DANNY LENNON: Ciaran, welcome back to the podcast.

CIARAN FAIRMAN: Appreciate it man. Good to be back here.

DANNY LENNON: Yeah, and then the, this time in person. So we get to hang out a bit and had some good conversations now and also a few months ago about the work you've been doing, which hopefully we're going to get into today.

CIARAN FAIRMAN: Yeah.

DANNY LENNON: Before we get to that point, just for maybe people who didn't catch the last episode we did, probably a couple of years ago at this point, give them an instruction into your area of expertise, your kind of, I suppose, journey to that point in terms of research you've been involved in, where you're currently based and that type of stuff.

DANNY LENNON: Yeah, so I'm currently a postdoctoral research fellow at Edith Cowan University. I mean in their exercise medicine research institute where we focus on the field of exercise oncology and looking at how different types of exercise, nutrition and supplementation interventions can improve a variety of outcomes in individuals with cancer.

So the last time we talked was coming towards to the end of my PhD at Ohio State where the PhD was in exercise physiology, and a lot of what I did there was doing similar stuff in prostate, endometrial and breast. Kind of before that, a lot of my education and experience was in sports nutrition and human performance. I did my Master's in Kinesiology at Georgia Southern, and did a lot of sports nutrition research and kind of human performance research. Coming into this field, there is a really clear need to draw from those principles and bring it into this field to really improve what we're doing from a research perspective in terms of design of our interventions, more specifically tagging our outcomes, and I think just overall an improvement of the work that we do and somehow or another have been able to carve out a niche and being able to do that. So that's resulted in me being here at ECU and kicking off from there.

DANNY LENNON: Yeah. I think the last time we talked, you had said that there's obviously been a lot of work going on in the field of exercise oncology, a lot of that very novel, very interesting, and there was more awareness I supposed in that decade leading up to that point from a place of relatively nothing being looked at in any great detail to now lots of good labs around the world. But you'd also mentioned that there were still all of things unanswered but more so there was a lot of in terms of practical application for people that really need that advices where maybe some of the messaging was getting lost too. I suppose two years on from that conversation, how would you kind of sum up the field of exercise oncology since then? One in that, I suppose the current state of it within academia and where you feel it is, and then kind of two, has there been any improvement in getting more of that into the places where it needs to be in the real world.

CIARAN FAIRMAN: Yeah, I think it's a good question because there's been a wealth of -- I mean the field is

exploding. From the time that we talked to now, the amount of labs in different areas that are conducting research in this space has exploded and that's brought with it a lot of different lines of research. Some of the most important areas of research, one of them is the implementation that we just talked about and actually getting the information to people that needs it. If I was to say kind of what are the most important areas of what we're doing, well, to summarize what's been done up until now, pretty much the safety and efficacy has been demonstrated in a variety of cancers. Most of our information comes from breast, prostate, lung to a certain degree, and colon. We're now starting to spread into more rare forms of cancer and things like that and different types of treatments, but overwhelmingly we can kind of say if you'll exercise into all cancer treatment, it's at minimum safe, there's no risks of adverse events in relation to treatment. There's always risks of muscle strains and things like that, but overwhelmingly it's safe.

The efficacy varies because of the field is so new, a lot of the research initially was, was surrounded by safety. So that resulted in programs that were very watered down to confirm safety. So oftentimes people are underdosed, which then effects the efficacy. So where we're at right now is we're really starting to kick on in terms of, one, developing more strategic interventions that are tied at the specific outcomes. So originally, it was kind of charter kitchen sink at them and see what sticks. Let's give them a combination of rowing and resistance training, let's test everything under the sun, and then whatever is significant, we'll publish it. I think there's more of an appreciation now for specific conditions. My specific focus is on muscle wasting and muscle loss, specifically as it relates to different types of treatments such as androgen deprivation therapy or conditions such as cancer cachexia, which is a whole different beast.

The other area is the implementation science, and actually getting that information not just to clinicians and practitioners. The implementation science is a broad field. A lot of what we think of is the usual stuff like behavior change and how can you actually get this to the communities and keep people active. One of the most important areas of that and what we do is the referral and actually getting a physician to click a button that says you go and see x. There's so much work to be done in that space. We've got a phenomenal PAC, Mary Kennedy, who is working on this. It's taken her to go to two years to get into one of our local hospitals and work with physicians to get them buy in into our program and to get them, when they're going on the list of checking everything off, to discuss with the patient. They've at the very least mentioned exercise and or diet and at the very least at least click the button that pings a referral out to us.

I think beyond our field that area is going to be one the most important areas moving forward in a lot of chronic conditions. And actually what I've come to learn with the implementations from that perspective is how we have to minimize the burden on the physicians. We can't shout from the rooftops and say it's on them to communicate all this stuff, particularly in our field. Like they're talking to these people that would have cancer diagnosis and their upcoming treatment schedule and dealing with the psychological impact of that and whether this person should tell their partner or their boss. We can't be so arrogant to come in and say, look, tell them to do a few squats as well, plus they're not trained to do that. What we're trying to now establish is a clearer pathway to where it's easier for them to say, look, I think this is going to be really important for you to have a chat about some lifestyle factors. I'm going to click this button, it's going to ping your info. Are you okay with that to this person, to go down the hall and go chat with them? And I think that is going to

open up so many avenues into actually demonstrating the value of what we do.

