pmpc046

Kendal Williams, MD (Host): Welcome, everyone, to the Penn Primary Care Podcast. I'm your host, Dr. Kendal Williams. I'm very excited about today's podcast, and we've been working pretty hard to try to get it set up for a while, because we're going to talk about exercise. We're going to talk about exercise and the heart with noted experts here at Penn. And I'm excited about this for a few reasons. First, I'm worried about my own cardiovascular health and I want to know how much I should be exercising and how to interpret everything that's being told to me about how much I should be exercising and then my patients are asking me the same questions.

Those who are not yet having cardiovascular problems and want to prevent them. And then we also have this whole group of folks who have established cardiovascular disease and need some guidance on how much to exercise and how to exercise. So in order to address all those questions, I brought on an expert at Penn, Dr. Neel Chokshi. Dr. Chokshi is an Associate Professor of Cardiology here at Penn. He is the Medical Director of the Sports Cardiology and Fitness Program and the Director for the Center for Digital Cardiology. Neel, thanks for coming.

Neel Chokshi, MD, MBA: Thanks for having me, Kendal.

Host: I've also brought back a great friend of the program, Dr. Dan Soffer. Dr. Soffer is now the President of the National Lipid Association. He is an Internist at Penn and a Preventive Cardiologist, someone I refer to, patients to very frequently. Dan, thanks for coming again.

Daniel Soffer, MD: Thanks for having me on again, Kendal. Always fun to be here.

Host: The other reason I brought Dan on for this one is also because we are making a major change to how lipids are calculated at Penn and how they're being presented to physicians. So we're going to talk about that a little bit at the end. So stay tuned and if you're interested in that and you want to fast forward to the end to hear that, that would be fine.

But I encourage you to stay and listen to the rest of this. So let's talk about exercise. So, I have all kinds of questions Neel. Let's just start with the basic question. When a human being starts to exercise, what happens to their body, basically?

Neel Chokshi, MD, MBA: I mean, that's a pretty broad question, Kendal. And I guess I probably would bucket it into two paths. One is there's physiologic changes that help with performance, that enhance performance. And there's a series of things that happen and we can talk a little bit about that. And then the other is probably what more commonly we people think of when you talk about, do I get enough exercise, which is it kind of reverses a lot of the more pathological changes, and gives you some of the preventive benefits that we talk about when you go to see your physician or, or you're thinking about longevity. And a lot of these are cardiovascular in nature, but a lot of them are musculoskeletal in nature, probably at the cellular level as well, that sort of then contribute to longevity in general.

Host: You know, it is interesting that it does appear that exercises reduces cancer mortality as well, at least preventatively it seems to have an impact there as well.

Neel Chokshi, MD, MBA: So exercise probably has many benefits across cardiovascular disease, musculoskeletal disease, and even cancer. We've, we think that probably, you know, it has something to do with a lot of these oxygen radicals or at the cellular level, a lot of toxicity that occurs that then sort of these natural mechanisms to repair the body itself. It's a little theoretical but there are some pathways that have been linked to it. So I think, it makes sense that some critical amount of exercise is valuable for everything.

Host: So, if a person, let's say a person like me, begins a regular exercise program I know that their blood pressure can reduce, I read today, you know, on average maybe three to five points just as a result of that exercise itself, that exercise regimen.

I know their resting heart rate will reduce. And I always thought of that as their body is just becoming more efficient at utilizing the oxygen it's receiving, and for that reason, the heart doesn't need to work as hard. Is there more to it than that, Neel?

Neel Chokshi, MD, MBA: So with exercise, with each heartbeat, your stroke volume would increase. And so you don't need as many heartbeats to pump the same amount of blood. So that is one example of the gained eficiency. You also, at the cellular level, when that blood gets to the muscle that you're using, you see the mitochondria become more efficient. The gas exchange crossing from the blood into the muscle becomes more efficient. Your vascular health, so the actual plumbing that takes the blood from your heart, that becomes more efficient.

And that, you know, as we see with lower blood pressures, the energy use as we can also see, so all of these little gains that you make, improve your overall efficiency and in your metabolism and that kind of contributes to sort of, all the general just feeling better, and being able to do more.

Host: And we know, Neel, that more exercise is associated with a longer life, a more fulfilling life, a higher quality of life. We know that its reduction has effects to reduce anxiety and depression, and so it has a plentitude of benefits. Now, there's a whole sort of industry out there, if you will, now, about training.

You know, it used to be somewhat limited with endurance athletes that would really be measuring themselves but now with Apple watches and other devices, other wearable devices, people are getting a lot more data about their bodies. And I want to deconstruct that exercise lingo a little bit. And then I want to transition into what a realistic exercise prescription is for patients. But, oftentimes when you read about this stuff, they start talking to you about zones and VO2 max and so forth. So let's just start with VO2 max, which I think is the thing that is out there quite a bit. What does that mean?

