DANNY LENNON: Mr. Brad Dieter, welcome back to the podcast, but thanks for this time in person.

BRAD DIETER: Yeah, it's not from my home office, it's in a hotel room.

DANNY LENNON: Yeah. So for a bit of context for people, I've just finished sitting in on Brad's awesome lecture at the moment, and so my head is kind of full of some questions that I'm hopefully going to try and throw at you now. I suppose the first thing, maybe to give some context for the rest of the talk, some of the things that you discussed, they were around diabetes, and so I definitely want to ask that. And then more broadly, I would like to ask about chronic diseases related to lifestyle and obesity and things like that. Can you maybe touch on some of your work in the past that has got you, I suppose, interest in those areas, specifically what type of research you've done that may explain why this came across your radar, I guess?

BRAD DIETER: Yeah. So I guess my formal academic training was all in chronic disease. My master's was a little bit less, but my PhD and postdoc work was definitely, basically all in diabetes, and then end-organ complications. So basically, chronic disease and comorbidities – it's very rare that we see somebody with one chronic

disease that doesn't lead to something else. So my PhD work was in cardiovascular, my postdoc work was in the kidney, and it was kind of all on the disease process. So not a specific disease in the end, but what is it along the way of healthy normal people to chronic disease, and like, what is the fundamental process that occurs, and kind of trying to understand that. So that was a lot of – my academic work was kind of understanding that at a lot of different levels, whether it was the molecular progression of disease, kind of the lifestyle, socioeconomic pieces that were going into it. And then kind of layered on top of that was this idea of disease progression and risk.

And I think what a lot of people don't really think about is most of these chronic diseases are like accumulations of risk over time. There's a reason that, as you age, the risk of all diseases goes up, it's kind of like, every day you're exposed to a small amount of risk for disease and every day you're exposed to a small amount. And as those days add up, that risk adds up. And so when we start to really think about whether it is heart disease, whether it's cancer, whether it's diabetes or any of the end-organ complications, it's really understanding that process, the key pieces, and then how risk plays out over time, and this accumulation of risk with each day and the year that passes.

DANNY LENNON: Yeah, like that understanding of how this is almost this risk equation was such an important lightbulb for me to realize, and I think actually it was some of the discussions with you that really embedded this from a chronic disease point, I think when you were on the podcast where we discussed saturated fat, atherosclerosis, things like that, and you'd mention that point around risk equation. And it's been something I've gone back to and can only bring up that now when these discussions happen, because nothing else makes sense until you understand that piece. So if we translate that instead of from the kind of atherosclerosis piece and now think about diabetes, we'll start

with and maybe we'll go elsewhere, but when we're thinking about a risk equation, maybe to draw a parallel, a better way for me to ask is with atherosclerosis it seems that there's, rather than someone say LDL a specific time that matters, it's this exposure to high LDL over many decades, that is the real thing that would indicate something here. Is there a parallel in that with something like type-2 diabetes that we see that is this long term exposure and then how does that fit into this wider discussion if any of that made any sense?

BRAD DIETER: Yeah, that's a great question, and some of the processes that occur in atherosclerosis are analogous in diabetes, especially at a cellular, molecular level is the things that kind of precipitate the initial insulin resistance we just covered in the talk, energy excess, disordered fat metabolism, inflammation, oxidative stress, all kind of have these core underlying metabolic and molecular pieces that really do result from just risk accumulation over time. One of the analogies I like to give people is even sports injuries, your likelihood of tearing your ACL only playing one basketball game is pretty low; your likelihood of tearing their ACL playing 10,000 basketball games is pretty high; that likelihood of that injury occurring just accumulates each time you expose yourself to that risk. And so, if we think about diabetes disease progression, it's fairly similar. So if we know, if you have a state of energy overload in a cell that kind of leads to all these downstream pieces that cause insulin resistance regardless of what the mechanism is, your body is going to continue to accumulate this risk every day that there's some obese phenotype. So whether it's you have excess adipose tissue for a week, a month, a year, a decade, as that goes by, your likelihood of these pathogenic processes occurring continues to add up. So it's kind of the same thing even in atherosclerosis, if you have high blood pressure, high changes in metabolic pieces, LDL, all that kind of stuff is that likelihood of the disease progressing or initiating is there too.

