessarily put everybody on the same type of exercise program. I want to manipulate that exercise program in a way that I know it can specifically address the problem that I'm trying to solve. Once we have understood what the problem is, and we think that we've designed the right intervention, we run a clinical trial to test the efficacy of that approach. I will say that oftentimes this leads us back to observation. Then we run through the cycle again, but this generally describes a lot of the work that I do in my approach to clinical trials development.

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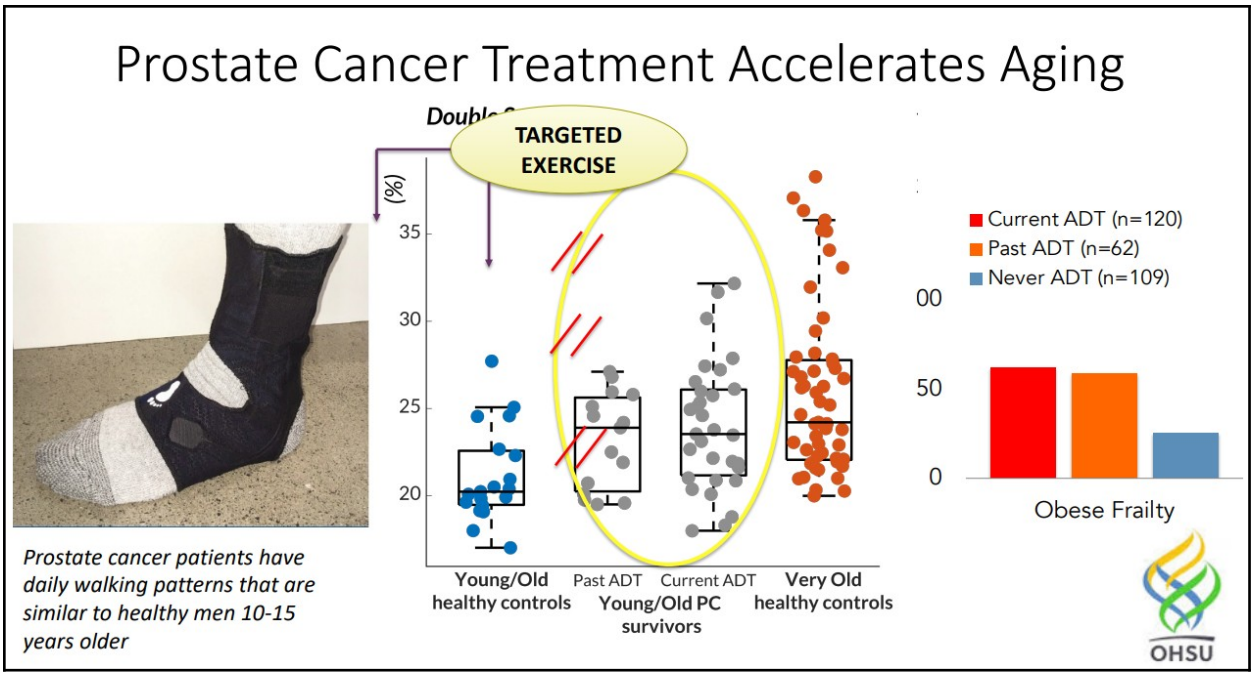
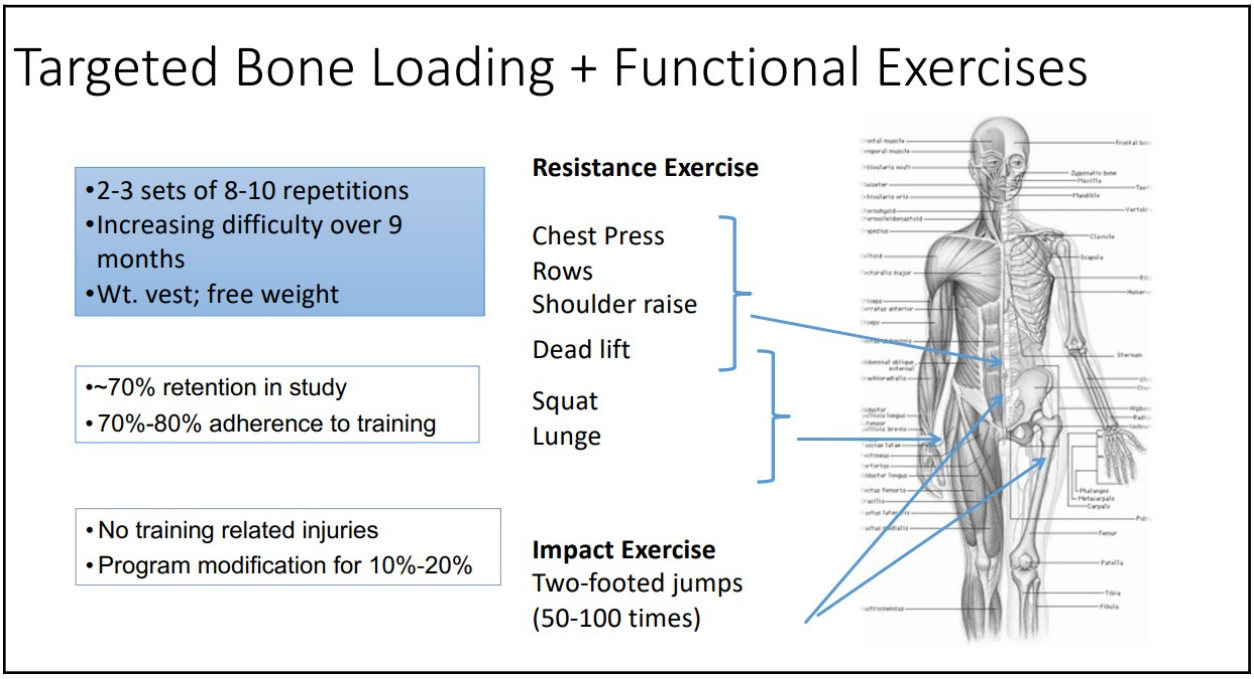


In the case of prostate cancer, one area that I've been working on for a long time is the impact of cancer treatment on accelerating aging. These are the kind of the typical changes that will accompany androgen deprivation therapy. It changes body composition, causes extreme fatigue, it can result in neuromuscular changes that cause slowness or weakness and instability. It can also make it really difficult for people to stay active. I know that this is a very engaged group and a lot of you work very hard on your exercise program. But a lot of men are not able to do that or have a lot of difficulty and then that only compounds this trajectory that can lead to either a longer term late effects that we know are increased from ADT like cardiovascular disease, diabetes, frailty, and loss of independence. We've done some descriptive work, like I mentioned before, to understand the impact of treatments like ADT on frailty, which is this kind of accelerated aging phenotype. We did a study as part of trying to get a grant funded to convince reviewers that there were persistent and troubling problems from ADT, and that it accelerated aging. We did a study where we characterized this frailty phenotype, that we've also combined with obesity, because together they ended up causing greater problems than either condition alone. We hypothesized that men who were currently on ADT would have the worst frailty profiles, men who were on ADT for a shorter period of time and were no longer taking it might have intermediate profiles, and that men who'd never received hormone therapy would have the best profiles. What we observed is a little bit different than what we thought. It turns out that whether or not you're currently taking ADT, or you've had it in the past, that the prevalence of frailty is quite high, and it's not that different. We're not seeing recovery from ADT, at least in this domain. That means there are a lot of men who've been exposed to ADT throughout the course of their prostate cancer treatment, and are now at risk for this condition.