Neel Chokshi, MD, MBA: Yeah, sure. So, to be very basic about it, people would ask or say that I'm in very good shape or you're in very good shape. And so therefore I don't have to worry about about my heart health or how long I'm going to live. So what does that mean? And that is basically what the peak VO2 addresses.

So it's the gold standard for the measure of someone's cardiorespiratory fitness. And essentially, oxygen is the primary fuel for energy in the body. And so we can measure how much fuel or oxygen or capacity you have to burn this fuel. And we can get a sense, it correlates very nicely with basically your overall fitness level.

And then this has been studied across many, many different diseases, including cardiovascular health. And we found time and time again, that this correlates, the ability or your peak oxygen consumption ability correlates with cardiovascular health, longevity and so on and so forth. It's been studied in cancer um, and in terms of outcomes.

So that is essentially, what peak VO2 is. How do we measure that? So there are lots of ways to measure it, and like there's you know, these devices have come up with ways to sort of maybe estimate it, but the gold standard, or the true way to do this, is a cardiopulmonary exercise test.

So that's, you've seen these commercials on TV you know, these fruit drinks or these energy drinks that you see the individuals running on the treadmill, they're wearing a mask. And this is a mask that's actually measuring how much oxygen they're consuming and how much carbon dioxide they're producing while they're exercising.

Host: So, my Apple Watch here tells me my VO2max, and frankly, it's a little disappointing, and I don't think it's quite accurate. How accurate are these on these wearable devices that we have?

Neel Chokshi, MD, MBA: Yeah, that's a good question. You know, we're actually talking about doing a study on this. I have a couple of trainees, but it's not really clear. I haven't looked as of late, if anybody's actually verified or validated these things. But the general idea is that these are proprietary algorithms. Apple actually has a patent out on this. You can look it up, but, what they're doing is they're using the accelerometer data in the watch, and then they're using the heart rate data on the watch. And they're essentially making some assumptions, but they can see that, based on the accelerometer, how hard you're working, and then what is your heart rate response to that work.

And then it, and it, has a formula that will calculate your peak VO2. So you can imagine that there's a lot of assumptions that they make. Like for example, if you're on a beta blocker it might overestimate, they probably are pretty sophisticated, but that's the idea. But the true, the really, the true way to, to get your peak VO2 is you'd come in, we'd put you on a graded exercise protocol, and we'd measure you know, how your consumption increases and then we try to max you out.

So we, try to fatigue you to a point where you cannot go any further and we can actually see the trend in the VO2 and then based on that, those patterns that we see, those technical patterns and how your oxygen consumption increases and how your carbon dioxide production also increases; we can sort of make some assumptions about sort of where you are broadly into your aerobic metabolism or versus your anaerobic metabolism.

Host: So I suppose more realistically for folks and it may evolve with the VO2 max measurements on the Apple watches and so forth, what most people can use to judge the quality of their exercise is probably just simply their heart rate, right? And there are calculations out there, you know, max heart rate you know, 220 minus your age, and then you want to hit, say at least 50 percent of that for, I think, moderate exercise, up to 70%, and then if you're over 70, you're considered a little higher intensity, and so forth. These sort of zones that they

talk about for heart rate. So sort of measure where you're at and whether or not you're exercising intensely enough.

Neel Chokshi, MD, MBA: Yeah. So, Ithink what we're getting at is how do you self assess the intensity of your exercise? That's basically what we want to do. And there's, the gold standard way is through testing. But heart rate has historically become a surrogate for that. So the idea is, is that at your peak heart rate, your maximal achievable heart rate; you are essentially performing at your peak VO2, or you're at maximal oxygen capacity. And the story behind how to calculate that is you're right, we use 220 minus age. That is not scientific by any way, it was just an empiric number that was created and then over the years and decades, it's been validated. It works.

It falls apart at the edges. So, very young patients that they'll frequently get well above 200 and we get lots of consults for that. My heart rate goes to like 210, should I be worried? And same thing at very older ages sort of super fit people that sort of falls apart. But we can use that to basically correlate to the idea is that it, the heart rates track along with where you are on that curve of how much anaerobic versus aerobic metabolism you are at different work rates.

And so that's where those training zones that people often talk about come about. So the heart rate is the easiest to talk about. It's, now with technology, we can utilize them. And for most folks, they work really well. And so we can get into a little bit more about where do you want to be or how should you, what's the formula or what should your approach be.

The other way though, is you want it all to kind of correlate really well. So the other big bucket is your just rate of perceived exertion, what we call RPE. It's a scale of one to 10 or one to 20, but just how hard are you working. So when you're working on a scale of one to 10 with 10 is max exertion, a five to seven should correlate to about moderate intensity activity, or maybe 50 to 70 percent of your maximally predicted heart rate.