DANNY LENNON: With the idea of a risk equation, there's a few ways that I've tended to think about this and one place that some people could go, and this is probably being talked about in medicine quite a bit, this idea that there's certain things are almost like a black box, we know the inputs going into them, we know the outputs at the end and some outcomes, but the stuff in the middle is kind of a bit messy to try and work out. Other areas where we kind of do know maybe mechanisms that play so, for example, with diabetes, all those different factors you mentioned today, the difficulty I suppose becomes in how do we weight each of those in a certain equation, because people are going to come to you and say, well, if I do this with my diet, what will that do to my – is that going to cause them to be diabetic or not. And it comes down to how do you even weight that in a hypothetical equation.

BRAD DIETER: Yeah, and I don't think there's a great answer, and I think it's, you know, part of it comes down to, and somebody had asked me this right after the talk is how do we best manage this risk. And I always think about it is, in any scenario, there's risks you can manage and there's risks you can't manage, and understanding what those are. So if we think about diabetes, we know that obesity contributes to risk, it's not the only thing that will cause disease but it is a risk factor. So is that something you can control and how can you control it, physical activity is a risk factor, can you control it, how much you could control it – those are two things we have control around about interventions. We can have dietary interventions, we can have physical activity interventions. Even with maybe some of those pieces we can have medication interventions, pharmaceuticals. Some of the other things that we know, genetics, how much genetic intervention can we do, you may have a very low genetic risk, you may have a very high genetic risk, but regardless, you can't really do much about that. We're not quite at the splicing

genome era as much as the Silicon Valley people who inject themselves in the garage want to be, we're not quite there yet. So you kind of got to be like, okay, what can I manage and what can't I; and then, of the things you can't manage, how can you quantify it, and then how do you assess that. So for something like diabetes, if I have a big genetic risk and a big family history, I'm probably going to try to do more prevention and disease management with a physician than I would otherwise. I don't have a big family history, I don't have a huge obesity problem, my physical activity levels are probably adequate, not super high, but they're pretty adequate, so how much do I need to go get yearly blood work done, how much – if I do see, my A1C is creeping up, do I need early pharmaceutical intervention versus do I just need to start being more active, whereas somebody who has a high genetic risk, they probably do need more medical intervention earlier, maybe they start with pretty low dose pharmaceuticals early, because they know, if I can delay it, I have better prognosis. So it's kind of understanding those and quantifying those unmanageable risk, like those things you really can't have a solid intervention for, for managing disease progression.

DANNY LENNON: Right. One of the things I really loved about your talk was before even trying to get into some of the nutrition interventions around diabetes, was trying to actually get people to understand diabetes, because it seems like people think intuitively they know what it is, but really they probably don't because that kind of sound bite that most people think of it, oh diabetes, that's a disease of blood sugar. So maybe to get our listeners on the same page there, what is the best way that you would suggest them start conceptualizing what diabetes actually is?

BRAD DIETER: Yeah, it's one of those things where kind of visual representation, one of the slides I use, it's probably one of the easiest ways to describe it. But the way I like to tell people whenever I'm

just talking about it is if you think about any disease like a diagnosis is really just describing what's happening, it's not what's causing it, and diabetes is very much the same way. So we diagnose it based on an elevated blood sugar, but what's causing that elevated blood sugar? If we think about heart disease, for example, like cardiovascular disease, it just means you have disease of your cardiovascular system, that doesn't really tell you what is it, what is causing it. So diabetes is very similar. You see elevated blood sugar, but what's causing that? And so you kind of go back to why is your blood sugar increasing. Well, it's because you can't get it into the cells properly and your liver's pushing way too much out. Well, what's causing that? The cells are not responding to insulin. Your liver is not responding to insulin, so it's making too much. So you kind of go back, you ask like the five whys, like "why is this cup white?" and you go back to what is the initial thing.