Brad asked me to talk about wearables. We use wearables in our work increasingly, not necessarily as an intervention, but in part to help us characterize some of the problems that we're trying to better understand. We've been doing some work lately, with this wearable called a Smart Sock that you can see on the left. There are wireless sensors in the sock on top of the foot and along the ankle, and we have men wear these for three to seven days in their home. It measures what we call free living mobility, and gives us a sense of how men are really moving in their own environment, not when we ask them to walk down a hallway, which everybody tries

to do their best. We use these smart socks to try and characterize and see whether or not what we're observing with our first study is persisting and what we see when men are in the home. We used these smart socks and measured this construct called Double Support. It's how much time that you spend with both feet on the ground, and it's an indicator of a worsening gait pattern. Usually, if you ambulate really well and freely, you have a lot of time on one foot. When you start to slow down, you spend more time with two feet on the ground, and shuffle or stutter step. What we saw when we used these instruments is that men who were exposed to ADT had really high gait patterns that were similar to much older men and worse than men who were age-matched. So again, more of this proof of concept that we're seeing this accelerated aging phenotype with treatment. If we go back to the model, what we're trying to do is use targeted exercise to interrupt this trajectory so that we delay or prevent these downstream consequences of hormone therapy.



I'm going to walk you through just a couple of the trials that I do, and then we can get into a discussion. In addition to those mobility issues, I think you're all familiar with the adverse effects of hormone therapy on bone health and on bone strength and increased risk of fracture. Back to what I was originally talking about my work at Oregon State University, some of the first studies that we did in prostate cancer were to try and use this type of exercise program that we had developed that we found to be effective at improving bone health and improving functioning in people without cancer and whether or not it could effectively be a countermeasure to individuals who are experiencing changes because of their treatment. It wasn't a no brainer in terms of whether or not this would work for a couple of reasons. The program was effective at addressing age-related changes, it had not been tested on whether or not it can be an effective enough countermeasure. Was it strong enough to counter the powerful effect of something like hormone deprivation therapy where testosterone and estrogen levels are basically wiped out? It might be that exercise just isn't strong enough and it takes more of a pharmacologic approach. This was a reason why we wanted to test whether or not exercise could be an effective countermeasure. This is a pretty rigorous program. We also had to determine whether or not it was tolerable, and if it wasn't tolerable, the load we thought, or the dose we thought would be effective, was still effective. This was the premise for a study that we had funded by the Lance

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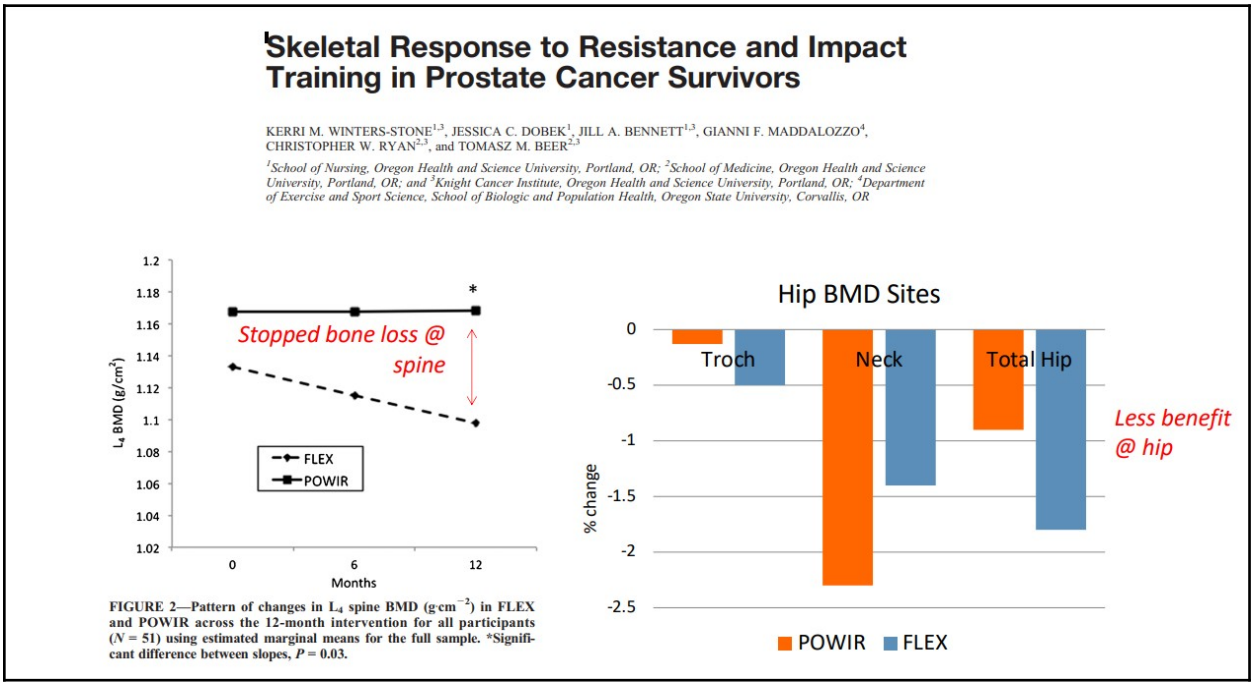
Armstrong Foundation back when it was the Lance Armstrong Foundation. That's been a while now. We tested a very specific bone loading program where we selected specific exercises that load the spine and the hip in ways that we think are osteogenic, or bone loading. We add an impact component of jumping exercise that generates ground reaction forces that we think also load the skeleton in a way that causes it to adapt. This is what the training program looked like. You can see it may not look like the training program that you guys do, but it's because it was very selective for these exercises and those had been shown to be effective in other populations. This was a year-long study that we ran in about 80 men who are currently on ADT for prostate cancer. This was conducted at OHSU three times a week, obviously pre-pandemic. We have decent retention and decent adherence and decent tolerance to training.



What we found was that with this exercise program, we were able to completely stop bone loss at the spine. Men who are in a control group continue to lose bone at a steady rate as we would expect it but the exercise program stopped that entirely. We did not have as much of an effect at the hip and we think that's because we were very conservative in our jumping program. We would increase the dose next time. But when we saw it, we started to see a little bit of a benefit. It's possible the training program wasn't long enough.

