DANNY LENNON: Professor Jason Gill, thank you so much for rejoining me on the podcast.

JASON GILL: Thanks, Danny. Great to be here.

DANNY LENNON: For people listening, you were on the podcast a number of years ago now at this point. For those who maybe didn't catch that episode or maybe haven't come across your work before, Jason, can you maybe give an overview, a bit about your background, where you currently are at, and what type of research you look into?

JASON GILL: Yeah, thanks Danny. So I'm Professor of Cardiometabolic Health in the Institute of Cardiovascular and Life Sciences at the University of Glasgow. My work's looking at lifestyle, broad lifestyle, so physical activity diet, and now increasingly, I'm doing bits on sleep, on the prevention and management of cardiometabolic diseases. And I work in three main areas, I do epidemiology, so looking at big populations and looking at how different aspects of lifestyle and different populations influence risk of disease. I do work trying to understand the mechanisms by which physical activity or dietary changes might influence health. So, for example, changes in your lipids or changes in insulin sensitivity, and increasingly, I'm doing work on intervention

trials to try and say, how do we get people to be more active, and with that, I'm particularly interested in people that are hard to reach, so people who we struggle to make more physically active, and I'm increasingly trying to do work to try and actually get to the point where you can implement it and actually change population health. So how do you actually do large scale interventions that you can roll out to change the whole population, And I'm really interested in the people that do very, very little activity. So I guess, many of your listeners are people who are interested in diet and physical activity, and they're all pretty active. I'm very much interested in the people that maybe are less like your audience, the people that sit on the couch and are not bothered about doing anything, and I want to try and help them to do something and make it easier for them to do something because that's where I think a lot of the public health gains are going to come, getting the people that do nothing to try and do something. So that's where I'm setting out how to get something that's doing nothing to do something, and what's the benefits of that that first bit of activity or that first change that you get.

DANNY LENNON: In recent times, we've discussed and tried to make clear some of those distinctions within nutritional epidemiology, and that difference between public health nutrition versus what we may look at on an individual basis in an ideal world, and being able to think about large interventions or policy changes that could be rolled out on a nutrition front. And so, I think much of that relates to work you're doing, but primarily with physical activity as well as nutrition. So to kind of set the stage with that, when we're thinking about at a population wide level, we want to get people in that are doing the least to be able to increase their amount of activity and what interventions may be useful. Where are we currently at with physical activity guidelines and recommendations, can you kind of set the landscape for people just to give us an idea of what we're talking about?

JASON GILL: Yeah. So guidelines have evolved over the years, the first guidelines were out in the late 1970s, and over the last, was that, 40 years or so, they've changed. And in 2019, the UK guidelines were updated, and I was involved in that process. And so, basically the key messages are, the first thing is some is good, more is better. So we have a number for the amount of physical activity you want to do, how many minutes you want to do, and that's something to work towards. But a really key aspect of the guideline is even at levels below what the guideline amounts are, you're going to get some benefits. So the person's doing nothing on the couch, everything they do is going to give them a benefit. That's the first key thing. And the second thing is a subtle change, it wasn't a guideline before, but we've switched the order around. So muscle strengthening activities a couple of times a week has now moved up to become closer to the headline part of the guideline. It was always in the guideline, but it was the bit that people didn't do. So less than a quarter of the population report meeting that aspect of the guideline, whereas about half of the population just underreport meeting the aerobic activity part of the guideline. So we've just switched the order around to increase the emphasis on muscle strengthening activities.

And then the third part of the guideline is then do at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity activity per week. And there is a bit on doing shorter durations of what we call very vigorous intensity exercise, and this is to reflect the growing evidence that high intensity interval training is something that people do and that the amount of activity at that sort of level that you need to do to get health benefits is likely to be lower. In terms of guidelines, it's very difficult to look at the evidence to give an exact number on what needs to be done when you're talking these very, very high levels. And we don't really have enough evidence to say whether doing 30-second intervals or one-minute intervals or four-minute intervals is better. So in terms of

which protocol for very high intensity activity, I don't think the evidence is clear enough, but if you're doing these very, very intense forms of activity, you can probably get away with less than 75 minutes per week. And then the final point is minimize the amount of time spent sitting, and maybe this is something that we'll come to later on in this talk. But I think there's a there's a bit of subtlety in whether sedentary behavior or sitting down too much is really as bad for us as some people think; some people are saying the chair is the killer and sitting is the new smoking. I have a slightly different view on that, and maybe that's something that we can talk about a little bit later.

DANNY LENNON: Absolutely. And having seen some of your ideas and conclusions around the evidence in the area, I definitely want to dig into some of that, as with some of those other points you mentioned. Just to start maybe with the strength issue, seeing as that was the one you mentioned as kind of been elevated within those guidelines, I know you've highlighted before how strength can act as a predictor of risk, for example, something as simple as clean grip strength, can you maybe talk through grip strength as a predictor of risk and maybe how does it compare to others and how we should view this as a potential predictor of risk?