DANNY LENNON: And presumably that would, in and of itself that action would speak louder than just saying exercise is important, because it almost validates this as a serious thing, right. In the same way as if someone's in talking to their doctor in and they get told, okay, you're going to go and speak to professional x now in a moment about this course of your treatment. That seems like a, okay, this is part of what I do, whereas if you're just told that you should probably exercise as well. That doesn't have the same feeling of seriousness to some degree.

CIARAN FAIRMAN: Yeah, it's huge because the majority of our trials compare exercise to usual care and usual care for all intents and purposes is we'll hand you a flyer that says, eat your fruits or veg, activities is good, go for a walk, and our flyer ends up in the bin on the way out. So the usual care doesn't work, and I think there's also a lot to be said for the buy-in of the physicians. I mean there's a lot of work in examining the fitness of physicians and how willing they're. If the physician themselves is fit and he understands the value of fitness and they feel it, there'll be more bought-in. The clearest example I can give you is two phenomenal physicians at Ohio State. One's in prostate and one's in head and neck. One of them is overweight, inactive, drinks coke all day, all that type of stuff. A super Intelligent dude but is partially sold on what we do as he sees as kind of a an adjunct, which is fair enough. But his conversation, if it comes to him, will be to refer. The other gent has a personal trainer, works out three times a week, loves it, and as you said, the conversation is not necessarily not a choice, but it's just a part of their treatment. So as part of your treatment, you're going to receive this type of treatment. You’re going to meet with your surgeon and you're also going to meet with this crowd who are doing this work, and it's almost like creating that opt out strategy rather than opt in. You find that that's

at least in getting people starting with the conversation that it's a little bit more effective.

DANNY LENNON: What would you state the strength of the evidence is and does that matter up to how that's being maybe viewed in some quarters or is it people just not aware of it or have they heard about it but just not convinced by that or what's kind of going on?

CIARAN FAIRMAN: It’s such a big conversation right now in our field, I think because there's so much emotion tied to cancer diagnosis, and I put myself in this category, we can fall into the dangers of being blind advocates, and kind of it's great for everyone. Everyone should do it, and it's not the case. Physicians are looking at this through a different lens. They're working with people who some are young and active and some could get some benefit or people are bedridden or in palliative care where exercise might help a little, but so could pissing off to the lake for three months while they're getting their affairs in order. And a lot of that stems from what you said is the evidence and from two perspectives. One is the evidence around fitness outcomes. And they're not actually that important to clinicians because the field now is moving to almost as they should just serve as a proxy that they actually did something.

So, for example, cardiotoxicity is a big concern in certain chemotherapy agents. So a lot of the work is focused on maintaining markers of that whether that's left ventricular ejection fraction or VO2, but in terms of something like improving strength, doctors don't care about that. So if we're designing interventions to improve strength, then we come back and say, look, all these people with breast cancer, they improved their strength, like I don't care. A lot of what they care about is, one, quality life, but more importantly the biological plausibility. So there was a phenomenal symposium this year at ACSM where one of the bigger areas that we're moving forward into is the kind of

biological impact of this, particularly as it relates to tumor physiology.

So there's been a couple of really interesting preclinical studies that have essentially posited that the tumor vasculature is messy. It's all over the place. The veins can't really go to specific areas of the tumor. There's leaky vessels which results in hypoxic regions of a tumor where there's no oxygen. Those areas where there's no oxygen actually feed "the metastasis of the tumor". Secondly, does the fact that the vessels are leaky and broken means that the draw can't actually get to areas of the tumor. So there's a lot of work done in the pharmacological space to try and normalize that vasculature that will result in a less hypoxia and better efficacy to drug. If you can improve the vasculature trial and surrounding of the tumor, more the draw can get to the tumor and you can potentially arrest the growth.

So there's been a couple of really interesting preclinical studies that have actually demonstrated that exercise plus chemo is better than chemo alone at improving this vasculature, at arresting growth, which then it's so funny because the main author Allison Betof Warner presented this data and we as idiots on the applied side saw this paper a few years ago and we're jumping from the rooftops and say everyone needs exercise because it approves tumor vasculature. And she presented last month that was kind of saying, look this difference in tumor growth size isn't statistically significant, but it's isn't exactly clinically meaningful and not for me as an unbiased physician to jump onboard and say everyone has to do this.

So they did a great job of outlining the model by which pharmacological drugs go from phase one preclinical trials all the way through to phase three and phase four and randomized controlled trials, and the need to create the biological plausibility in the initial phases to

actually determine if RCTs are worth it. Because if we're presenting preclinical data as evidence that everyone should, they'll laugh at it, just like you would present preclinical data from pharmacological research, and we haven't got the translation down yet in terms of actually developing randomized controlled trials to do this in humans because it's infinitely more difficult.