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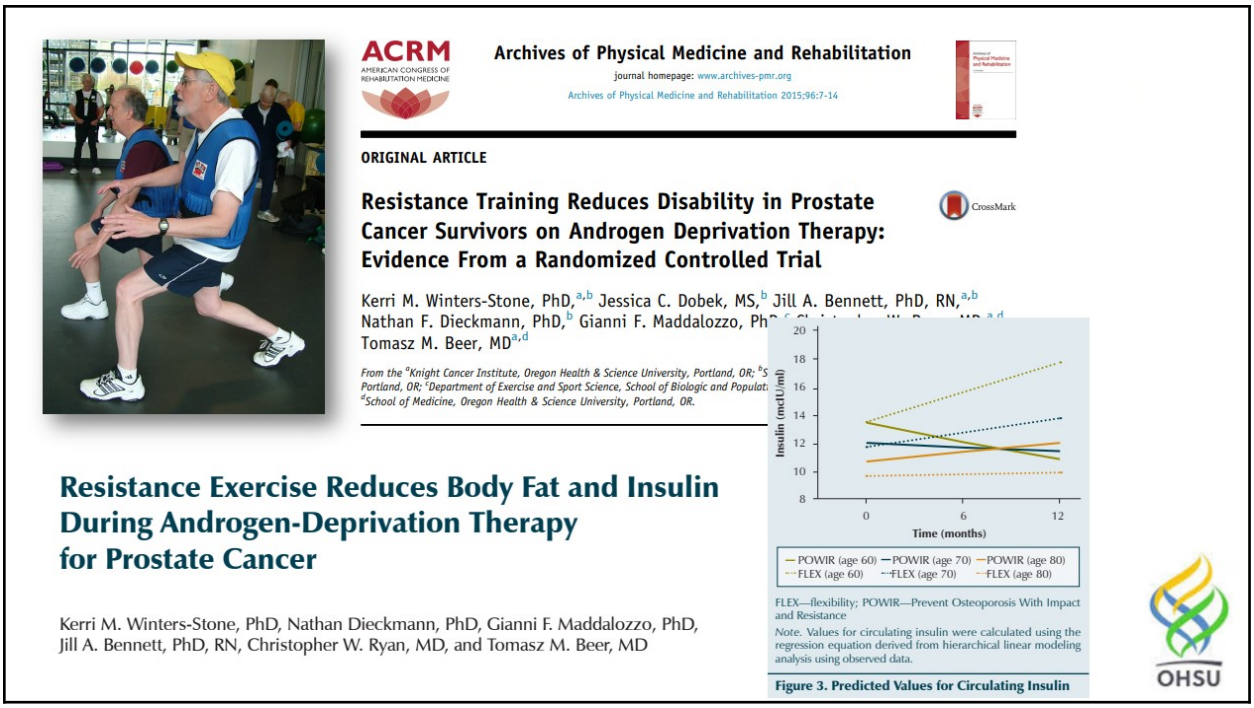

This is the first type of work that we did in prostate cancer. In that same study, you can see men here in the upper left in our trial. They wear a weighted vest to weight their lower body exercises. We do a more functional resistance training program because we are also interested in not just preventing bone loss, but improving functioning and reducing fall risk. We don't put people in machines. Machines unweight you and even though you can get pretty strong on a machine from a bone loading perspective, it removes gravitational forces. We didn't want to do that. We also try to create improvements in functioning by using functional movement patterns in the exercise program. Instead of putting you in a leg extension machine, we would have you do a squat or a lunge with a weighted vest to increase the intensity because this is the type of way that you move in your day-to-day life. You don't sit in a chair and extend your leg and accomplish anything. But you might lunge forward when you're gardening or working or in an activity. We are specific in the way that we apply exercise that way. This exercise program had additional benefits besides the impact on bone. We were able to reduce self-reported disability in men, which means that men were able to do more activities without any assistance. They were able to fully engage in the activities that are meaningful to them. We also found a metabolic impact of resistance training. As you're thinking about doing aerobic exercise or strengthening exercise, resistance exercise has a good cardiovascular and metabolic impact. We're able to observe reductions in circulating insulin levels and in body fat with this resistance training program to give you an idea of the broader benefits achieved by a single program.

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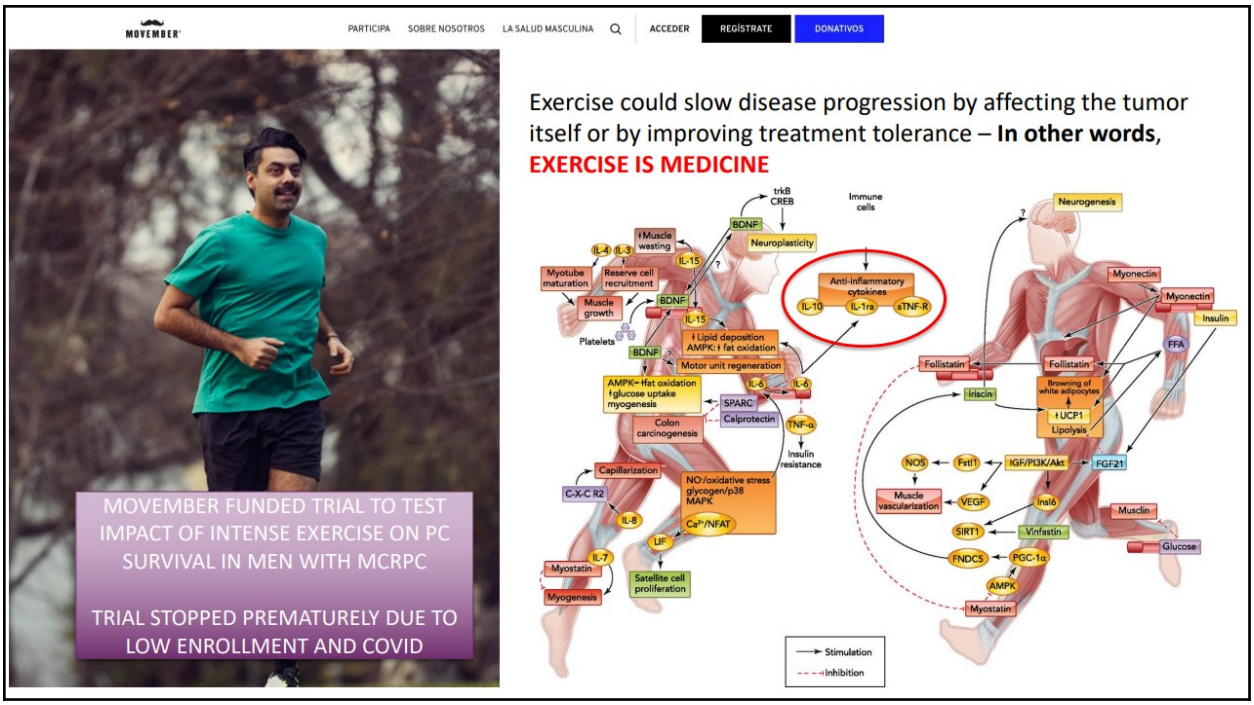