JASON GILL: I think that's a really important point, Danny. So there's now increasing evidence that strength is associated with a number of adverse or low strength is associated with number of adverse health outcomes. And generally, in large population studies, they measure strength using grip strength, using a hand grip dynamometer. And that's not because grip strength is causally related to any of these adverse outcomes, it's just there's an easy measure of strength that you can do in 1000s of people. And the evidence suggests that grip strength actually correlates very strongly with other markers of body strength. So it correlates very well with leg strength, for example. So people who have strong grip strength have strong legs and strong

upper body strength, so it's just a measure of overall body strength. And what you find is people at higher levels of strength appear to have lower risk of mortality from any cause, lower risk of cardiovascular disease, respiratory disease, type 2 diabetes, some cancers, and a whole range of adverse health outcomes are associated with having a low level of strength. And we've done some work using data from UK Biobank, which shows that if you add a measure of grip strength to other measures that doctors typically use to identify people at a high risk of developing a disease, which they might use to, for example, decide whether they're going to prescribe you with statins so looking at age, sex, whether you smoke, your BMI, whether you have diabetes, and your blood pressure, if you take those factors and say, based on those, you can predict what your risk over the next 10 years is of dying or having an adverse cardiovascular event. And what we've shown is if you add grip strength as a measure, you actually improve your prediction. So what we think over time, we're not there yet, is that in a doctor's office, as well as having a blood pressure monitor, and scales to measure your height and weight, you might have a hand grip dynamometer and measure strength, which might be something that they use in the future to try and predict future risks. So I think strength is becoming a potentially more important indicator of overall health than maybe we appreciated previously.

DANNY LENNON: Yeah, for sure, I've had some good conversations with Brendan Egan, who's based over here in Dublin City University, and a lot of their work centers around not only sarcopenia, but looking at that muscle mass and muscle function as it relates to other chronic disease risk later in life. So it's definitely great to see more of this emphasis being placed there. And, like you say, being able to use something like grip strength, you have this very easily scalable way to screen people to improve prediction.

JASON GILL: Yes, I think that's exactly right. And another piece of work, which I didn't mention was some

more work we did in the UK Biobank. And if you look at people's levels of physical activity from sort of low to high, and what you can do is look at people's levels of physical activity and look at their risk of mortality or risk of developing cardiovascular disease, and what you can also do is stratify people into having high, medium, and low levels of grip strength, and what you find is if people have a higher level of grip strength, so they're in the top third of the population for their age and sex, it doesn't seem to really matter how physically active they are, they seem to be at low risk; whereas if you take people who have low grip strength, and they are very active, they're at low risk; but if they have low grip strength, and they're inactive, they're at high risk. So it appears that it's not everybody who's inactive, that's a high risk. If you have a high level of strength, you're protected.

So what we might have going forward is, as I envisage an example where you might have hand grip dynamometer in community settings such as supermarkets, and you can identify people who have low strength, and then try and develop interventions to try and get them in particular, to be more active. So I think, we might need to become more focused in who we target to become more active, because we've got limited resources, and the evidence suggests that if you get somebody who's not very strong to become more active, you're likely to get a bigger public health gain than take somebody who's already quite strong, and they seem to, to some extent, sort of get away with being less active if they're sort of naturally quite strong. So I think we're kind of maybe moving to this idea that certain people really, really need to be physically active and people that are not very strong seems to be one of those groups.

DANNY LENNON: And I suppose, it's having not only that shifting of the whole population bell curve in one direction, but now the ability to target specific at-risk populations. When we see those differences between people with higher strength versus lower strength and that risk, what exactly

are we putting that mechanism down to, is it the fact of just the training they have to do to get there, or are they able to effectively put glucose back into muscle cells more easily, or is it a combination of too many things that becomes a complex web to untangle?

JASON GILL: You're right, it probably is complex. So there's a couple of things. So we know that muscle is your biggest sink for glucose. So that if you have more muscle, you've got more capacity to take glucose out of your bloodstream and regulate your blood sugar levels. So that's some of it. There's also this possibility with epidemiological studies, you might be predicting risk, so people who have low strength may be at high risk, but we've got less evidence that if you try and make them strong, you actually then reduce their risk. And some of that is due to the inherent difficulties of doing endpoint studies of lifestyle intervention in general population. So I'll give you an example. So if you take a 50 to 59-year-old woman who doesn't smoke and is physically inactive, her risk of dying over the next 10 years is about 3%. So it's very small. And if you want to measure whether making somebody stronger is going to reduce the risk of dying, you need to have enough people die, to be able to determine the difference between those two. And what happens is these studies need to go on for decades, and have huge numbers of thousands or tens of thousands of people to actually to measure that.