Or put another way, I tell people that if you're exercising at this and someone tries to talk to you, you're going to be a little winded when you're trying to talk to them. And there are different strategies to meet that. And you can get super precise, but in clinic, you might, depending on the person, like you said, Kendal, you have different patients.

You have the super quantified self person that likes the reels of data that we all get and then there's the other person that just like doesn't have access to the

technology and there's different ways to do that so you could write an exercise prescription based on any one of those strategies.

Host: So the World Health Organization has said that we should all be getting 150 minutes of moderate intensity exercise a week, which as I understand it, Neel, just putting it in those terms of, having that you can have a conversation, but it's difficult. And then you know, 150 minutes, is I always tell my patients, it's five sessions of 30 minutes each during the week.

But there appears to be mortality improvement up to 300 minutes. And then beyond that, there are you know, some sort of, if you look into the details of that, ideally 75 minutes of that should be a little bit more high intensity, right, into the higher heart rate zones and even adding some strength training in twice a week.

Can we kind of just go over what those World Health Organization guidance are and how do they tie to the heart rate data that our Apple watches are telling us?

Neel Chokshi, MD, MBA: Yeah, it might be helpful for a lot of clinicians to understand where this came from. So basically there's a pretty well known meta analysis that looked at all exercise studies and there are a bunch of different types of interventions, different durations, moderate intensities.

And so they just plotted them, you know, on a curve, they created this curve and they figured out, basically, that there's essentially the more exercise you do, the better, the outcomes are better. So there was, there's officially, there's no limit. I mean, we're going to get to this idea of extremes, but for the majority of people, more is better.

And if you look at the curves, there's maybe sort of like an inflection, like around 150 minutes of those studies where they were doing moderate intensity that maybe that, that's okay. There's a slight diminishing return there. So they just drew this line at 150 minutes and they said, and this also seemed like kind of feasible for people like, you said, I do the same thing in clinic telling people 30 minutes a day, just go walking is, is kind of like a manageable thing of course they freak out when they think you're going to tell them 150 minutes per day.

I don't know if you've had that experience, but um, yeah, so that's basically where it comes to, and then the other idea is so. All activity is beneficial, so, that's the other piece of it. All walking, it's incremental, but probably like the idea, if you truly want it to count, then making them get to this like sort of

critical threshold of intensity, this moderate intensity, which is what's been studied and done in different ways is probably really very important. And so like, we said, you know, how you can assess that. I, for the simple folk that are just going for walks, I tell them, start basic, go for a walk. Go long as you can for 30 minutes. If it's too easy, then pick up the pace, walk at a pace where like, you're going to get a little short of breath if someone starts talking to you or if you're talking on the cell phone.

Some folks are like, that's a little too abstract. I said, okay, do you have, they have an Apple watch and then we'll do some basic math. Either I'll put them. I'll do a VO2 or I'll do a treadmill test and I'll actually give them heart rate zones, but more often than not, we could just use the formula 220 minus age and I'll ask them to do the test.

When you're in this heart rate zone walking, how do you feel? Is this like too hard? Is this too, too light? Most times you're in that five to seven range. So that's like the bulk of people. And then it only, and then the data also goes along with that. It makes more, it makes sense. Like if you're working harder and you're doing more high intensity stuff, you don't need as much exercise and more activity.

And there's probably, Kendal, we can talk about that. There's some interesting studies that have been done around things like the seven minute workout where, because time is a big factor. People just might say, I don't have time to do this. Well, you can get similar gains to working out 150 minutes in a much shorter period of time as it relates to your peak VO2.

Host: That's interesting because you get into this high intensity interval training stuff and you know, this idea of doing shorter workouts that are higher intensity and getting benefit from that, which is actually good because it really can push your VO2 max because you have to sort of squeeze it in, as opposed to a long five mile walk, you're doing 30 minutes of a really more aggressive sprint type activity. And those are somewhat equivalent? Is that what you're saying, Neel?

Neel Chokshi, MD, MBA: Yeah, yeah, so probably the study that worth referencing is they looked at people that were essentially jogging three times a week for 45 minutes at a time. And for over a duration of six weeks. And then they had, they randomized folks to this other arm, which was seven minute, high intensity interval workout.

And you can find this workout. It's been anywhere. The New York times has covered it. It's basically like calisthenics. It's, 30 seconds on, 15 seconds off.

You can get through the whole workout in seven minutes. And they, at the end of six weeks, they saw similar gains in people's peak VO2s. They had them do the test before, the peak VO2 test before and at the end, and they showed very comparable gains.