And so that's what I always try to explain to people is the end thing you see is not the thing that caused it. Another example is like a good analogy for a lot of people is think about like your retirement account, is when you see somebody with $2.5 million in a retirement account, it's like, okay, they didn't just make $2 million at one time, they invested it and then the market grew it. So what was the mechanism was it was an initial investment and then market growth. The diabetes is the same thing, what's this initial thing that causes the result in the end.

DANNY LENNON: Again, we're getting on this like parallel with atherosclerosis and cholesterol I was thinking but the same way that we wouldn't say high cholesterol is a disease in itself, it's telling us something might be going on, it might be a marker for something, but what is really going on atherosclerosis wise, the same way as we don't just say, well, the high blood sugar is the disease, this a symptom of something that's going on. The second kind of part was that when you start working backwards, it's

probably important for, like you say, not to look at the end and say, well, that explains what causes it, because the obvious place people jump to then is, well, if someone has type 2 diabetes and they can't really tolerate glucose, maybe it's too much glucose that's causing it, this person doesn't tolerate carbohydrate which we obviously know is not necessarily the case. And one of the big points that you made and I think is a really important point people miss was around the fat metabolism base, and this impaired fat metabolism in diabetes. Can you maybe talk a bit about that and why that is so relevant?

BRAD DIETER: Yeah, and that kind of comes back to the, like, what's the initial underlying cause. So one of the things that's, to me the most interesting part about that disease is the kind of fundamental thing that happens early in the disease is you kind of get – and the only word that I know how to describe it is disordered fat metabolism. As your body normally, you take up fatty acids in your peripheral tissue, primarily your skeletal muscle, and then you store what you need, you oxidize what your body is requiring and you just kind of maintain it. And as you store more energy, you store some in your muscle tissue, you store some in your adipose tissue, and then you just kind of use that. But what happens in kind of the diabetes state is you kind of get this weird, like just feed-forward cycle, where you start getting more energy than you need, your body has to store more than it can oxidize, and it starts storing it as things that I can't ever really use again. So you start kind of getting this – the word we use is ectopic fat accumulation. So it's just fat that's stored in places it's not really supposed to be, and then what that does is it kind of changes your molecular machinery in your cells, and then your body gets less efficient at oxidizing fatty acids, and you start to get some bad waste products. And then those start causing to be less efficient, and that causes kind of damage to your cell, you become insulin resistant, and then you start storing

more fat. So it's kind of this fat metabolism just gets kind of, the whole thing gets out of whack, and you can't really correct it by just eating a specific type of food. As you kind of have a general over storage problem, your body is not handling things the way it's supposed to be, and then that's leading to all these other downstream metabolic problems.

DANNY LENNON: And that comes with cyclical process in many ways. So if you're having this extra ectopic fat, that's going to lead to more, let's say, inflammatory cytokines being around, that itself, as you mentioned today, can cause problems, and that would probably suggest why we don't see benefits to just saying, I will anti-inflammatory foods, for example, without addressing those other causes of that.

BRAD DIETER: Yeah, exactly. And that's been one of the really interesting pieces of a lot of the diabetes research is we've kind of – we've tried almost every intervention at the individual pieces. So we've done the kind of massive antioxidant studies in people with diabetes. So for about a decade, there's a lot of data that was like, okay, oxidative stress is a key part of insulin resistance in people with diabetes; maybe if we just give them a ton of antioxidants, it'll kind of free up that piece of it, and it'll help. Absolutely nothing worked. We had tons of clinical trials and none of them were beneficial. Same thing with inflammation – we started to see some hints that there was an inflammatory component to diabetes, there are some really cool mouse model studies where they just knocked out either receptors for some of the major inflammatory cytokines like TNF or they knocked out the actual protein itself, and it basically prevented diabetes in animal models. So they did anti-inflammatory therapy in humans – also yielded basically no benefit. And so then they started looking at, this is in the 90s, they started thinking, okay, if it's just glucose that's the problem, we can give these people carbohydrate that doesn't elevate blood glucose. So they started doing all these fructose

interventions in people with diabetes, and it helped manage glucose levels a little bit but it did almost nothing for actual disease progression. And so then it was like, okay, there's all these pieces of individuals we've tried to address and none of them had been beneficial. But the one thing we do know is if we relieve the energy excess burden, we see all those downstream things kind of go away, yeah.