I'm going to move on to what I think is probably of interest to this group. The other really important question that we're still trying to answer is whether or not exercise can help improve survival. There are some epidemiologic data that suggest an inverse relationship between physical activity and prostate cancer mortality. Ever since some of those epidemiologic findings have come out, everyone's been very eager to design the randomized controlled trial to test that observation. I think in 2016 Movember Foundation started what was called Gap 4, also called Interval Trial, which was a large worldwide randomized, multi-site randomized controlled trial to test whether or not a pretty rigorous exercise program could improve survival as an endpoint in men with advanced prostate cancer. We have been a site for the Movember trial ever since it started. The premise of Movember is really to think about all of the potential physiologic metabolic improvements, or adaptations that happen with exercise that should also be anti tumorigenic. A lot of this is based around lowering inflammation levels and this study has been ongoing for a long time. I am sad to tell you that it was stopped prematurely because of a lack of enrollment. The original goal was 1000 participants. I don't know what the final enrollment ended up being, but due to COVID and some difficulties with enrolling patients in a pretty intense exercise program and clinical trial it was closed. They're currently in the process of gathering all of the data from multiple sites and trying to find what they can and maybe look at their secondary endpoint. I just want to let you know that we participated in that program.

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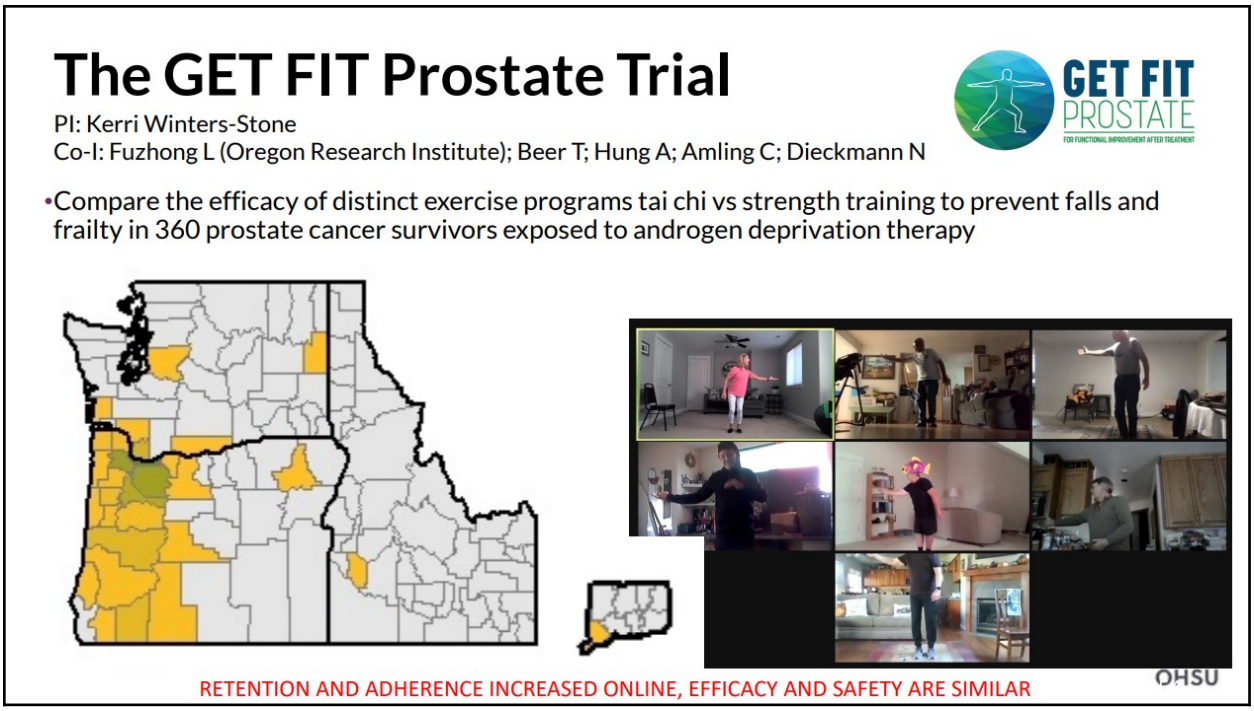


Back to the work that we're currently doing. On the theme of musculoskeletal health, our first trials were really focused on using exercise in a specific way to improve bone health. In the interim, we became very interested also in trying to figure out whether or not there are elevated fractures from ADT. We know bone weakness is probably playing a part. But as someone who's studied fractures for most of her life, I can tell you that very few fractures are truly osteoporotic fractures, meaning that the bone breaks first and then the person falls down. On the other hand, most fractures are associated with some type of trauma, and it's oftentimes a fall. We also did some work that showed that ADT increased the risk of falls in men with prostate cancer.

That led us to design a trial called the Get Fit Prostate Trial. This is a fall prevention trial. We are comparing two types of exercise that have been shown to prevent falls that are related to age, not cancer treatment, to see whether or not they might also be effective programs at reducing fall risk due to ADT. Get Fit Prostate is comparing tai chi, which is aimed at improving postural control. It's a very effective program at preventing age-related falls and older adults. We're comparing that to a strength training program which is also known to prevent falls, but through a different mechanism. We compare that to a placebo control exercise group. This trial aimed to reduce falls in 360 men exposed to ADT with our trial starting in 2019. Obviously we got hit by COVID and in a bad, bad way. We provide an exercise study in older adults with cancer and so we deliver group exercise and we were among the first first types of human subjects research to get fully shut down from COVID. Due to the risk of exposure, we converted everything online. You can see my group down here on the right. I'm doing their Tai Chi online, we did that within 72 hours of shutting down in-person classes. On the left is Friday and on the right is Monday. We've been online ever since. Interestingly, our retention and our adherence rates are just as high if not higher, now that we've moved online and the efficacy looks to be similar between online and in-person exercise and the safety profiles are the same. The other advantage that we've gained from moving online is we've spread our program across the state of Oregon. If you know where Portland is, it's in the green shaded area on the map and the yellow areas represent counties where our participants now reside. If you recognize your state on the lower right, that's Connecticut. We've actually had people find us on the internet and asked to

participate. There's really nothing that stops us from offering these programs to anyone across the globe, except for time differences.

Amit Gattani 31:18

Is this a trial that has a start and stop enrollment date? Or, do you take rolling enrollment? If so, you have to manage the data of how and when people enrolled and the effect. Can you comment on that?

Kerri Winters 31:42

Excellent question. I was just about to get there. These are six-month intervention programs. They have a designated start and stop time. We enroll about 50 to 60 men at a time. We start their exercise, we randomize them, we start their exercise programs, they train as a group, they end as a group, and then we start all over again. We've had nine groups of men participate. So far, I'm happy and sad to say that we graduated our last group last Friday. We converted the trial online. We enrolled 328 men in the program, which was 91% of our target even with COVID. This program is inclusive of men with bone mets, whereas a lot of trials are not out of safety concerns. The trial is going to be completed, so we finished our last exercise class last Friday.