And so now, I don't know, Kendal, if you've probably seen the, there's this, these concepts of these micro workouts, like, as short as like three minutes a day or even shorter than that, that have shown gains. And there's probably something to that. It's, this idea of, you know, when I was in residency, one of my preceptors told me, use it or lose it.

So if you don't practice it, you'll lose that functionality. And I think just goes towards that. So there's lots of creative strategies, and I use that to figure out what makes the individual tick or what's enjoyable, what's feasible, and then tailor their regimen to that, especially if it's just for longevity and for general health.

Host: Neel, do you make a distinction between aerobic activity, you know, walking, running, cycling, swimming, and weightlifting you know, sort of strengthening?

Neel Chokshi, MD, MBA: I do, I mean, it's a spectrum and cause there's a little bit of both and depending on what the activity is, but there's probably differing benefits and officially, you both may know this, the recommendation is not only the 150 minutes of moderate intensity, but it is also at least two to three days depending on what guideline you look at and probably around 20 minutes of resistance training per session per week.

And that's purely resistance training. And I think that's beneficial probably even for longevity and as we have an aging population, probably maybe more important than aerobic training. I don't know if you guys have thoughts on that, and for diabetes and uh, metabolism and just general wellness, I think, you know, and I personally have built that into my regimen as well.

Host: You know, it's interesting when I got this Apple Watch, which I got for another purpose, but I got it and then I wanted to test it out and see what, so, you know, I, I would run, you know, mostly with my dog and he would stop and then we'd only do three or four miles. But, I'd run and then I would cycle and I would cycle into Radnor, which is about seven and a half miles.

And then I would weight lift. And I didn't do these all in the same day. I was just sort of testing out these workouts. And, you know, when I weight lift, it was

machine to machine to machine, you know, with little rest, you know, so I try to make it as aerobic as possible, just. You know, you do your bench, and then you do your lats, and then you go back and do your bench, and your lats, and so forth, so you're not just standing around.

And I found that the weightlifting actually, done that way, was very similar to the other two. The cycling was actually the highest heart rate on average. But the running and the weightlifting were about the same. That was just an observation I had.

Neel Chokshi, MD, MBA: Yeah. If you structure it with a time element to it, then that kind of gets into this interval training workout. I space them out. There's some, Dan may have some experience with this too. There's some resistance workouts, you know, where you just go to the gym and you're kind of beat and you just like, take like two hours to probably do the work you could have done in like 20 minutes, but there's something relaxing about just like doing a purely resistance set, not much of an aerobic element, but it's a mix.

I think there's value to it. And I think a lot of it is around core strength, at least for longevity. I mean, I, think I've really started telling my elderly folks as the population, and I don't like the word elderly because I think we're all going to be like a hundred by the time we, because we're getting really good at longevity, but core strength and functionality and balance, and that's kind of starting to be built into the guidelines as well.

Host: Before we leave exercise prescriptions, I just want to ask Dan uh, Dan, for your, both your primary care population and your preventative cardiology population, is there anything you want to add in terms of how you frame this and how you prescribe it?

Daniel Soffer, MD: Kendal, I didn't hear the last part of what you said, but I gather what you were asking about is, is there anything else that I recommend, that maybe Neel didn't touch on, in my practice. And I will say that it's been a real pleasure listening to Neel. I wish he was in the office with me all the time when patients come in, because I have all those same questions that you were asking.

And our patients have all those same questions. And having him respond in the way that he has, very thoughtful manner uh, very evidence based. And it's comforting because I think I give the same types of answers, maybe not with the same depth but Neel hasn't said anything that shocked me or turned anything upside down that I wasn't already saying, but it's very comforting to hear.

A lot of our patients are tracking their heart rate variability also, and Neel, I wonder, is that something that we should encourage our patients to do? Is that just another metric of cardiovascular fitness?

Neel Chokshi, MD, MBA: Yeah, it's an interesting metric. There's some data to suggest maybe we should just sort of start by mentioning what that is. Basically heart rate variability is just that, it's looking at your beat by beat, the time between each heartbeat and there should be sort of a baseline level of variability and when that ability to, or that variability, the change between beats decreases that is often a sign of increased stress when your heartbeat doesn't vary. It's, it can be detected over time and there's potentially a sign of quote unquote increased stress on the body. That can mean a number of things.

It could be something disease related. It could be recovery related, inflammation, whatnot, a hard workout, you have the flu. And so a lot of, a lot of these device companies have tried to capitalize on that to say, Hey, can we, and it's really interesting. Can we use this like a sort of leading indicator to say, okay, maybe there's something brewing.

Maybe you need to exercise less today. Take it easy. In theory, it's really great. But you know, what I tell my patients, it's not quite ready for prime time. What I mean by that is like, you know, it usually when it makes sense, then it's great. But when it doesn't make sense, then it kind of falls apart.