So we have some difficulties in this field to try and understand whether the interventions that we put in place, be it a dietary intervention or a physical activity intervention or whatever, actually change hard endpoints, like, do people have a heart attack or do they die. So we're left with trying to triangulate from two other bits of, two other types of study. One is the epidemiological studies where you observe people who are strong or less strong or fit or less fit or active or inactive, and then follow them up over time and say, is there a difference in the incidence of the adverse health outcomes. Or we

can also do studies which say, you do an intervention, a strength intervention or physical activity intervention or dietary intervention, and then you say, do you change biomarkers of risk, so do you change your blood lipids, your blood pressure, your insulin sensitivity or whatever, and these factors that we know are causally related to an outcome. So we have to kind of triangulate from these bits of evidence.

Now, there is evidence that if you do a strength training intervention, you do improve some of these biomarkers of risk. There is evidence that if you do strength training in combination with aerobic training, you seem to get a bigger benefit than either of them on their own. And that's true, even if you normalize the total amount of exercise. So you do the same total volume of exercise and you are half resistance, half aerobic, you seem to get a better benefit than either doing all of it resistance or all of aerobic; and that might be because aerobic type exercise and strength type exercise work by different mechanisms. So by doing the two of them, you're kind of maximizing benefit there. So I think there's evidence that I'm doing both aerobic activities and strength training activities are likely to be beneficial. But it's really, really hard to get the endpoint data and in some ways, that's the Holy Grail, and I think we're not quite there yet with the evidence for that.

DANNY LENNON: Seeing as you bring up, aiming to do better quality studies over time and increase our evidence base here, if we talk a bit about some of the methodology and specifically related to measurement quality is one thing I've heard you discuss in a number of your lectures previously, particularly when it comes to physical activity, and how that data has often been gathered, i.e., from self-report surveys or so on. And you've done a really amazing job of kind of highlighting this discrepancy between some of that self-report data versus objective measurement data, and then showing how that can actually be problematic when we're trying to work out these associations with certain outcomes, can you

maybe talk through some of that discrepancy and what you've concluded?

JASON GILL: Yeah, thanks Danny. So what you find in most epidemiology, most epidemiological studies showing the association between physical activity and risk of adverse health outcomes of work by giving people a questionnaire to ask them how physically active you are. Some of the questionnaires are quite sophisticated and can ask you activities on different days and different domains, but essentially, you're asking people how much they do. And what you find is that if you measure how much activity people do using something like an accelerometer is you get a very different answer. What you find is people overreport how much activity they do considerably, And they overreport it by an inconsistent amount; some people overreport it by lots, some people less. So you can't just use a conversion factor to get from the self-report to the actual measure. And the effect of that is to attenuate, to reduce the apparent association between the activity that you do and risk of the adverse health outcome. It's a really nerdy thing. It's called regression dilution bias.

So if you measure activity poorly, it diminishes the apparent effect on an outcome. And this is important in terms of what we recommend people to do, because if we look at a lot of the evidence where you come up with your 150 minutes of moderate intensity physical activity or 75 minutes of vigorous intensity physical activity, this is based on a large body of epidemiological studies which have used self-report. And what you find is that if you take studies which have measured physical activity using an accelerometer and these studies have only been around for the last few years, and one of the things that you need to realize with this is you need to measure people's activity with an accelerometer, but then you have to wait long enough after the measurement for adverse events to happen, which you have to wait several years. And so, now we're getting to the point where we're getting a reasonable amount of

data, which has measured people's activity using accelerometers and follow them up over time. And what those data suggests is that the dose response relationship is quite a lot steeper than from self-report. So you appear to get benefits of being physically active when you measured objectively with much smaller levels of activity than you would from self-report.

So it's generally about two and a half minutes of self-reported physical activity is equivalent to one minute of accelerometer measured physical activity. So during 25 minutes of self-reported physical activity is about equivalent to maybe 10 minutes of measured physical activity. So this has implications in terms of how much activity we recommend people do. So most people have an accelerometer on their phones, a lot of people have Fitbits and Garmins, and if you actually look at the amount of activity people do in a measured way, you might be able to get away with substantially less to get the benefits. And an example of this is we did a study published a couple of years ago called EuroFIT. This was a really interesting study because men are much, much harder to reach with lifestyle intervention than women. So if you look at the large intervention trials, what you find is women are much more receptive to being asked to do some sort of intervention via physical activity intervention or dietary intervention. Men are much, much more resistant to that.