Kevin Fordney 33:50

While I was in the worldwide trial that she talked about that got shut down, but part of it that distressed Kerri was a trial that had a control group and intervention group, and I was randomized into the control group. I hired a trainer, and they gave a little support, but their specific regimen was proprietary. It was a strength and resistance kind of thing. I went to the gym and used machines and all that until I got totally wiped out last year on that trial. My exercise program is pretty meager right now. The thing that I was anxious for Kerri to talk about when we talked with her, Brad, is she seemed to indicate that they learned a lot from doing

things online, or they were forced into that from COVID. I am anxious to hear if she's going to be offering opportunities for people like us to enroll in a little more personalized thing like an Apple fitness where you're doing a program online.

Kerri Winters 37:39

Here are some of the clinical guidelines that I've been privileged to be a part of, and what we hope are going to help move exercise into the standard of care. A lot of the evidence-based work that we've been doing, we're glad to have contributed to some new clinical guidelines. In 2019, we issued the exercise guidelines for people with cancer through the American College of Sports Medicine. In 2021, we issued exercise guidelines for people with bone metastases, who tend to get left out of a lot of the exercise recommendations out of fears around safety. I also just wrote, and I'm glad to share with this group, some brief clinical guidelines for providers to prescribe exercise for men with prostate cancer. I was just sharing with you what we're trying to put forward in terms of clinical guidance that we believe will be the impetus for now starting to require that exercise get moved into standard of care. I think what's holding us up right now are some of the data that speak to third party payers. If they fund exercise and support exercise in clinical care, what is the clinical benefit and what is the benefit to the healthcare system in return for that. That's where our field is doing more work to make sure that we're including endpoints that are meaningful to those parties. I think they're meaningful in general, but they won't find exercise because it helps reduce your fatigue. They will find exercise if it helps keep you out of the hospital and if it helps reduce the cost of your medical care and so a lot of the trials are also now starting to collect those endpoints so that we're more effective at our overall goal.

Brad Power 40:05

I'm very intrigued by the notion of “exercise as medicine”. We've heard of “food as medicine”. But this is the first time I've ever heard exercise is medicine. We had a session with Nigel Brockton of the American Institute for Cancer Research, who said we spend a lot of time on nutrition. Why do we do that? Is it more important than exercise? He said, "No, it's just that it's

more complex." Think of this big picture as a pie chart. There are things we do with therapies, there's things we can do with food and nutrition, there's things we can do with exercise, maybe sleep or meditation. If you had a full wheel and the effects that can have on someone's care, which is I think the way everyone here looks at it, wow would you rate exercise in that pie chart in terms of its potential impact on your disease progression?

Kerri Winters 41:20

On disease? I would add another pie chart in terms of quality of life on that too. But I would say in terms of what we have seen from the epidemiologic data, there is potentially a 50% reduction in prostate cancer specific mortality and prostate cancer recurrence. That's pretty big effect. It's pretty big. Right? It's more powerful than chemo, it's probably more powerful than a lot of the current treatments.

Russ Hollyer 42:02

I talked to my MO extensively about exercise, and she feels it's the most important thing that we can do for ourselves.

Kerri Winters 42:12

I would agree. It makes me sad that you don't have a warm handoff to someone to tell you what to do and to put you in a program. What we need is cardiac rehab which includes phase one, cancer rehab - the time you get diagnosed, phase two - you're coming in and out a little bit to the cancer center, and then phase three - you're out in the community and it's lifelong. You don't necessarily graduate, you just might move on to another setting. I think that's the gap that we're needing to fill that we just simply can't fill fast enough because a lot of people struggle with knowing what to do.

Brad Power 43:04

Can you provide a simple summary of advice? We trust that the research is backing up the evidence for whatever you're about to say. You don't have to prove it to us, but what would you do? I always love this phrasing, “What would you do if you were us?” That is, what advice would you have for anyone with advanced prostate cancer, most of whom have been on ADT, as you've been discussing.

Kerri Winters 43:39

From an exercise programming standpoint, I think you should work towards aerobic exercise, three to five days a week, 30 to 60 minutes at a time, resistance training two to three days a week, and flexibility mobility every day. That's a lot. What I'm saying isn't any different than the public health guidelines. But each one of those have different benefits and an ideal program would contain those different modalities and those are the doses in which they are effective.

Russ Hollyer 44:31

When you mentioned flexibility, did you mention any stretching?

Kerri Winters 44:35

That's what I mean by flexibility. Flexibility, mobility, or you can call it yoga. It's got a little bit of other stuff in it too. It's got some strengthening and some stability exercises. But flexibility means stretching. In order for you to do the other two types of exercise like strength training, aerobic exercise, and function in your day to day environment, you need range of motion, and you need mobility. If you don't have those, and you do a squat, for example, and you have poor ankle flexibility, and poor hip mobility, you're going to do the squat wrong and you're going to get hurt. The flexibility provides that foundation for movement and it doesn't take a lot. We recommend about 15 minutes every day. That's a morning stretching routine, or an evening stretching routine. That gives you that foundation for movement.

Mike Yancey 45:55

I've got significant bone mets, and particularly in my vertebrae clear up and down my spine. Even though I'm able to do some weight work, my doctors have pounded in my head that they don't want to load my spine up at all, so that limits what I can do. They're really afraid of a vertebrae just crushing. Do you have any suggestions or recommendations?

Kerri Winters 46:21

Yeah, I do. And that's always difficult. In the absence of having super clear guidelines, everyone's going to err on the side of caution, and that's what they're doing. They're erring on the side of caution because we don't know, even from the osteoporosis field, where you've got weakened bone and we're trying to be careful. We still have never been able to do the right study to show if you do a squat, with this level of bone mets, it is risky. We just don't know that. My advice tends to be this. If you do bodyweight exercises, where you're doing unloaded exercise and your form is correct, the risk is relatively low. As you start to increase weight and if you start doing things incorrectly, the risk is going to increase. The other things you should avoid are highly dynamic, rapid loading kind of exercises, twisting exercises, hyperflexion hyperextension, or any extreme loading on the bone. I would also be careful of exercises where the weights are away from the midline of your body. If I'm doing crunches with a barbell up here it's no good. The further away you move the weight from your midline, the more pressure it puts on your spine. The classic osteoporotic fracture is in osteoporotic when a woman leans over to get the turkey out of her oven and fractures her spine. That's like picking a heavy load that's way away from the midline of your body. It's almost like if anyone's had to go through NIOSH lifting mechanics for how do you safely lift a load? Similar to Occupational Safety, it's the same kind of guidelines. You want to keep things close. Does that help, Mike?

Mike Yancey 48:45

Most of what I've been doing so far is weight work in the upper body, like laying down on the bench and doing that kind of work. Sometimes I will also lean over that bench, but I will rest my elbow on the bench to pick up the load so that my spine is not picking it up. That's most of what I've been doing. You mentioned aerobic and I love to walk but unfortunately recently I've had significant hip pain. That's put me on the sidelines. I swim 40-45 minutes a day when I get a chance. Would you consider it an aerobic exercise?