So the typical thing is like, you know, I had like 10 drinks last night and I tried to work out this morning and my workout was terrible. And my heart rate variability was spot on. It was like terrible. Well, I could have told you you had 10 drinks and, you know, so there are very few scenarios that I've seen quite yet, and I've tested these out myself, but it's a I think we'll get there.

I think, you know, especially with AI and as we bring in a lot of other data to couple it with heart rate variability, I think we'll probably have some interesting signs. I think some of these device companies, like where it became interesting, a lot of the proteams were using wearables to, to maybe detect COVID before COVID was like positive. And that was kind of interesting because we, at the time we were really struggling to like figure out a leading indicator for that. So there's probably, the heart rate variability is probably not quite there yet, but it's getting there. think it'll be interesting to see.

Daniel Soffer, MD: I remember about 20 years ago, there was a device company that did in office heart rate variability testing and, said it was a leading indicator of the autonomic nervous system balance. And a good general

indicator. Of course, it was just a one time test. It wasn't something that you wore on your wrist at all times and you got

moment by moment or day by day variability. So, but it was something that I think had some clinical utility in concept anyhow.

Neel Chokshi, MD, MBA: It's interesting because I wonder if everyone's heart rate variability was like very low because when you're in the doctor's office you're just basically amped up like it's like your blood pressure's up. So I wonder if they were kind of skewed. But uh, yeah, it's gonna be interesting I think once they have like more data to pull apart the signal from all the noise. Yeah, it'll be interesting.

Host: So, the other question I have when I'm thinking about patients and thinking about their cardiovascular risk, is how much I shouldn't factor in their fitness level and their level of exercise. I have an assumption that the ASCVD scoring systems were developed out of cohort studies, obviously that may or may not have included patients baseline fitness, and I'm assuming they didn't, because I often see patients who have, let's say, a coronary calcium score that's much lower than you'd expect based on their cholesterol level or their LDL level, which is largely genetic. So how much does exercise modify our existing ASCVD scoring systems? Do we know the answer how much it modifies?

Daniel Soffer, MD: Kendal, I have no idea, but I imagine it's one of the variables that is not measured in estimating cardiovascular risk. I, think I've said this on podcast before. I know I've said it in meetings before when asked how I use ASCVD risk scoring, and my answer is really hardly ever, because I know risk when I see it, and I find the risk scoring for the individual rarely changes my thought process.

But I can sometimes use it to justify a point of view that the patient and I have come to for medical legal reasons, but the risk scoring systems are devised from large population databases. And they're relevant to the populations, but I find them far less relevant to the individual management decisions.

Neel Chokshi, MD, MBA: Yeah, I tend to agree with Dan. I think they're not unlike the heart rate variability metric in that when they fit to the person, then it's nice. But there are rarely scenarios where it adds sort of a novel perspective on things. So I think, some of the newer calculators, I think, again, these scores will get better, I think, as we have newer data and we're able to handle more data.

So I'm still not entirely against it and it might prompt folks, but, Kendal, to answer your question, I think, there's two big buckets of things that are not incorporated and exercise for sure is not. So, so a lot of my clinic is high volume exercisers with traditional risk factors, or maybe without traditional risk factors, calcium scores.

And I don't think their risk is the same. In fact, we have data to suggest that. So, they come to me looking for this answer that I've, I exercise so much. And yet, why am I being grouped with the same individuals for the general population? And I agree with them. I think that, exercise is protective and we can talk about specific scenarios, but so I agree that's excluded.

And then, similarly, like, sort of, and oftentimes, conversely, is their whole, and Dan will probably agree, their diet and nutrition. I mean, we have people that exercise a ton, but their diet is, because that, it's kind of a work hard, play hard mentality, they feel they can eat and whatever they want, and that negates all of that.

And again, that's not incorporated into any of these scores or they are sort of inflammatory milieu or so, so I think, yeah, I agree. I think there's still a role to sort of tailor risk based on exercise and lifestyle in general.

Host: So largely from Dan's input on previous podcasts, I have really taken to using coronary calcium scores and find them extremely helpful. But there's an interpretation problem here in relation to exercise, both in terms of folks that exercise seem to have less plaque than you'd expect.

And then sometimes they have a lot more plaque than you'd expect, right? And so, or they have more calcium than you'd expect. And Neel, I sent you a patient maybe six months ago I think 50s year old heavy cyclist, 200 miles a week, not bad lipid profile, as I recall, did a coronary calcium score because he was 56 and I was, you know, I do this usually in people that are about that age, men about that age, and it came out very high, and so that was confusing, and I sent him to you to help me solve that.

Can we talk about coronary calcium scores in relation to exercise?