You've got things like serum markers of hypoxia that aren't exactly closely related to tumor levels of hypoxia or you can look at MRI and tumor perfusion, but all of that work takes so much money, takes a lot of participant burden to actually sit in MRIs and get this data and a ton of research in terms of it's easier to look at different doses of exercise and preclinical models. It's easier to get mice to run for 150 minutes or 300 or whatever your metrics are, but when you extrapolate that out to all the stuff we talked about and get on untrained people to work out at different doses or intensity, I think we're so far away from actually getting to the point where we can put something down at ASCO as the American Society of Clinical Oncology and say exercise can actually improve tumor physiology.

And it should also be noted with that, Allison brought this open, another great point that there's also a few studies that have shown that aerobic exercise preclinically can actually facilitate tumor growth. So by overemphasizing the vasculature, maybe you're facilitating growth by some other mechanism. So we also have to have caution there. It's worth noting that I think if we would have seen that given there's several large randomized controlled trials during chemotherapy and radiation, STAR trial in 2007 was one of the biggest with 242 I think. I think we would have seen that in humans if that hypothesis was there, but it's definitely worth adding caution to.

So in terms of one of the biggest areas to get clinician buy-in, they want hired science and I

think we're years away from that. So it's a really challenging area that a lot of people are trying to dig into now, because in addition to that, the tumor physiology will vary based on cancer type. So we may do some phenomenal work in breast cancer and see some really good outcomes, but someone with lung cancer will say, well, the mechanisms for growth of metastases is a little bit different. I'm not sold on it. So in terms of embedding it as a standard of cancer care, we've come to realize the gravity of what we're asking for and how much evidence we will need to actually implement it.

DANNY LENNON: Right. At least that it's impacting cancer specific outcomes itself as opposed to things like strength or so on. Yeah, it's kind of, presumably you can kind of see the position where how physicians would be looking at that from of saying, well, it's great now that we can kind of hypothesize that this is going to happen, but what evidence do we have, and then what is the magnitude of that effect? And probably more so, is it worth putting the resources where that's like mentally or otherwise for me and the patient to actually go through what would we need to, to implement this stuff for the return on that investment in the end? Because I mean this person has just had, their world shattered. There's all this stuff going on that we need to attack in terms of the treatment and then also their support. So they probably quite rightly are having some kind of questions there too.

CIARAN FAIRMAN: Yeah. And I think you made a good point in, I shouldn't also go too far, but there is support for quality of life and outcomes. VO2 as an outcome is important in terms of mitigating cardiotoxicity. Increasingly, body mass is important against mitigating cancer cachexia and things like that. So there we can make those cases, I think you nailed it where we just have to be careful of what we're advocating for. If we're advocating for conscious specific outcomes and then saying that that's going to lead to reduce recurrence or mortality, we're

nowhere close, but if we're saying we can improve the overall fitness and that may lead to less hospitalizations, it may need to a smoother treatment course, higher quality life, that's a way we can kind of get around it.

DANNY LENNON: Yeah, that makes sense, because especially if you're saying like there's long a period of time needed to get that level of work done before you can make some of those stronger claims that doesn't need to mean so well. We're just going to wait until then before we start advocating something that we clearly have of evidence showing there's some benefits here. Instead, you can almost use those as a way for it to become part of practice, but you're just advocating on a different basis, right, where you can quite clearly tie it to quality of life if you're improving someone's ability to function and move around and so on.

CIARAN FAIRMAN: Yeah, exactly. And I think that's a way of then facilitating the ability to look at other outcomes. If we can use that as a way to push towards standard of care, we have a bigger patient pool to draw from to look at other outcomes. There's a couple of big trials that are looking at survival and there's one in colon cancer called the CHALLENGE trial that actually has a fair, I think it's got 300 out of 800 they're trying to get, and GAP4 -- so the challenge is looking at aerobic excises and colon cancer. It's kind of a lot more self-directive where people are just checking in, telling you what they're doing. The GAP4 trial is absolutely insane. They're looking at trying to get 900 individuals with metastatic castrate resistant prostate cancer. So these dudes are just ended the line and they're trying to see if they charter kitchen sink at them, take them through an aerobic and resistance excise program, can they somewhat delay the progression of disease and time to mortality. It's a really, really challenging trial to run from variety perspectives. The ethics, and trying to get ethic true to talk about the patient population we're using.

We've got a pretty strong support in Australia for this type of work. So it's not as challenging, but to open up sites in America is a nightmare and then some European sites starting to open now. But we've only got I think 60 out of 900 recruited. So that trial, if it comes to completion, will answer a lot of questions. But in terms of coming to completion, I would say 5 to 10 years at least, and then as we were talking about fair. I'd also be very cautious about the outcomes of trials that look at survival, because it looks pretty on paper and saying, we ran 900 people and saw that exercise led to a significant improvement in survival. Because you're working with so many people, you may find that three weeks of a difference is a "significant difference". But I keep coming back to picture myself sitting in front of someone and they are in the palliative stage of care and I say then we'll the [inaudible 00:25:39] and see what happens. We have to be very careful about the gravity of what we're suggesting to people.

So it's a weird phase I'm in as a researcher, as I move out of that passionate advocacy stage to actually now trying to build the evidence. I've become more cautious in how and what I'm saying and the message I'm delivering.