Kerri Winters 49:28

Absolutely. Yeah. 100%. Any aerobic exercise is if you're using the larger muscle groups in a repetitive way, and it's not against high loads. Swimming and cross country skiing, the Versa climber, the elliptical trainers, those are all whole body aerobic kind of movement.

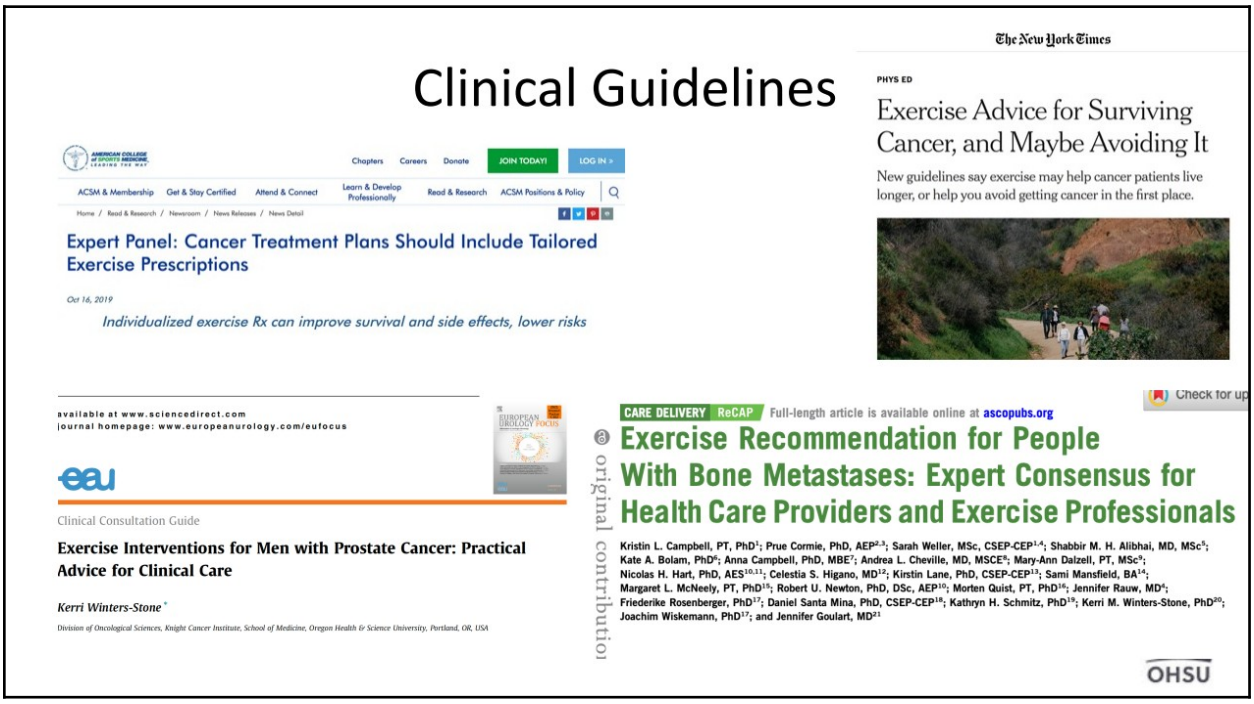
“Exercise as a Countermeasure to Hormone Deprivation Therapy Side Effects and for Bone and Mental Health” (Kerri Winters-Stone) [#48]

Mike Yancey 49:53

Thank you. Appreciate it.

Amit Gattani 49:59

You mentioned that there are some guidelines available. Can you share the links for those guidelines, especially for the bone mets? I'm actually pretty much in Mike's situation with very similar conditions and issues. Recently, because of this spinal cord compression, I've developed more neurological issues as well. I think some kind of published guidelines that you can share would really help. What's the best way to find a trainer who's actually certified in this? We've seen a few links in the past, but I would like to pick your brain on the best way to find a trainer.



Kerri Winters 50:46

I'm happy to share those guidelines. They don't necessarily specifically prescribe exercise. They are around clinical guidance. For example, "can you send a patient out to community exercise if they've got extensive bone mets? Or, do they really need more one-on-one training?" It's a little bit more like that than the same type of guidance that I just gave Mike. I'm also happy to talk to anybody on a separate call or have an email discussion because that is tricky. The one thing I forgot to say to Mike but also say to others is, this is in my opinion, knowing bone, bone adapts to its habitual stresses, and it gets strong in those ways. So the type of exercise that you're doing, Mike, it's probably accustomed to. If you do something different, or excessive, that puts the bone at risk. I just say that because the things that you're already doing, if you're tolerating that, you're probably going to be able to tolerate it. That tends to be the way that bone behaves. In terms of getting a trainer, and this may be what people have told you, there is a certification through the American College of Sports Medicine for cancer exercise trainers. That individual has advanced education and experience working with people with cancer. There is a directory

for cancer exercise trainers through the American College of Sports Medicine that I will send you guys the link to. I believe you can search by zip code and then you could reach out and contact those individuals. I will say that we don't have enough of them across the country to be available to all the people who need it. But that might be one one place for you to be able to find someone.

Amit Gattani 53:08

Are there online group classes? If you can share some information about that, that would be helpful.

Kerri Winters 53:16

I can share that too. We have a resource list that we give to our participants. Once they finish a trial, Kevin, you might have gotten one. Oh, I don't think we're able to give you yours yet. But I'll look for ones that are not local to Oregon. I will tell you that one of the things that we have done from our research programs, due to demand, is a nonprofit that's called Fit Together. We deliver our evidence based exercise programs in a community setting because people from our trials didn't want to stop. We ended up creating a nonprofit. It is supervised exercise classes for people with cancer and their partners because our work extends to partners. We also allow partners to participate. I'll send you guys the link to that. We have yoga classes. Someone said in the chat, "I don't know how to stretch." I have a yoga class that I think could help you. I have lots of YouTube and online videos. I prefer to know you before just sending out a video to you to follow, but we also have stretching routines that we have created that we're still working on publishing to our OHSU website, but let's continue to talk about that. The Fit Together classes would also be a group class that you could take if you're interested in that. Can we reach out via email individually? Absolutely.

Russ Hollyer 55:22

I have like 20 or 30 questions. So what's your email address? I don't want to take up all your time. We're almost done here.

Kerri Winters-Stone

wintersk@ohsu.edu

Russ Hollyer 56:12

With ADT, have you heard of transdermal estrogen therapy, either in addition to ADT as a low dose replacement, or like the Patch trial in place of ADT, (or in place of the standard ADT drugs because I don't want to say in place of ADT because it is ADT)? What do you think about the bone loss mitigation results that have been found through the Patch trial and other trials or studies?

Kerri Winters 56:39

That's even been shown in postmenopausal women that a low dose of estrogen is enough to have this bone preserving effect.