Daniel Soffer, MD: Yeah. That's a question that comes up a lot, Kendal. I'll take it and maybe neel has some other thoughts on it too. There is a literature on endurance athletes and select group with a higher coronary artery calcium score. And there is a thought that, Neel was just talking about a few minutes ago that

they seem to be at a lower than expected risk based upon their coronary artery calcium score.

And it's, Largely based upon expected better outcomes that you see in these patients compared to others in their cohort who aren't exercising at the same rate. I don't think the physiology of why endurance training should increase your coronary artery calcium is fully understood.

I'd be curious to hear if Neel has some thoughts on it. I've talked to some experts in the uh, physiology of coronary calcium. And they speculated that there's some microtrauma that occurs as part of high endurance training, but that's, it sounded like speculation on top of speculation as a response to that.

So I don't really think we understand exactly why endurance training might increase coronary calcium. It's still a marker that there is atherosclerosis present. But it may not be the best marker for cardiovascular outcomes. And hopefully both of you may have heard that at Penn, the coronary CT angiogram program has new software that was incorporated in the last few months.

And Neel and his colleagues in cardiology like it because they're able to now measure fractional flow reserve in a non invasive way. So for determining who may benefit from intervention, now they have a non invasive FFR. But internists like you and me, Kendal, who take care of asymptomatic patients, we may learn more about plaque morphology that is very interesting to the management of our patients from the same software package. And learning about the plaque morphology differences may help explain some of the differences we see in these endurance athletes. So if they have very fibrous calcific atherosclerosis, and that's lipid poor, it's not full of all that gooey cholesterol, it doesn't seem to have the same inflammatory predisposition or the same predisposition to uh vulnerability that a lipid rich plaque might have, that might help explain the prognosis for some of our patients, like what you just described.

Neel Chokshi, MD, MBA: Yeah, I agree, Dan. I think to piggyback off of that, so the question really is in the general population, a calcium scan or elevated calcium score implies lots of plaque, but specifically the concern is that the implication is they have a lot of soft plaque or lipid rich plaque. And that's the real question that we have for athletes.

Is that plaque or is that score on that scan have the same prognostic implication as it does for the general population? And the answer is probably not. It's still a mixed bag of folks and, but in general, we think it's probably not the same. And

I think we'll have better answers to that in the coming year with a lot of the studies that are ongoing as Dan said.

But, I would say that a good takeaway is that athletes are not immune from traditional cardiovascular risk factors. I mean, there are studies that they have maybe not as high a prevalence, but similar prevalence of hypertension, smoking, hyperlipidemia, you know, diet, as we talked about.

And so they're not immune from a lot of these plaques that we, the general population have that put them at risk for events and sudden death. But, you know, I think what you're getting at, Kendal, is to touch base on there probably is some from very ultra high risk or high volumes of exercise in a small cohort for whatever reason their predisposition is; there's probably more calcification that occurs, whether that we should be as robust or aggressive with that risk is still to be determined, but we tend to, in our practice, with shared decision making, I tend to be just as aggressive and looking at that.

Daniel Soffer, MD: I wanted to add one more thing to that, Neel, because I think that's a really good point. For example, you know, course I'm going to always make the case for, you know, very good LDL and apoB lowering in our patients who have high risk as evidenced by a high atherosclerosis burden. So high calc calcium score tells me that person is at very high risk.

And one part of their treatment is going to be with intensive LDL and apoB lowering. In the past, that has always meant statins and high intensity statins. And our athletes can't stand it. When you tell them that you want them on statins, especially high intensity statins, it does have an impact on sports performance and exercise performance.

So you have to be mindful about that recommendation. And I like that you brought up a clinician patient discussion about how best to achieve that. And I think if this were a decade ago, that's basically the issue. But now, of course, we have non-statin therapies that are very effective and being able to leverage the use of non-statin therapies to lower the LDL cholesterol to levels that you're more satisfied with while keeping your statin dose at a more reasonable dose that's less likely to affect the muscles and allow them to exercise at a high level. I think there's nothing wrong with that. And we do that all the time in our clinic.

Neel Chokshi, MD, MBA: I will just add though, Dan, just to be clear about it, there have been studies about the impact of statins on performance, on peak VO2 over six months has not shown any impact on it. And while it has shown

maybe at the cellular level, some changes. There isn't any strong evidence to suggest that statin impairs performance.

And so I just want to say that out loud, cause Kendal, you probably deal with that a little bit in clinic and we all do. So, again, it's a choice. Fortunately it's a preventative choice. So there's a little bit less I won't say urgency, but you know, it's not as necessarily life threatening to them.

And the one other thing that we should, Kendal, I don't know if you want to talk about is worth mentioning is the study that Dan was referencing on endurance athletes and calcification. I can sort of chat about it for a second if we have the time for it.