DANNY LENNON: Yeah. I mean there's so much, and I think one thing we talked about that last time that makes all cancer research so difficult or so much that needs to be done, and particularly in this case is, as we mentioned, every type of cancer is vastly different. And even you take one specific type of cancer and you can have differences in how different tumors are reacting and so on. So given that we have all these different cancer types, if we're looking at cancers with specific stuff, presumably that would need to then be repeated across a number of these different types.

CIARAN FAIRMAN: Yeah. There's a couple of different approaches and I don't know if there's a right answer. You can almost go in terms of chemo specific, so

different chemotherapy agents will have different side effects. Doxorubicin and some types of chemo are really associated with cardiotoxicity. Other types of chemotherapy are more associated with peripheral neuropathy. So you could go the chemo agent route, but then cancer types will have different combinations and doses of chemo. So peripheral neuropathy is associated with not only the type of chemotherapy but the time on chemo and the cumulative dose of chemo. So based on the agent you could have more or less symptoms and then it could dissipate as you remove the agent. So the chemo agent I think is an interesting rule. You could also go by condition. So cancer cachexia is really prevalent in pancreatic cancer, in GI Cancer, head and neck cancer, places where digestion and absorption of food alters, and also things related to the tumor as well that are beyond level of comprehension.

I think that's an interesting way of tackling it whereby the mechanisms might be different, but it's broad enough to where if you intervene aggressively enough, you might be able to catch it. If you take it from the condition perspective, if you could say we enrolled x amount of head and neck, pancreatic and GI cancers, and found out their nutrition supplementation training protocol was effective at delaying the progression of cachexia, that may offer support for a variety of cancers rather than saying, we're going to look at cachexia in pancreatic dem, we're going to look at in head and neck, because the condition is bananas. And if you look at a lot of the criteria for it, it is continuously evolving and it's basically a muscle wasting condition with or without fat loss that kind of gets progressively worse.

I make the analogy to diabetics and we'll get to a point where just like the cell debt, diabetes isn't reversible. It gets to a point where cachexia is so progressive that the muscle wasting isn't reversible. And I mean, I've seen it and it is insane how quickly that drop off

happens. So the broad definitions are kind of around greater or less than five pounds of muscle loss or 5% of body weight loss in about six months. So if you've less than 5% of body weight loss, your pre-cachectic. Over 5% body weight loss, with or without some water conditions, you're in the cachectic stage. And then as it progresses, you're in this, what they call, refractory cachexia stage, whereby time to mortality is as low as three months.

So it is insane to watch how people can literally be walking around look high function, for all intents and purposes look normal, and then just tank. And muscle loss goes through the roof. They're losing three to five kg a week and there's nothing you can do. You're just watching it, which screams to the importance of not just interventions but appropriate screening. So I would hazard a guess and say that depending on the type of oncologist and the cancer type they're working with, they may or may not be as in tune with how dangerous this can be, and busy clinics are a nightmare to deal with anyway. So I don't know how often people are screening for this. In addition to 5% body weight can go in six months is a fairly broad criteria, so it may go missed if people aren't thinking about it. And then the imaging that's required to identify the body composition itself. The gold standard are CT scans, but who has the time, money and resources to get regular CT scans.

So there's a lot of issues with the screening, but the standard response to cachexia or at the end of that sentence where the definition of cachexia is muscle wasting with fat loss that can't be ameliorated without traditional nutritional guidance. The traditional nutrition guidance is, sorry dude, eat more. And if you look at that, it's not just an imbalance in energy, it's not just a progressive muscle wasting. There's a lot of things that go into the energy requirements of the tumor. Malabsorption depends on the tumor site. Head and neck cancer, they can literally have

parts of their throat, and head and neck removed, so they can't eat, radiation to their throat where they can't digest foods. It's too sore to where you're looking at people taking two or three hours to get a bowl of oatmeal or a smoothie down. And then you've got a lot of inflammatory side of clients that either directly or indirectly impact all this.

So if you look at all the mechanisms that are involved, it's not enough to say eat more. I think we need this kind of -- and there's a couple of trials that are ongoing right now. One of them is called the MENAC trial that's looking at exercise, nutrition and antiinflammatories to try and just charter kitchen sink at it, which is a different approach where purist researchers might look at that and say, you have to look at efficacy of one first and then look at the additional, whether it's synergy or additive effects, whereas I think it's such an aggressive condition. It's worth going to kitchen sink approach and working backwards.

DANNY LENNON: Right in that any one of them alone may not be enough to see a big enough of effect.

CIARAN FAIRMAN: Yeah, and I'd almost has it I guests in -- we're working with some great dieticians at the minute but identifying these patient populations that are at higher risk. And if you know, going into treatment that they're going to experience this dramatic weight loss, is it worth putting them in a caloric surplus and maybe an aggressive caloric surplus for the days and weeks leading up to that to do anything to, head and neck cancer, 20 kg in six to eight weeks, you know, it's bananas, and then what their recovery looks like and how difficult it is. Most of the time one of the hardest things is to put on and we write these papers as if it's just a natural consequence of what we're going to do with. It's a very difficult thing to do.

In addition to the likes of head and neck and breast will have a lot of impairments that

preclude them from being able to get sufficient types and volume of training in that will allow them to put on muscle mass. So there's a lot of things that we're trying to tease out and really what the most appropriate way is to tackle this, but in terms of the translational impact, I would urge people to look at the types of cancer that are highest risk for this, and have strong conversations with the individuals and their caregivers and professionals and asking them what's going on and is there actually a conversation around the risk of this.