Russ Hollyer 56:55

I actually did the Patch trial myself four or five years ago, or their high dose estrogen. I'm now on something called bipolar androgen therapy and when I go on my low ADT cycles, I do a very low dose estrogen replacement. Do you think that should be standard for guys to do that? I've spoken with a number of MOs and urologists about it. When it comes down to it, does adding little estrogen affect ADT, low testosterone? Their answer is always either crickets, or "no, I don't think so."

Kerri Winters 57:39

Because I'm not a clinician, I'm going to avoid any comments there. I always get a little bit weary of doing that. But from a bone preservation standpoint, you don't need a high dose of estrogen in order to have some bone preserving impact. I would say the other thing, for those of you worried about fractures, if you don't fall, you're probably going to avoid fracture. The other thing is don't stop moving because you're afraid of falling down. There's this U shaped curve that we see that not enough exercise increases your fall risk. When you're super active your fall risk goes up too because you're just taking more chances. It's not because too much exercise increases fracture. It's an environmental hazard more than anything. I would also think about keeping yourself strong and working on balance control and being aware of the potential fall hazards that exist in your environment and taking care of those low lighting, small dogs, rugs, and seemingly innocuous things that can be dangerous. The other thing from a fracture prevention standpoint is that we know exercise is the only way to stop a fall. There's no drug for that.

Jeff Krolick 59:29

When I was first diagnosed and started androgen deprivation therapy, my oncologist actually screened trainers who had a certification that you were talking about. I actually worked with one

virtually for about a year and a half and learned all the routines, and I try to carry on with that although it is nice to have a cheerleader. I just put this in the chat with the address, or with the website, so it may be a place to start to check that out.

> From the chat: My oncologist screened trainers and recommended Adebola and Clinton at https://www.gymguyz.com/sw-portland/

Mike Yancey 1:00:16

That's great. I'm going to look at it myself.

Russ Hollyer 1:00:24

I was wondering about the research, or what you think of whole body vibration plates. I've seen a little bit of research about it. It makes a little bit of sense to me when I'm working out. I tend to do a whole body vibration plate in my rest periods, or do an elliptical cycle.

Kerri Winters 1:00:42

It's so interesting you bring that up. I used to have a platform. I used to have two of those. I don't know for those of you guys who aren't familiar with this whole body vibration. It's a high frequency, low amplitude platform. It's like a shaker plate. I don't know if you know the origin of that but it was originally developed out of SUNY Stony Brook by a skeletal physiologist as a way to stop zero gravity induced bone loss because you can't use weights in space. The things they have to do to keep astronauts from losing bone are crazy. They've had to strap them to their treadmills and use these really heavy bungee cords and things. They developed this opposite approach using high frequency, low amplitude to improve the bone. He did a bunch of experiments in turkeys. The guy has been in Time Magazine. It works from that perspective, but it's been slow on the uptake in the human trials because there's now a worry that too much vibration could be harmful. I think it's had a difficult time making it into the medical world. It has made it into the performance world. You'll see these plates in training rooms and you'll see them in gyms. From a scientific standpoint, the evidence is kind of like so-so. Some trials show that there's a benefit other trials show there's not. I had a platform and I was able to see some benefit really around bone loss. I'm using it now more for peripheral neuropathy. I know a lot of you guys get neuropathy. I mean it can't hurt. I don't know from a scientific standpoint, if I can say really confidently that it's doing a whole lot more.

Russ Hollyer 1:02:59

That's kind of my take on it. The research is pretty sketchy in my opinion. I'm not a turkey. I'm not a rodent.

Kerri Winters 1:03:07

You don't want to shake until your eyeballs come out of your head.

Russ Hollyer 1:03:09

I heard one guy say he had a brain aneurysm or something like that on a whole body vibration plate. He said his teeth were chattering first, his jaw was hurting.

Kerri Winters 1:03:35

I haven't had success getting a trial funded with the type of vibration I think you're talking about. I've moved more toward a very low vibration. It's almost like a hum.

Russ Hollyer 1:03:47

What type of frequency are you using?

Kerri Winters 1:03:50

I'd have to look back and see what the Hertz are on that. I can definitely send it to you. But it's been hard to get that because of occupational vibration loads and concerns over that. When you do use it, make sure that you're in a semi-loaded position. If you're squatting on it, you don't stand straight legged and just let it vibrate because there's nothing to dampen the vibration. If you're doing push ups on it, I wouldn't go to straight arm push ups. I wouldn't go to full extension if you're doing squats on it. I'd always stay a little bit loaded if that makes sense.

Russ Hollyer 1:04:38

Did NASA also do some research on PEMF (pulse electromagnetic frequency)?

Kerri Winters 1:04:52

Not sure about that.

Russ Hollyer 1:04:56

What do you think of vitamins and supplements like calcium, VK, boron, phosphorus, etc.

Kerri Winters 1:05:04

I'll only go so far as to talking about what I know for calcium and vitamin D. For women who are hormone deficient, e.g. postmenopausal women, the recommendation is about 1500 milligrams of calcium a day. For men, it's 1000 because we don't account for hypo estrogenism or low testosterone. I would go with 1500 milligrams a day and you should break up your doses throughout the day. The gut can only absorb so much calcium, and then it's just going to pee it out. About 500 milligram doses is the maximum that can be absorbed at any given time. If you're doing 1500, I would do a dose in with breakfast, lunch and dinner. Calcium citrate tends to be the most absorbable followed by calcium carbonate. Oyster shell calcium is not as good as Citric Cal or some of these other supplements that are on the market. With vitamin D, it depends on where you live. For those of us in Oregon, we don't get vitamin D in the wintertime so you might benefit from a supplement.

Rick Stanton 1:06:32

How much, 500 or 1000?

Kerri Winters 1:06:35

Probably 1000.

Russ Hollyer 1:06:42

It seems to me that because we're an ADT, we're like post menopausal women. When we're not on ADT, we're not necessarily sure if our testosterone has recovered and estrogen has recovered with it.

Kerri Winters 1:06:53

But from a calcium standpoint, the worst that's going to happen is you'll excrete it, unless you're a stone former. But hopefully, then you're under the care of your urologist.

Brian McCloskey 1:07:11

I'm concerned about cardiovascular health. I've been on ADT for over six years. I'm curious if you have any sort of bell curves that show over time, how your risk of some type of cardiac event increases the longer that you're on a ADT? I've got a Fitbit that I use when I'm running, or when I'm on a peloton, or any kind of exercise. I noticed that I seem to be in zone five a whole lot more than I should be. It could be because I'm just coming off of some surgeries and whatnot. But I'm a little worried about having a cardiac event because I've been on ADT for so long. My Fitbit is telling me that I'm overheating my engine.

Kerri Winters 1:08:17

It's a good question. I don't know the answer to the long term trajectory of risk. But now, I'm really curious. I will look and see what I can find. I would say the best thing to do if you're concerned is get a graded exercise test.