So what we did is we took advantage of the fact that a lot of men like football, top level soccer, and so we designed an intervention where we did the intervention in top level football clubs throughout Europe. So there were five clubs in England, I think it was Everton, Arsenal, Newcastle, Stoke, and one more I can't remember. And there were three clubs in the Netherlands, So PSV Eindhoven, clubs like that, three clubs in Portugal, Porto, Benfica, Sporting Lisbon, three clubs in Norway. And what we did is we designed an intervention which was delivered by the club coaches. So we trained the coaches now to design a fit into how to deliver a

physical activity intervention, and they delivered it to their fans within the clubs. It was a big study, it was about 1100 men across Europe, across 15 clubs, it cost 6 million euros. We tried to get to increased physical activity of one year, so that's another key thing that we tried to do. We tried to look at a long term change, because one of the things you find in interventions is it's relatively easy to get people to change physical activity for a few weeks. But the difficulty that people drop off and try to look it over time. So what we were very interested in is we delivered intervention for three months, and then we actually measured how physically active people were at one year, after we didn't have the intervention for nine months to see how well they kept doing it. Because in terms of public health, what we want people to do is to keep doing the intervention, essentially forever.

And what we found is that 12 months, we changed accelerometer measured physical activity by about six minutes per day, so it's sounds relatively disappointing. What we also found is we changed self-reported physical activity by 32 minutes per day. So people reported doing 32 minutes more, but when you actually measure it, it was only six minutes more. But the really important thing was it was enough. So people lost 2.6 kilograms in bodyweight, they reduced their blood pressure, they improved their lipids, improved insulin sensitivity, reduced their liver enzymes. So although we only changed actually measured physical activity by six minutes per day, it was enough. And I think that's really important, because if the target is, say, five to 10 minutes of physical activity of actually measured physical activity per day, rather than 30 minutes, it changes the way you do an intervention. Because you can get to five to 10 minutes per day by asking people every hour to go and do a brisk walk for two minutes, and that's a very different type of thing from saying, go for a run for 30 minutes. It's very, very different. So I think this evidence opens up new ways that we can try and do interventions to get people that are doing

nothing to do something if the target, when you actually directly measure the physical activity is less than we thought. And if our target's five to 10 minutes, then maybe that makes our job easier, and maybe people who thought, this isn't for me, thought, yeah, I can do that.

DANNY LENNON: That makes a lot of sense. It's not this overwhelming, complete lifestyle change that is so often talked about, it's we can build this into the existing lifestyle and structures people have. I really, really like the EuroFIT RCT that you just mentioned. And so maybe to recap on that, the fact that it was a three-month intervention, but then, for the next nine months, it was kind of up to people to continue on with things or not, and measure that at 12 months. The difference between their actual measured was six minutes versus they were reporting that they were doing 32 minutes more activity. But that six minutes alone was able to improve those markers like bodyweight, blood pressure, lipids, and so on. And importantly, it kind of speaks to the fact that here's an intervention that is actually targeted at some of those groups who are most hard to reach, which is what you mentioned right at the start, in this case, particularly, men and getting them through their support of certain football teams. I did want to ask about a review paper of yours in, I think it was sports medicine, from maybe 2008-2009, and in that you talked about the amount of exercise that's needed to get to a low absolute level of risk of cardiometabolic disease is more for people in a high risk population versus a low risk population. Can you first just explain that?

JASON GILL: So what you find with the physical activity you do is you get benefit in a curvilinear manner. So the first bit of activity you do gives you the biggest benefit, the next bit gives you a little bit less, and then the next bit gives you a little bit less. So if you go from doing nothing to walking 10 minutes a day, you get a bigger benefit from that first 10 minutes than you go from 10 to 20, and then smaller. And once you're walking for an hour a day, doing an extra 10 minutes, that

benefit is much smaller from the first 10 minutes. So you got this curvilinear manner. And if you think about public health, what we want to do is to try and get people to have a low level of risk. And if someone starts off at a low level of risk, say, they are young and thin and of European ethnicity, because we know there's differences in risk, depending on ethnic group, what you find is, they probably need to do a relatively small amount of physical activity to get to be this low level of risk. Whereas if you are a middle aged, South Asian, who is obese, they're at high risk, and so the amount of activity that they need to get to be at low risk is going to be more. And what we're doing in the guidelines currently is recommending both people do the same amount, whereas the person at high risk probably needs to do more. And if we are suggesting to people that they don't need to do more than other people, then maybe we're doing them a little bit of a disservice, and maybe recommendations might need to be different in different groups, and we need to target the high-risk groups more.

And I can give you an example with relation to body mass index. So we typically say that normal bodyweight is a body mass index of between 18 and 25, overweight 25 to 30, obese more than 30. And that's true if you're White European. But if you're South Asian, those thresholds are shifted down. And now, it's probably not far enough, but it's moving in the appropriate direction what you would regard as being obese, if you're South Asian with BMI of 27.5, it probably should be 22 or 23, but it’s lower. So what we're saying is in different groups with different levels of risk, what we're saying is an appropriate bodyweight is different. And what I'm arguing is for physical activity, we've got a general guideline, and it might be that if you're in one group, you might need to do a different amount of activity as people in another group. And again, this is moving to this idea that one size doesn't fit all, and different people might need to do different amounts. I think we're not quite there in terms of putting

numbers on it, but I think I'd like to get that concept out there.