DANNY LENNON: Yeah. One of the things that just as you were talking about it reminded me of that. I know you've said to me before of when we're thinking about, oh, well it's obvious that exercise and specifically some degree of resistance training, it would make sense that that could help at least mitigate losses in lean body mass at least because that we know that happens in healthy people and so on, and we know how that impacts hypertrophy for example. But all of that is with the big presumption that it's prescribed where you're putting enough of a stress on the muscle that it's causing an adaptation. Whereas, I think one of the big things you've been talking about is specifically in the field of exercise oncology of making sure are we getting an appropriate intensity in dose and workload. That's going to at least cause an adaptation to see if we're even measuring the right thing because even if someone exercising but it seems it works or not, but it might not be enough of a stimulus.

CIARAN FAIRMAN: Yeah, it's huge. And I think that's a lot of what drew me to the field initially, and as I was looking forward and my career. Look, if I go for strength and conditioning, I'm a tiny fish and a massive pond and I don't know if I would have the intelligence in that specific area to have an impact the way I wanted to, whereas when I was looking at the field of exercise ecology, there some glaring gaps, specifically because are related to the exercise prescription that. I think I was young, naive and probably arrogant

and pointing fingers and saying, this is wrong, this is wrong, and now I've kind of moved into a space where I'm running these kinds of larger trials that are multisite, I've become more forgiven. So I understand why these exercise interventions are where they are, but I refuse to accept that's the only way you can be.

So basically to sum up the field of exercise oncology, it's leg press, leg extension, leg curl, shoulder press, seated roll and chest press. You might have some modifications here or there, but the majority of the work started with people who are trained in behavior change. So that was kind of gentle physical activity. Then it moved to a lot of aerobic work, and only in the last, I don't know, 15 or so years have we actually moved to resistance training. And to be fair ECU is to my mind one of the best to do it because they've got Rob Newton who was a trained sports scientist who brought a lot of the principles of sports science to our field. But beyond that, a lot of it is done in hospitals where the equipment isn't great. You're running multisite trials where you've got anywhere from 5 to 15 clinics that you have to manage where there's different equipment, different expertise, different logistical challenges, different people and the politics you've got to navigate.

My primary -- and that's all to me has become a big challenge for me in navigating some of these trials and actually understanding how difficult it is. But at the same time, my biggest gripe is that we don't even try. We kind of just accept that. I've talked about this a lot, but even in the same cancer type and you've got the same treatment core. So I work a lot of prostate cancer. So men on prostate cancer with androgen deprivation therapy, it castrates them, dilutes all testosterone. That comes with dramatic losses in muscle mass, profound increases in fat mass, bone mineral density, physical function to works. So inherently an automatically too, okay, resistance training. Even in that population, whether on ADT, you

can have someone who was 45 and a former athlete and super fit and you can have someone who's 89, never active, 150 kg and has a lot of orthopedic limitations.

My gripe with our field and what we need to do better is that to try and standardize our protocol. We water it down to what the lowest functioning a person could do. And it's phenomenal to see improvements in those lower functioning people. The problem is that all the higher functioning people end up being underdosed. So if you give people the same type of protocol, there is large heterogeneity in the response. So what I've been really trying to do is actually push the field forward and making sure that we're selecting appropriate exercises, make sure that we're actually sticking to principles of progressive overload and pushing them, and you'd be surprised at how uncomfortable it is.

Look, there's a lot of things you have to work in a space, understand about the pharmacology of treatment and how that relates to recovery. For example, chemotherapy is given, again accommodated standardization, the chemo is given a variety of different ways, but breast cancer is a pretty easy example where the majority of times, and it's always evolving, people will be given a standard course or a standard cycle of treatment, which basically means they'll have an infusion on day one, they'll have three weeks of recovery, then another infusion, and they'll repeat that for about six cycles, and that's your full course of chemo. So six cycles of that you're looking at six months, and generally, people will be given corticosteroids right before they're getting a chemo fusion, which does a pretty good job of buffering the side effects for about two days. So they feel, okay, corticosteroids wear it off and then they're just wrecked and they're spending the next days and weeks recovering, they get back to a point where they're okay, hit them again with chemo.

So there's a real air fluctuation in fatigue, energy, sleep, nausea, where that relates to their propensity to train, which requires us to develop some sort of autoregulation model to match their propensity to train. But also the acute side effects will compound over time. So you will have similar side effects in the sixth cycle than you were in a fourth cycle, but because you're getting chemo every so often, the sixth cycle will feel a lot worse, so all the more profound side effects where it may take longer to recover. So coming back to clinical outcomes, a lot of what we're working on now is actually mitigating dose reductions in chemo. So depending on the fitness level, they could prescribe x amount of chemotherapy, whether it's relative to body weight or whatever the standard is, and that could be too toxic to where when they come back for the second a dose of chemo, they're not, well, they're not recovered enough so they have to delay chemo or they've given a lower dose.