Brian McCloskey 1:08:45

Like a functional test such as on a treadmill?

Kerri Winters 1:08:47

Yeah.

Brian McCloskey 1:08:48

I did that years ago and I was fine but that was probably two, three years ago. So I guess I could do it again.

Kerri Winters 1:08:57

You could. Where are you Brian?

Brian McCloskey 1:09:04

San Diego.

Kerri Winters 1:09:04

You got access up the wazoo down there. But if you do it in an exercise science lab or something, and then they can actually look at your heart rate response to your VO to your

oxygen consumption and get an idea of what your training zones are and what is your cardio like when you're in your zone five, or whatever heart rates those are for you. Are they seeing any cardiac arrhythmias or is anything popping up? If you end up having some symptoms, what's your symptom? But if you're asymptomatic when you're in those zones I don't necessarily know that you're at any more risk than when you're at a lower zone, but I'm not a cardiologist.

Brian McCloskey 1:09:38

Given the fact that so many people now have Fit bits and wearables, there's all this data, right? I’ve got truckloads of data, and I could go in and have a functional test, but it seems to me that it would be far more insightful if I could upload my cardiovascular data to some site that would tell me where I sit on that bell curve. Is anybody working on that?

Kerri Winters 1:10:48

Not that. I know exactly what you're talking about, and I know there's a lot of interest in that. Not that I am aware of, but it doesn't mean that it's not happening, potentially out of the oncology context.

Brian McCloskey 1:10:58

Okay. I think we've got Mike Snyder coming on in April, maybe maybe he can help us.

Kerri Winters 1:11:05

Oh, yeah. He's the big guy. He's the guy down in Silicon Valley, right? .

Brian McCloskey 1:11:10

Yeah.

Rick Stanton 1:11:29

I used to get my aerobic exercise with swimming. I would swim it all at once. No bursts. We used to call it LSD for long, slow distance when I ran. Then I heard about HIIT. I haven't even done a mile time lately since I've learned about HIIT. I just exercised for 30 seconds. It's hard to recover, repeat. And then I got some guidance from the Block Center and US Integrative Oncology Center, which said 30 seconds as hard as you can, then 30 seconds rest, repeat three times, then take a little rest, and then repeat that 3x3 kind of approach. So I stopped at a long, slow distance for HIIT. Is that a good plan?

Kerri Winters 1:12:49

Yeah, if anyone's not quite sure what we're talking about I'll try to explain. Training for a marathon is a really good example. You've got a long slow distance, right? You're doing 15 mile runs, 20 mile runs that you do on the weekend. Then you've got interval training, which is what you're talking about, the high intensity interval training, that's boosting your fitness. They both serve their purpose. But right now, there's really a movement toward using HIIT as an efficient way to improve fitness, cardiovascular fitness, and the data are pretty strong. It's like interval training. If you guys were runners, it was called Fartlek training. You do these bursts of high intensity kind of like 90 to 100% of your max. And then it's followed by a recovery period,

walking or jogging. Then you do another short burst. In terms of improving fitness, like cardiovascular fitness in an efficient time efficient way, HIIT is a really good program. If you're trying to improve muscle endurance because you want to run a marathon or you want to do a long cycling event, you got to run for a long time or you stay on your bike for a long time in order to develop that level of specificity. Again, it's this specificity of training. It depends on the outcome. If you're interested in bolstering your fitness, and the metabolic adaptations, I think HIIT is a nice efficient way to do it because it doesn't take much time.

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Follow up by Kerri on questions raised during the meeting:

From: Kerri Winters <wintersk@ohsu.edu>
Date: Thursday, March 16, 2023 at 2:17 PM
To: Brad Power <bradfordpower@gmail.com>
Cc: Brian McCloskey <brian.j.mccloskey@gmail.com>
Subject: Re: [EXTERNAL] Thanks, Next steps -- Exercise and cancer

Hi gentleman,

This is a long email with a lot of attachments, including my slides as a pdf. If I forgot something that was asked about / requested yesterday please let me know.

Three of the attachments are articles that the group might be interested in:

- Campbell 2022 is the exercise with bone mets guideline
- Campbell Winters-Stone is the American College of Sports Medicine exercise recommendations for cancer survivors
- Winters-Stone is a brief clinical guideline for providers wishing to recommend exercise to prostate cancer patients

I have also attached the list of exercise resources that we provide to participants in our clinical trials at the end of their study period. Most of these are local to Oregon, but with online offerings I’m sure they may be accessible no matter where someone lives (file name is: Community Online…).

Relatedly, many people asked about our FIT Together community exercise program. This is a nonprofit I run outside of OHSU as a way to provide access to our exercise programs outside of the research context. Here is a link to the website, which is very basic (and is a work in progress), but shows the classes we offer and a little bit about our group. https://www.fittogethertraining.org/ . The costs look like they vary but they are all about $5 per session and the total cost varies by the length of the session. There is one class specific to prostate cancer, which is a yoga and mobility class, and the others include mixed cancer types. We also have created a once weekly online meeting space for our prostate cancer participants

per their request. There’s no cost and it’s just a gathering space for men to talk. We don’t facilitate anything. We are also going to start an intro to resistance training class in a few weeks, that I mentioned. That is not yet posted to our website, but you could contact us and we’ll let you know when it is up.

One person asked about stretching and in addition to the live classes offered through FIT Together, I’m including a link to a DVD / YouTube program we used in a research study in women with cancer and in persons with advanced lung cancer. The program is for anyone and is taught at three different effort levels so someone can follow whatever level suits them at any time, even from exercise to exercise. I love this program!

https://www.youtube.com/watch?v=ebjV2hy-Q1A&t=1126s

Here are two stretch routines we made for a prostate cancer study, one is in the chair and the other on the floor:

GET FIT Prostate Seated stretch program	https://youtu.be/azCFsWl8wjY
GET FIT Prostate Floor Stretch Program	https://youtu.be/4ArAjh9DJtM

Finally, someone asked about finding experienced trainers to help them and we are definitely under-resourced here, as a profession. But, the ACSM has a Cancer Exercise Trainer (CET) advanced certification for personal trainers and those would be the ideal type of trainer to seek out. Anyone outside of that, I would ask how much experience they have working with cancer survivors, other types of illness / limitations / considerations, and judge if they are the right person for you. Someone who can do their homework and adapt exercises as needed for your ability and tolerance is best. Some trainers have little education about chronic conditions and little empathy, so I generally discourage working with them and I would not hire them to work for me. But, there are a lot of good people out there nonetheless.

If you go to this website: https://www.acsm.org/certification/about/profinder, you can specify what type of trainer you want, including a CET, and your state/zip so this might be of help. There is also a directory of cancer exercise programs that can be found here: https://www.exerciseismedicine.org/eim-in-action/moving-through-cancer/exercise-program-registry/ .

I think that covers most of everything we talked about. If not, let me know and I’ll get back to you.

Pleasure to meet all of you – I hope we stay connected.

Kerri