Host: Yeah, I'd like to get into that just for a second. So I want to, but I just want to throw out a theory to you and I don't know, as I was exploring this for myself, I learned a couple things about coronary calcification. First off obviously, not all plaque is calcified. I read that about any one time, maybe 20 percent of the total amount of plaque is calcified. It depends on the age of the plaque, obviously. And that calcification is a positive process, as Dan alluded to. You know, you're turning something that's a gelatinous sort of flexible substance into something that's a little bit more rigid.

And so, I wondered if possibly the exercise was accelerating the body's own processes to stabilize the plaque and prevent events from occurring, and that that's why we just saw more higher calcium scores, because exercise was actually making more of the plaque calcified. I, don't know if that's true.

Daniel Soffer, MD: I like that theory, Kendal. Call it the uh, Williams hypothesis of coronary calcification associated with endurance athletes. Coronary calcification is not entirely benign. It'smostly benign, as you say, it's a marker of stabilized plaque, but calcified cholesterol crystals can induce some damage in and of themselves.

It's not presently a target of therapy. When we treat our patients, we're not trying to make that calcification go away. We, that's not a target. We don't have any intervention that is reliable to achieve that, nor do we have a way to reduce cardiovascular events by reducing coronary calcification.

But it can induce some injury to the endothelium, trigger a neutrophil response, and that can be partly responsible for future cardiovascular events. So that's thought to be part of the process.

Host: I didn't want to get off on too much of a sidebar because, Neel, I want to get back to this calcification and endurance athlete study. Can you illuminate us in that regard?

Neel Chokshi, MD, MBA: Yeah, so the study that we were referring to and probably worth is relevant. So this is from UT Southwestern and Ben Levine's group, who's a pretty well known physiologist and sports cardiologist. And they looked at 20,000, a very large cohorts, about 20,000 endurance athletes, predominantly men, about 52, 50, 55 years in age.

And these guys, just to give you an idea, they at least exercised one hour a day for a minimum of five days a week, between five and seven days a week. So very high volume exercisers. And there was a couple of things that are interesting. One, that when they stratified people by how much they exercise in terms of like the, the lowest third and upper third and middle third.

The folks that exercised the most tended to have more calcification. So there was the suggestion that in this cohort, volume correlated to calcification. The other thing that they looked at is comparing folks, the group with the highest amount of calcification and looked at their over 10 years, you know, who had cardiovascular events.

So first of all, the event rate was quite low in the high calcium group. There's like 10 in a cohort of like 20,000 people, there was like 10 cardiovascular events, which is pretty amazing. And the rates of events in those groups, looking at the cohort of people who were high volume exercisers, they were lower then the lower exerciser group or like a comparative sedentary group.

So the point of that is when a person comes to you in the office and asks you, should I stop exercising with the calcium score? And the answer is no, because your event rate is still lower. It's protective, even though, now probably it is still beneficial. If you asked me if I would have no calcium and be a high volume exerciser versus have calcium, there's probably still some benefit to having no calcium.

The point is that event rates are low. And exercise is still protective and we see that clinically in lots of people. We have tons of high volume folks that have coronary disease and um, maybe don't even feel it. So I think that's really important to highlight. And I point that out to patients so that it's a little reassuring to them because it's a little bit of a surprise when they have calcium when they've been super fit.

Daniel Soffer, MD: Neel, that was great. Thank you for clarifying that. You know, some of our patients who have these high calcium scores are not just athletes who are weekend warriors and working out every day. They're also competing. Can you say a little something about the difference between training versus competing? I do get a little nervous about our patients who compete.

Neel Chokshi, MD, MBA: Yeah, I think that's a good point. And that's a distinction I make. So competition is an extrinsic motivator versus self training is an intrinsic motivator. And that's important because you will push yourself beyond your means, your boundaries, if you're competing, and you've probably seen this, Dan, and I think you're still a competitive soccer player, or pseudo competitive maybe, but, and so that's really important because if you're truly a quote unquote athlete, and that's anybody that puts a premium on exercise, it doesn't have to be a professional athlete, you will push yourself beyond your means and competition.

And I extend that now in current generation; it's not just like traditional competition on the court or a race. It's like pelotoning, right? You want a personal, you, there's a leaderboard on there and you're trying to chase that leader or you're trying to beat your last record and you're pushing yourself beyond your means.

And you may, think that unless I'm having chest pain, I'm not doing it right. Unless it hurts, it doesn't feel right. And so yes, that does concern me, especially in the high calcium scores. And so those folks, I will put them on a treadmill or I will test them more often depending on what they're doing, if they're competing, if they're getting in the water and their competition and if they're looking to be elite, I tend to have a lower threshold to surveil and stent.