So we're actually trying to work in, if we can keep them fitter, will that help smooth that process out, will they get a higher relative dose of chemo, so the treatment is more efficacious, they're getting a higher tolerance, they're bouncing back quicker. That will kind of maybe smooth out those fluctuations, but it's a really challenging area. Going back to the original point is that if you understand that if you understand the fluctuations in fatigue and energy and acute side effects that come with chemotherapy, you can match the exercise program to that to where when they have the good days, you can really push them and it's perfectly okay for someone to sweat during chemotherapy. It's perfectly okay to have them to work out hard. There's quite a bit of data now coming out specifically with aerobic exercise with high intensity interval training. Safe, efficacious, the standard things apply like you're working on high intensity, making sure you're warmed up right, or there's risks of musculoskeletal issues. But beyond that there's nothing that the cancer diagnosis or the

treatment from a physiological perspective that will prevent you pushing these people. So that's pretty much Kell Bell that I'm walking down the streets banging.

DANNY LENNON: Right. Which is still pretty counterintuitive to a lot of people, and you probably see that also in presumably like cardiovascular disease too, and recovery from that type of thing.

CIARAN FAIRMAN: Yeah. One of the bigger ones is lung cancer. So there's kind of this disability cycle in lung cancer depending on the type and how advanced it is and the surgery they get, there's a lot of breathlessness. So that breathlessness, the feeling of being out of breath, have an air hunger, having discomfort with breathing causes them to avoid a certain intensity of exercise. Because they avoid a certain intensity of exercise, they become deconditioned, and the threshold at which they become a breathless is at a lower intensity, and that kind of cycle keeps continuing. So this whole thing is, is it safe for someone like that to exercise. I would ask the question, is it safe for them to not exercise.

DANNY LENNON: Right. It's basically raising that threshold for what it takes to get our breath. The same way is a person who never moves, walking up some stairs, gets him out of breath, but if you're a marathon runner, it takes a lot to do it. It’s kind of same thing here.

CIARAN FAIRMAN: Yeah, and I mean, to be fair, if you're someone would with lung cancer and you're getting a lobectomy and you're getting perished or half a lung removed, you're absolutely going to see some physical decline. But what we're saying is the exact same thing. It's such an important point to intervene because if you allowed a physical decline, you're in an impaired state, you've had your capacity. If you continue to decline, it's already hard enough to make improvements with a full functioning system. It's even harder when you have half a function system. So one of the areas of research I'm

really interested in is, again drawing sports science principles. We're actually looking at a study now to compare traditional sets versus cluster sets and using dyspnea as a marker of exercise response in advanced lung cancer. So I think it's going to be a really interesting study that's going to tell us a lot about how we can potentially modify the exercise, because I think, again, what happens is people will match the exercise intensity to the preferences rather than say muscular fatigue.

So if you're out of breath at a set of ten for 40 kilos, but you could -- your muscles could move 80 kilos, we dropping it to where you can do consistent 10 reps because that's what your breathlessness will allow. I hypothesize at least that if we can interject closer sets and we haven't figured out the configuration yet, but for example you do two sets, two reps, take 20 to 30 seconds, do two reps take 20 to 30 seconds, can that alleviate those acute feelings of dyspnea and breathlessness to where you can perform more quality, better quality reps, more volume, whatever.

DANNY LENNON: somethings that's more in line with the actual strength and endurance of the muscles as opposed to the limiting factor being your breathlessness.

CIARAN FAIRMAN: Yeah.

DANNY LENNON: Pretty cool.

CIARAN FAIRMAN: Yeah, isn't it?

DANNY LENNON: Yeah, that's pretty cool.

CIARAN FAIRMAN: Yeah. To be fair, again, it stemmed from listening to and reading a lot at the likes of Greg Hoff who is huge in in developing that or bringing that cluster set literature to the forward and kind of looking at the whole premise of it initially was to maintain power and quality of reputations in weightlifting and things like that. So the same premise applies.

It's just a different type of quality we're worried about and different outcome we're worried about. And I think if we can -- and this is another thing where I am caught -- this is something that's safe enough to where it's worth trying to clinics. You know what I mean? I don't think it's something that we have to wait for this study to say, you know what, they spent a year and they figured out and it's good. I think it's about all those practitioners thinking creativity like that to where I don't anticipate there being any adverse events using cluster sets beyond you would have a traditional set. So it's worth having a goal and checking out and seeing if your clients respond to it.

DANNY LENNON: Yeah. I think that's an empowering place to be regardless of anything else. If you know that, even in lieu of getting any more research. You're in a place where at the very worst there might not be certain benefits that you'd hoped there to be, right, but you can still prescribe and see how it goes. I know I kind of jumped around a lot of the questions, so maybe if I kind of circle back and I guess to summarize a few things within this field for people to take away. First, and again, this is going to be a super broad question so you'll have to do your best with it, but it just seems with so much going on and the kind of punchline being that the fact that there's a field called exercise oncology, in and of itself tells us that to some degree exercise is probably a good idea in a lot of cases. But when we're talking about exercise being good for people that are undergoing cancer treatment or after they've finished cancer treatment and the recovering, how would you kind of summarize the different distinct areas where there could be a benefit? Because we've kind of touched on it, right. There's these things specific to the type of treatment they're going on. There may be benefits to those things outside of that in terms of their quality of life. There's other benefits that we may have not got to, because one thing I don’t think I asked kind of relates more to some psychological things like wellbeing and

because in a general sense of exercise for the general population. We have lots of stuff to show that has benefits psychologically.