I mean, another thing related to this is we've done some work, which we published in Lancet Public Health. I think it was 2018 or 2019, which didn't just look at physical activity, it looked at a range of unhealthy life or healthy lifestyle behaviors – so whether you're active, whether you eat enough fruit and vegetables, whether you smoke, how much alcohol do you drink, how much television you watch. And what we showed is that if you are affluent and you have an unhealthy lifestyle, you get a bit of an increased risk of mortality. Whereas if you're in the most deprived socioeconomic groups, that same difference in lifestyle seems to have a much bigger adverse effect. So if you have an unhealthy lifestyle there seems to be some sort of multiplicative effect of living with deprivation, which seems to exacerbate these differences. So again, lifestyle seems to be doing slightly different things, depending on who you are. And one of the things I'm very interested in over the coming years is trying to unpick that further and understand what's going on, and to understand the implications of that for what we recommend different segments of the population do to optimize their health in terms of their lifestyle behaviors.

DANNY LENNON: Yes, that paper in the Lancet Public Health that you mentioned is one of my favorites to have read, I'm fascinated by the whole area related to socioeconomics and public health generally. So when I came across that, I found it fascinating. And there's a beautiful chart in there, which I've shared with people, that outlines just what you said, of between that degrees of social deprivation, going for like a score of one to five, and then for each one looking at a most healthy, moderate healthy, and the least healthful lifestyle. And, as you say, I found it fascinating that you see not only does the unhealthy lifestyle have this disproportionate increase in risk, but even those who were moderate healthy in the most deprived group, seem to have like the same

risk of people living with the least healthful lifestyle in one of the more affluent groups. And so that alone, to me is like the basis for why so much of this public health work and looking at some of these external factors is so important.

JASON GILL: That's really interesting Danny, and that's a really good summary. I guess, there's a couple of things that we can take from this. One is the people in the lowest socioeconomic groups are probably the hardest people to reach, in terms of lifestyle interventions. So what we're finding is when they're unhealthy, it has a bigger adverse effects, and we also know that they're the hardest people to try and change lifestyle behaviors. And so, we've got an issue there, and what we need to try and do is to develop interventions which work for that population as well as the more affluent ones who we often reach. And one of the challenges that we often see is we're developing an intervention to try and get people to cycle more. If you put in an intervention like that, what you might actually do is widen health inequalities, because it's the more affluent people that take up these interventions and they get better, whereas the less affluent people don't. And so, what you have is a difference between the most affluent and less affluent health actually gets wider or narrower. And one of the things we're often faced with is how can we actually deliver intervention to improve health, which actually doesn't make those inequalities wider. And I think some of this is we need to move towards system level changes.

So you need to actually change the system, which brings everybody up together. And so this argument that we just need to intervene at individual levels, I think is not quite correct. I don't think that works in the system as a whole, and what we need to do is actually intervene at multiple different levels. I don't know whether you're familiar with this concept of the socioecological model, and that sort of tells you that you can actually intervene at multiple different levels to have an effect. So you can

intervene at the individual level, you can intervene at a family level, a social level, an organizational level, a policy level, and one of the things that we need to consider if we want to improve the health of the nation by getting people to have healthier lifestyles is we have to intervene all of those levels. An example of a policy level and infrastructure level things might be to increase cycle lanes or to get people to ride bikes more, things like subsidizing healthy foods and taxing more unhealthy foods. And I think those types of interventions are likely to have a bigger effect than the individual level interventions that we're focusing on, and we maybe need to think about how do we do this whole society changes rather than trying to just target individuals do more going forward. I think that's a real challenge, and I think it's a challenge for me and also for the younger generation of scientists in this field coming forward to work out how can we do these interventions, which actually work at a system level to actually change the health of the largest possible number of people.

DANNY LENNON: And that whole area of looking at these policy changes could be a another discussion, so I definitely don't want to derail us too much. But I love thinking about some of these ideas. I talked with Corinna Hawkes about some of this. And, of course, what you unfortunately see sometimes is you can have areas where there's some really good evidence being done in public health epidemiology and cases where we may have evidence for certain interventions. But there can be also a bottleneck when it comes to politics and certain ideology that can sometimes prevent that, which is kind of unfortunate, but that is a topic for another time. I think one of the things I did want to come back to, and I think you had alluded to it is in relation to the importance of activity for those with a different genetic risk for obesity. And I think there was one paper that you were an author on that had assigned people a obesity genetic score based on a whole range of genes, and looking at differences between those who had a lower

versus higher risk for obesity, and looking at some of these changes. And one of them, if I remember correctly, was that for those with a higher risk of obesity, that sleep was a stronger influencer on body mass index. Can you maybe talk through a bit of that, but also the implications of some of those conclusions?