Kendal Williams, MD (Host): Neel, if you look at the folks that do have, say, cardiac arrest or cardiac event while doing exercise, particularly heavy exercise, how does it break down in terms of the cause of those events? I mean, sometimes we don't know, but depending on autopsies and so forth, but how much of it is coronary artery disease versus an underlying cardiomyopathy versus an arrhythmic event for which they may have been predisposed and so forth?

Neel Chokshi, MD, MBA: Yeah. Good question. So it's stratified by age. We see a clear inflection point. Another definition or terminology, Kendal. So, 35 years of age, 35 and above are considered master's athletes and 35 and below are considered sort of young athletes. And this correlates because we think there's sort of an inflection in physiology and risk factors.

In those 35 and above, from like sort of population based studies, it's predominantly, probably like at least the third to half of patients, the etiology is coronary artery disease is the cause of sudden death. As you get into the younger population, it gets into a mixed bag as you can imagine, these are tough studies to conduct, but probably the biggest bag is sudden death with structurally normal heart.

So these are folks that have true sudden death and on autopsy, they have nothing abnormal about them. So it's probably something genetic or arrhythmogenic. And then the next biggest sort of buckets are a cardiomyopathy of some sort, genetic or myocarditis and then hypertrophic cardiomyopathy, and then coronary anomalies.

Those are kind of the big, big buckets of things in younger population folks. And then in older folks, the sort of usual suspects, but nothing stands out. Coronary disease is the culprit.

Host: So this whole discussion, I think, segues into something that's going to be relevant to us that is happening at Penn, and that is a change in the way the LDL cholesterol is calculated at our laboratory, and I think this is happening in some ways nationwide. That's one of the reasons I brought on Dr. Soffer to talk about this. Dan, can you update us on that?

Daniel Soffer, MD: Sure. The timing is great. As of a month and a half ago at the University of Pennsylvania, we changed the LDL cholesterol calculation, on the basis of a preponderance of data supporting an update for that calculator. So up until then, we were using a calculation from the 1960s derived from the an NIH database of around 5,000 patients, at the time. And it was a sensible calculation for what they had. And it was compared against the gold standard fancy test that no one ever does anymore. And it worked fairly well. That's referred to as the Friedenwald calculation. And since then, in the last, about 12 years, there have been a few easy calculations that were derived.

One at Johns Hopkins, by Seth Martin and his team. It's referred to as the Martin Hopkins formula. And Quest Laboratory uses that as their principle LDL cholesterol calculation now, for at least five years, I believe. And at the NIH, the, they also created a new calculator called the Sampson NIH formula by Clara Sampson and Alan Romali down there.

And this is a mathematical formula that improves greatly upon the older Friedenwald formula. And at Penn, we've started using the Samson model. Not that it's superior to the Martin Hopkins. It just fits into the EMR a lot more

smoothly. And what you may see in the clinic is that your patients who, especially have high triglyceride levels, and by high, I mean, anything over really 120 milligrams per deciliter, that you're going to get a variance from the older Friedenwald formula, LDL cholesterol, to the newer Sampson formula.

And the higher the triglyceride, the bigger the variance you'll see. What that means is that for the most part, it's not going to change how you manage the care for your patients. But for some of your patients who are taking statin therapy and are at the lower end, who you think you're, that you would intensify the regimen if their LDL cholesterol is over 70 milligrams per deciliter, they, and before they may have had levels that were in the fifties or sixties and you were pretty satisfied, now you might get their level back and it's 80 or maybe even as high as 90.

You can see variance by 20 or 30 points. And so you may be thinking about your patient in different light when you get that back. And so, unfortunately what was happening is that if you were basing your decisions solely on the calculated LDL cholesterol, you weren't doing so with the best information available.

That's part of the reason why we talked about on previous podcasts why non-HDL cholesterol is superior because it gets around these complicated calculations and why apoB is superior for the same reason. It gets around these calculations and you're not relying on an older formula that's now outdated and had to be updated.

So, non-HDL cholesterol and apoB still outperform even the newer LDL cholesterol levels, but the newer LDL cholesterol level that we're using, is far superior to the older Friedenwald formula. So you can feel more confident in your decision making about the current levels that we're using since May 7th.

Host: And we should adjust our therapy accordingly. Like as you said, you have somebody who's above 70 and you're targeting below 70, you should adjust the therapy to get below.

Daniel Soffer, MD: Exactly, yeah. That you're, they're above the threshold for where you would wanna do more, so do more.

Host: Well, we've run out of time and it's a shame because I, really have a lot more questions because this is a really interesting area. And if anybody has more questions and wants to email me, we can always bring Neel and Dan back

on. But for now, we'll have to wrap it up there. Thank you all for joining the Penn Primary Care Podcast.

Please join us again next time.

Disclaimer: Please note that this podcast is for educational purposes only. For specific questions, please contact your physician. And if an emergency, please call 911 or go to the nearest emergency department.