And now if we're in a case where someone either has, let's say, received a cancer diagnosis and either the treatment has made them less active than they used to be, or maybe they are worried about training in that they've stopped or just not as active or maybe they've never been active. Presumably you could make a pretty strong case that just the inclusion of some training program is going to improve our psychological wellbeing that may then have other knock on effects. But even in and of itself it's probably not going to be a bad thing.

CIARAN FAIRMAN: Yeah, definitely. And and it's really interesting to look at the ins and outs of that in I suppose perhaps the mechanisms but also descending. So if you're -- the majority of, and I suppose all behavior change like that, that peer led group support session where you've got five to 10 people with a similar diagnosis working out together. It can be highlighted or it doesn't even have to be highlighted, but conversations arise of the shared challenges that they're having. We're going through different aspects of their treatment, their relationships with their spouse, everything else, that in itself, the cohesion, leads to improvements in quality of life. Not to mention, again, you've got people who are poor function, somehow throughout treatment come out the other end, higher function, that leads to improvements to quality of life. And then at the other end, an area I'm really interested in is athletes who get diagnosed.

If you talk about the psychological impact of losing your identity as an athlete, with people having to give up parts of their career, they have to retire because of this or they're getting told from physicians, family members, whoever to rest. If we can find a way to give them an ability to exercise or workout or train at the capacity they used to, maintaining that identity

as an athlete, is massive. So it's really interesting to look at again just the spectrum of how this can impact different people different ways.

DANNY LENNON: Yeah, sure. So where are the kind of next areas that you think is the research is either going to go or you'd like to see it go or maybe that's a couple of types of questions that are the next things to kind of work out?

CIARAN FAIRMAN: I think, and I hope this goes out to a broader audience than I have. I think we're past looking at a 12-week intervention in breast cancer survivors and quality of life. If I see one more of them at a conference, I am going to pull my hair. We figured it out 12-weeks of exercise improves quality of life in survivors. I think one of the important areas is the tumor physiology area, and specifically whether it's acute changes in perfusion, whether it's chronic adaptations in tumor physiology, or is it chronic adaptations in physiology that impact in the subsequent acute response. So there's a lot of areas in that. The other area is, again, as I said, the implementation science, and actually while all this sort of stuff is going on, can we get this to practice, because I'm at ECU and we have 15 years of research behind us and we've got six clinics.

So when I email an oncologist they say, yeah, I know ECU, I know the research, yeah absolutely, we'll get on board, but wherever I go to my next position, if there's no exercise ecology based there, it's going to be really difficult for me to set up my line of research. So that implementation science is so huge, not just for community programs but to drive research. And then I think an area I'm really passionate about is the combination of exercise, nutrition and supplementation research. I think too often we're working in our silos and looking at what resistance training can do and what supplementation can do, and I think there's a real need to look at combination strategies to target specific clinically relevant outcomes.

DANNY LENNON: It's just fascinating, because the more you kind of see these different moving parts, it's like almost the classic thing of medicine, like this kind of black box that we know these inputs and we've kind of already seen these benefits out the far end. It's now all the stuff in the middle. You need to work out like the mechanistic stuff and what is the appropriate dosing, what's the best way to put that into practice and all the messy things in the middle.

CIARAN FAIRMAN: Yeah. And a lot of it translates to more broad applications as well. You'll have academic arguments about is it worth figuring out that those, because we can't get people active and things like that, whereas I just think there's a why not to do them concurrently. Let people work on behavior change and do the appropriate work to get people active and keep them active. Let us do our work looking at different doses and types of exercise and supplementation strategies to optimize specific outcomes. And maybe the combination of the two is a watered down version of each. There's always going to be in terms of optimal, and when you're talking about what's optimal, well what's optimal for adherence is probably different than what's optimal for actually targeting specific outcome.

If I push you to put on the most amount of muscle mass you can, you probably aren't going to like me and aren't going to do that independently, especially if you're a 78-year-old man with prostate cancer and all that sort of things. So we also have to look at -- I go back and forth, like in the behavior change world, is it worth maybe spending the time in doing what we do to optimize a specific outcome and then while you're doing that, incorporate behavior change strategies and then figure out some sort of maintenance strategy to where it's not as aggressive. It's something where we can maybe lose the -- arbitrarily you gain 80 kilos in lower body strength, you gain a couple of kilos in lean body mass. If you lose 20 kg of

strength and half a kilo of muscle mass, if you're still doing a year from now, I think that's much more important than gaining 100 kg and losing it all, because you're not active anymore.

DANNY LENNON: Right. And that's probably something that you'd have a hard time people disagreeing with that it's almost those continued behaviors that matter more when it comes to physical activity than the outcomes, even in general populations, right, because the divergence and type of activity people do and all those types of stuff are so different, but you still see that it's just the behavior of being more physically active matters in a lot of cases.