JASON GILL: We published a couple of papers on this. So what you can do is you can – there isn't one gene, which makes you fat. There are lots and lots of different genes that you have, which have a small effect, and everybody has one or other version of those genes. And what you can do is – I think there's about 97 that have been identified, and what you can do is based on which version of each of those genes you have, and some of these genes have a bigger effect than others, and the effect of it, you can give someone an obesity risk score, which determines their risk of being obese. And if you have a higher obesity risk score, you're heavier than somebody that has a lower obesity risk score. So what you can then do is to say we can take people with different levels of obesity risk, so people at low risk, medium risk, and high risk based on their genetic score. And then we could say, well, if we look at these different populations, and look at their level of physical activity, so you can look at their level of physical activity measured using an accelerometer or their level of sleep, and you put people into categories of, say, low physical activity, medium and high physical activity, depending on whether they high or low genetic risk score. What you find is people have a high genetic risk score for obesity, if they are inactive, it has a much bigger effect on their bodyweight, if they have a low genetic risk score. So if you have a low genetic risk score, how active you are, influences your bodyweight to a lower degree than if you have a high genetic risk score.

So let's unpack that. So what you find is people say, well, look, it's not my fault, I'm fat, it's in my genes, or, I can't do anything about it, it's in my genes. What these data actually show is the

opposite. So if you have a high genetic risk score, the ability for you to change your bodyweight by being active is actually greater than if you have a low genetic risk score. So it's a really positive message that if you have been dealt the cards, you've got a high genetic risk score for obesity, your level of physical activity influences your bodyweight even more, so it's even more important for you to be the active if you have a high genetic risk score. We see a similar story for sleep. So what we know is that if you're a short sleeper, or you're a very long sleeper, you appear to have a higher risk of obesity. So the optimal level of sleep for your bodyweight is about seven to nine hours per night. And the issues with long sleeper are a bit complicated, they probably relate to people having poor sleep quality. The reason you might need to sleep for a long time is your sleep quality is less good and poor sleep quality is a risk factor. With short sleep, it's more straightforward. But what you find, again, is that if you have a low genetic risk score for obesity, the effect of the association between how much you sleep and your bodyweight is much less strong than if you have a high genetic risk score. So if you have a high genetic risk score and poor sleep, your bodyweight goes up more.

So again, it's even more important for you to have good sleep behaviors, if you have a high genetic risk. So basically, what the data show, to summarize, is that if you've got a high genetic risk, you're more susceptible to the effect of an adverse environment. So you have to try and focus on making your environment better, and that's more important. So if you have a high genetic risk score, it's important that you get your sleep right. And there's also evidence with sugary drinks, again, they have a bigger effect on your bodyweight if you have a high genetic risk score, and your level of physical activity, so it's much more important for you to get these things right. Whereas people that are lucky enough to have a low genetic risk score can in some ways get away with having a less healthy lifestyle, because they've sort of won the genetic lottery in

some regards which gives them a bit of protection.

DANNY LENNON: And I think it's crucial that the way that you frame it that rather than see this in any way negative, it can be viewed actually the opposite, that if you do have this higher risk, then these lifestyle factors matter more. And so, therefore, by placing emphasis on those, you can actually get that risk reduction, as opposed to if you had low activity or poor sleep, etc., that you can offset that to quite a large degree. So I think that can be framed in a much more positive way.

JASON GILL: I agree. I mean… so both my parents have type 2 diabetes. So that means I've got a 90% lifetime risk of developing type 2 diabetes. So I know for me, it's even more important that I try not to get too fat, and I try to be active than somebody that does. And that knowledge means that I really need to focus on those lifestyle factors. I know that for me, if I get too fat, I will get diabetes, so I really need to work harder. And it's a similar sort of story with this genetic risk score for obesity, if you've got a high genetic risk score, you just have to work a bit harder; but when you do work hard, you get a bigger benefit for doing it.

DANNY LENNON: Jason, I did want to touch on the sitting and adverse health risk data, because, as you said at the outset of this discussion, this is an area that you've not only looked at, but have came to conclusions that maybe run counter to some of the presumptions people make in this area, particularly, because we hear so much about sitting right now. Can you maybe set the stage for us about what is that typical narrative we hear about sitting, and then how that may be slightly different to some of the conclusions you've came to based on looking at some of the evidence in this area?

JASON GILL: About 10-15 years ago, there was a thought that the amount of time you spend sitting down, what you call sedentary behavior, was maybe a separate risk factor for adverse health outcomes

like diabetes or heart disease or mortality, that how much physical activity you do. And there was the argument that even if you go to the gym and are really active, if you spend lots of time sitting down, you still have an excess risk because of that. And there was a narrative that went forward and said the chair is the killer, sitting is the new smoking, which has become quite popular. And if you look at the literature, and look at the evidence, I think the story is very subtly different from that. I mean, the first thing to think about, if you look at the relationship between how much time you spend sitting down and say risk of mortality, what you find is that the line is flat until about eight or nine hours, and then it sort of increases modestly. So it's not that all sitting you do is bad, and I like to say you get the first eight or nine hours free. The first eight or nine hours of time you spend sitting doesn't influence risk at all. Beyond that, it increases risk modestly.