DANNY LENNON: And that translates to weight loss interventions.

BRAD DIETER: Yeah, exactly.

DANNY LENNON: So on the podcast before I've talked to Nicola Guess who is now based in Kuwait, just a real superstar in diabetes, and she actually wrote a paper last year that was a really good overview of what we kind of see with nutrition interventions, and again that same type of punch line of weight loss is the most potent thing we see right now, and then there's some other areas where we just don't have good data, if any, including low carbohydrate interventions specifically for this. We are starting to see a few now I think, but it seems that weight loss is this most potent thing we can have. But one of the suggestions around why low carbohydrate diets maybe useful is in terms of management, you're just putting less exogenous glucose into the system. Even if you were to match weight loss with other diets, do you think there's any inherent benefit from a management perspective of just having less exogenous glucose around so that you don't need this insulin secretion?

BRAD DIETER: Yeah, and I think it's, you know, there's kind of twofold here. One is the kind of the disease load itself. And I think part of the question there really is at what stage of disease are we catching people, and so I think low carbohydrate diets, you know, there may be some additional benefit for like, okay, let's just lower the overall insulin load needed from a

physiological perspective, maybe early or in the disease. When we start to see insulin levels going up, your body is requiring your beta – your pancreas and beta cells function to ramp up. There may be some benefit kind of early there. Later stage we have no beta cell function. It's like, well, it doesn't matter. It's like your body is not going to be doing any different work anyway, you're relying on exogenous insulin or exogenous things like that.

So I think there's some interesting questions around there that we just don't have like, early stage, what does that mean, and how does that translate to long term beta cell preservation. We don't think we have any data that I'm aware of, and I don't know how much that would matter if you match weight loss. So I don't know. The more pragmatic question is, from a pharmaceutical perspective, we know that people who are especially later-stage diabetes require insulin, and it can be incredibly expensive, especially in the United States. Our cost – some people pay thousands of dollars a month for getting the medication they need. So if I have clients who need weight loss and they have late stage and they're relying on insulin kind of to manage their blood glucose and we have options and they're pretty open to it, sometimes we'll be like, okay, if we can adopt a more low carbohydrate model, and for the next three to six months while we're losing weight and we can start to see some improvement, maybe we can lower your actual total medication bill by just having a little bit less that we have to push into your body. So those are some considerations that I think kind of practitioners who've had some experience go, okay, if we have two ways to do this or three ways to do this and you have some limitations financially and we can test it, and be like, okay, can we get away with less insulin every day that you have to administer and maybe your medications can last longer.

DANNY LENNON: Another good point that you made today was that key distinction between reversal and

remission of type 2 diabetes, because there's many claims in different places about different diets that can reverse your type 2 diabetes. But the point you made is, if it's true reversal, essentially that would mean when someone goes back to eating normally “like a ton of carbohydrate", they would have a perfectly normal glucose response which is probably not the case. The only thing I can think of from a nutritional intervention sense that seems to hint that some, not even true reversal, but something is going on, is some of the very low calorie formula based diets so like some of the stuff at Roy Taylor's lab, and they were the only ones that actually seem to stimulate some sort of return of beta cell function, at least to some degree but I'm not totally sure. Have you looked at any of those kind of very low calorie formula interventions and what is the kind of current state of evidence there?

BRAD DIETER: One of the things that's really interesting about a lot of the very low calorie literature is when are they getting these people their disease. Is beta cell function completely exhausted – that's a question. Or are you catching it where there's still some function and then you can actually kind of bring them back a little bit from just getting really rapid results really quickly. And then also is there some benefit to extreme caloric restriction that causes some sort of like, okay, we can bring this back from an actual cell differentiation piece. And those are questions I don't think I have good answers to. Those are things that's like, okay, there may be some data, I'm not aware of it. So it is possible. But I think a lot of it would be just from the way we think about it is where are we catching these people in the disease, is it kind of where they still have some function maintained or is it completely gone and now it's like, okay, no matter what we do, we're not getting it back.