DANNY LENNON: One of the things that I'd like to at least reinforce is that I've found a steel fear and both from a condition perspective but also from a practitioner, whether it's personal trainers or exercise physiologist, when you hear the word cancer and you hear, particularly if it's active treatment, there's a fear of touching these people and what they can do and what they can't do. And there are some phenomenal guidelines. The American College of Sports Medicine has guidelines that released in 2011. They're updating those and publishing them this year, so that'll be out this year. Exercise Sports Science Australia just released some guidelines as well to give some phenomenal in-depth practical takeaways of, for example, someone has a port to administer chemo. How do you modify exercise to make it safe?

We have guys in our clinic who are doing heavy dead lifting, who are doing heavy leg pressing, who are doing movements that are outside the norm for this population. And they love it. They love it, so much so that other people in the clinic are saying, why can't I do that. I think if we have people coming to our clinics and we're just sticking them and shoving them in a leg extension machine, having them do a three says of ten, you wouldn't do it. You'd be bored out of your mind. So we have to be able to treat these like normal people, push them within

reason, with all the safety constraints around that book, but let them enjoy their training and treat them like normal people. There's nothing about this diagnosis or the treatment they're going through that would justify within reason, you watering down the program.

DANNY LENNON: Right. Yeah, we've quite a lot of fitness professionals obviously listening to this particular podcast. So I think that messaging for them is particularly important that you can help people, because quite rightly, I think the type of audience we have are very familiar with things of like scope of practice, being wary not to be going outside that and may be sometimes can worry that, oh, this is something that is obviously beyond what -- I'm not having no expertise in cancer, so maybe I shouldn't be working with this person. But as you said, there's some things that you can do without fear of actually doing any harm, and it's more a case of you can do that without, I suppose, making any claims about what I think is the big thing, right. You can still work with this person and still train them the way you try and train someone else within the kind of caveats of what they can actually do without overstepping and claiming that you're doing anything outside of that, right.

DANNY LENNON: Yeah, that's exactly it, yeah. The message gets messy. There's absolutely and considerations of how you have to modify exercise, but people need to understand that modification does not mean limitation and we'll have to tailor their exercise program around their treatment and around their comorbidities, and whatever's going on, but we can absolutely give them a program that's going to lead to some degree of improvement in whatever area they're interested in. We just have to make the case that our job in terms of screening and working with these people is not to create more barriers for them. Our Job is to understand the side effects of treatment to where we can enable them and empower them to exercise rather than limit them.

DANNY LENNON: Yeah. And for those of you that are in a position like that working in the fitness industry and you want more information like this I will link to all of Ciaran's stuff in the show notes as well as anything else that you tell me ends up being a relevant link that they might, or a resource that they might want to follow. So I'll include that for you people. So kind of with that, that brings me to the question of for people who do want to get in contact with you, follow you on social media, look at more of your stuff. Where are some of the places they should go on the Internet?

CIARAN FAIRMAN: Yeah. So I'm mostly active on Twitter @ciaranfairman, and that's where, to be honest, there's a good group of us that have a lot of really cool conversation about different patient cases and where the research is going. I'll have my own podcasts called Reach, Research and Exercise in Cancer Health. That is on reachbeyondcancer.com. And then I'm on Instagram as well, @ciaranfiarman where I'm trying to share some of that.

DANNY LENNON: Great. And as I just said, all of that will be linked up and I'll add some other resources that Ciaran deems places you should go and check out. So we'll come to the final question. You've probably had the luxury of having this before, but yeah, you can have it again, because I'm sure in that time you change your mind or at least I changed my mind on this question every day. So if you could advise people to do one thing each day that would be positive for any area of their life, what would that one thing be?

CIARAN FAIRMAN: Oh, really put me under pressure to be profound. It's like 300 episodes later, okay, tell me something that no one else has said.

DANNY LENNON: How about go for something that's the least profound maybe then?

CIARAN FAIRMAN: I would say, be present, be present. I had a phenomenal conversation a few weeks ago where one of my line managers who was literally saying, look, you need time to think. In your role, I need you to just chill for an hour or so and just think about areas of our research and where the field is going on, and it's been huge for me. I think we get caught so much in like living this busy lifestyle and I'm bored just on the call, and we're on our phones and all that stuff and you just need time to chill out and let your brain think and bring that creativity back. And I think for me it's been huge and actually allowing my mind to wander and think about different areas both professionally and personally.

DANNY LENNON: Yeah, it's interesting because I think the fear people have is of doing nothing, but the ironic thing is that's literally impossible. Like if you try not to do anything, your brain is going to do something for you, and then then actually a lot of good stuff happens, right?

CIARAN FAIRMAN: You do look like a weirdo, which is so strange. Luckily, I live just around the corner from the beach. If I go down and sit on the beach and just sit and look, it's uncomfortable.

DANNY LENNON: There's that creepy guys, watching us again, staring into the space. Yeah, well, I'm not worried about looking weird. I was in the airport the other night, wearing my light orange, blue blocking glasses and people were like, why is this guy wearing sunglasses. It's like a midnight flight. Yeah, so I know what looking weird looks like.

Man, thank you so much for conversation and it's been awesome to see all the work you're doing. It's so fascinating to me. So thank you for talking to me about it.

CIARAN FAIRMAN: I appreciate it.

Find me on Instagram: @dannylennon_sigma