Now, if we think of the magnitude of the risk increase, what you find is that you take someone that's been sitting about 10 hours a day, and they reduce their sitting time to nine hours a day, what you find is you get about a 17% reduction in risk of mortality. Now, put that into context, if you take somebody who does no physical activity at all, and you get them to walk for two and a half minutes, you get about a 17% risk in mortality. So in some ways, my argument is it's easier to get somebody to walk for two and a half more minutes than it is to get them to sit for an hour less. And that is reflected in the intervention trial data. When they do interventions to try and get people to sit less, what you find is actually quite hard to do. And the study shows that you can probably change sitting by between 10 minutes and an hour, mostly sort of between 10 and 30 minutes per day with an intervention to try and get people to sit less, which isn't enough. You need to get people to sit less by hours, and my argument is it's much easier to try and get people to do a few minutes of moderate intensity physical activity, which is likely to have a bigger benefit. If you

take somebody that's sitting down all day and doing no physical activity, and you try and get them to change their sitting by four hours, the change in risk in mortality is equivalent to changing the amount of walking they do, and this is self-reported walking, so it's probably smaller, by about 20 minutes per day. So maybe eight to 10 minutes of actual measured walking is probably equivalent to changing sitting by several hours. And my argument is, it's probably easier to get people to be more active than get them to sit less for hours and hours a day. And the evidence suggests that we can't do that really, at least with our current interventions.

The other thing that I think is important to think about is, what is the minimum increment above sitting which is necessary for benefit. And we've done some studies where you sort of interrupt sitting with either static standing or just light self-paced walking, just up and down the corridor. And what you find, in terms of metabolic benefits throughout the day, in terms of the levels of insulin and glucose in your blood and levels of lipids in your blood, that self-paced walking, slow, easy walking is enough to cause changes, whereas static standing isn't really. And so what you find is a lot of people say, well, sitting's really bad, what we'll do is we'll get a standing desk and that'll stop us sitting. And I think the evidence, and I've looked at this quite closely, in most studies, and we've done a number of these studies, suggest that standing probably isn't enough, it probably needs movement. And if you need movement, rather than standing, the message of sitting less, might not be necessary. You can just say move more, because if you're not sitting, you can be standing or moving. And if standing isn't enough, it's just about moving.

So I think a message of move more and more often is probably a more effective public health message, which fits with the evidence more strongly. And let's think about it, sitting down for a long time is probably not good. But if we say, well, every two minutes, every hour, go walk

up and down the stairs for two minutes. That's an approach to say move more often, rather than get a standing desk and stop sitting. So I've got a slightly different perspective. I think a number of people are coming round to that perspective, not everybody has. But my view is just focused on getting people to be more active at any intensity under any opportunity, rather than saying that sitting per se is a bad thing.

DANNY LENNON: So in that scenario, you could have a condition where let's say someone's total amount of time spent sitting over the day could be greater than a separate condition. But if it's broken up throughout the day, with some periods of just some light walking, even for a very short period of time, that feasibly is going to have a more beneficial impact than having less total time sitting, but the rest of that may be spent statically standing in place in that there's something about movement that is the key to the benefit here.

JASON GILL: Yeah, I think that's what the evidence shows. So basically, so moving's enough, static standing probably isn't, and again, I'm going to caveat this because people sometimes come back to me with this, is I'm really focused on cardiometabolic outcomes. So things like levels of risk of cardiovascular disease, looking at levels of lipids and glucose and insulin in your blood. What I'm not considering with this is things like musculoskeletal effects, sitting down all day gives people bad back. So in some instances their standing might be beneficial. In terms of my focus, which is basically cardiometabolic health outcomes, it looks like standing probably isn't enough.

DANNY LENNON: One thing that I did want to discuss was this distinction between fitness versus activity per se. And I know the last time when we had discussed some of the data related to race and ethnicity and seeing differences in cardiometabolic risk based on cardiovascular fitness I think VO2 Max and some of those studies. Does the impact therefore of activity

relate to how much it can change one's degree of fitness, or is it just being more active regardless, that's going to have that benefit?

JASON GILL: So I think the answer is it's both. So what we know about fitness is it improves with physical activity, and it's also a strong genetic component. So about half of how fit you are is going to be related to how well you chose your parents. So some people are going to be fit even if they're not very active, whereas other people might be very active and still unfit. And let's think about this, so a person who is very active and unfit is the people who are basically trained to run the London Marathon, but run it very slowly. So they've done a huge amount of activity, but they're not fit enough to run it fast. Whereas some people who just pick up a pair of trainers and then can run a really fast 10k without any training, they're naturally fit. And there are two distinct things, and what you find is that if you have a high level of natural fitness, in some ways, just like if you have a high level of natural strength, you can probably get away with not doing very much physical activity and you have a low risk. So a fit person inactive is probably still a relatively low risk of adverse health outcomes, whereas if you take somebody who has a low level of fitness, if they're inactive, they're at high risk; and if they're active, they're at lower risk. And what the activity can do is two things, one is increasing activity per se, even if it doesn't change fitness is likely to reduce their risk. So if you think about doing light and moderate intensity activities, they might not be enough to change your fitness. But they do have metabolic benefits. But then they've got an extra benefit is if they do the activities at sufficient intensity that increases their fitness, they get an added benefit from having more fitness as well. So physical activity can do two things. It can have a benefit in its own right, even if it doesn't change your fitness. And it can make you fitter, which gives you an added benefit from that as well, if that makes sense.

DANNY LENNON: Yeah, absolutely. And so that reminds me of the work that you have published in the area of race and ethnicity, particularly those comparisons between South Asians and White Europeans, in that, there is that difference in risk predicated on overall fitness, but it seems that it was the amount of activity that would be needed to get to a certain level of fitness differs between groups as well, which, therefore, if we're looking at how do we come back to some overall guidelines is one of the bases for why there may need to be differences between groups. Am I remembering that correctly?

JASON GILL: Yeah, well remembered. So what you find is that if you become more active, your fitness increases broadly. And we've shown that if you take South Asians and you look at their measured fitness using an accelerometer, so measured physical activity using an accelerometer, and measured fitness on a treadmill test, and you look at the relationship between the two, and you look at that same relationship in people of White European descent, is you've got a steeper relationship, if you are – no, what you find is the relationship is such that if you are South Asian, for any given level of physical activity, your fitness is lower. So to get the same level of fitness, South Asians needs to do more physical activity than Europeans. And the evidence suggests that having a high level of fitness is protective against diabetes, it's protective against cardiovascular disease. So South Asians probably need to do more to actually get to that level of protection than people of White European descent. So that's another reason why the amount of physical activity that we recommend for different groups of people for optimal health is maybe a bit different.

DANNY LENNON: I know the last time we discussed that in certain places, and certainly, certain people were advocating for different guidelines, and I think they're referenced in the nice guidelines, or at least were at the time. However, there's maybe not a consensus across all public health

guidelines, and we still do have these default, generic recommendations. Where are we currently now in terms of guidelines, and are we at a point where there's going to be differential guidelines across the board?

JASON GILL: Yes, that's an interesting question. So one of the things to think about is the threshold that you need to change a guideline is actually very high. And you default to what you're currently doing, unless there's strong evidence to suggest that you're doing something different, and I think there is evidence that's starting to accumulate, but it's not yet there. So I think over the next several decades, if there's more, or several years, that we might move that. An example of this is, with high intensity interval training, there's loads of studies which have been done in high intensity interval training, suggesting you can probably do very, very small amounts of high intensity activity, which will give you really big changes on fitness and other outcomes. But it's not there in the guidelines yet, and that gives you an idea of what's the thresholds that you need to actually change a guideline. The guidelines are, by nature, relatively conservative, and so I think we'll get there. I think it's probably going to be closer to 10 years than five years before we get there. And we're doing work to try and build that evidence base, so that when the guidelines are reviewed in future years, there may be enough evidence to suggest that we do different amounts of activity for different ethnic groups.

DANNY LENNON: Jason, where can people find more about you either online, your work, social media, any of that type of stuff that you want to mention?

JASON GILL: So I don't really do a lot of social media. I've got my university webpage, which should link to most of my papers, I mean, that's probably the place where you'll find most of the additional information about the work I talked about.

DANNY LENNON: Brilliant. Yeah, and as I often say to people, there's probably a correlation between those

who don't spend a lot of time on social media and are prolific in their publications of research. So it's a very smart idea, I think, stay away from Twitter, it's a good idea. Jason, to round this off, if you could advise people to do one thing each day that might benefit their life in any particular area, what might that one thing be?

JASON GILL: As somebody in the field of physical activity, I think get some activity. And the evidence is the first bit you do gives you the biggest benefit. There's also evidence that doing activity outside is important. So I guess, I'd maybe say, make sure you go for a walk outside every day.

DANNY LENNON: So with that, let me say, thank you so much, Professor Jason Gill, it's been an absolute honor to be able to talk to you about some of your work. It's been incredibly insightful and informative for me to be able to read it and to see the work that you continue to do. So thank you so much for taking the time to come and chat with me.

JASON GILL: Thanks, Danny. That was great, I really enjoyed it.