But the other question that, and this is a little more kind of in the weeds work but there's a lot of data coming out about the epigenetic changes, and we were working on this in my

lab before I left, is a lot of these, whether it's due to the early exposures, kind of the energy excess or it is the glycemic conditions, is we do see changes to the epigenome. We see this in kind of a large observational studies where we do bisulfite sequencing, we look at methylation patterns on genomes, we see it on chip sequencing where we actually look at histone modifications, or we look at transcription factors, how they're affected. So we do see this change in the epigenome and some of those are permanent. So we do know there's some epigenetic changes that are labile, so they'll go on and come off, but there are some that are permanent. So a lot of these DNA methylation where you actually methylate the DNA base pairs don't ever go back.

So there is some evidence that even if you were do a very low calorie diet, they're not going to come back. So some of those changes do appear to be permanent, and the function of those, we haven't really worked out. We are working on some of the inflammatory genes in our labs. So we are doing a lot of cell culture work, we're exposing things too hyperglycemic conditions and then looking at inflammatory genes and seeing that some of the repressive marks were basically being removed from these genes, so they were just kind of expressing inflammation even after we put them back on normal conditions. So there's some weird long-term changes that appear to be kind of sustained around.

DANNY LENNON: A moment ago you mentioned medication and probably one of the main drugs, if not the main drug used here, is going to be metformin, which the more I try and look into it, the more it seems to be almost a wonder drug.

BRAD DIETER: Yeah.

DANNY LENNON: It's hard to find too many downsides and just like every time I read something there's something new that it does. But certainly from a glycemic point it seems to be extremely

potent, pretty safe, and effective. However, one of the papers that you brought up, the diabetes prevention program I believe, was just really interesting, that goes to highlight I suppose the impact we can have from a lifestyle standpoint. Can you maybe just talk through a very brief overview of that and why that's so relevant?

BRAD DIETER: So the DPP, the Diabetes Prevention Program, was a study that was done for quite a while, several cohorts went through it over several years; and it was basically, they took people who had pre-diabetes and they randomized them to a placebo, so nothing, metformin which is kind of standard of care, first drug that most people get at least at the time now sometimes people will get a different one depending on where they're at or lifestyle, so basically diet and exercise. And they followed these people for four years. Basically, what they were able to show is that if you get people metformin, they see their risk of progressing to diabetes go from 40% to about 30% roughly and people with the lifestyle intervention saw a reduction from 40% to 20%. So the lifestyle change is actually almost twice as effective as the medication. And basically what we think that comes down to is the metformin helps with a lot of – it kind of targets one of the pathways that's involved in insulin resistance, it's AMPK, it kind of helps with some of the metabolic issues that are going on with the impaired fat metabolism and glucose metabolism, but it's not hitting everything where kind of the weight loss, the diet, the exercise starts to impact a lot more pieces, and those risks are kind of reduced for a longer period of time, yeah.

DANNY LENNON: When we think about diabetes and the association with obesity, we've talked so far about weight loss being that main intervention from a nutritional standpoint that's going to benefit. There's people that would have reservations. Is that association as strong as people suggest it is? Is it as causative – and primarily I'm thinking about some discussions

I have had in the area of health at every size, weight neutral approaches, of which I think there's a lot of value in those and I've kind of voiced those before. But one of the points I struggle with is this disassociation between those two things, and what I think might be a missing piece is something that I've heard you talk about before is almost this lag time when we're looking at the rates of obesity and some of these chronic lifestyle diseases, and that lag time that people are saying, look, they don't match up, that there's an explanation for that.

BRAD DIETER: So with the lag time piece and this is I think a pretty interesting and important point is to go back to our initial discussion of kind of like the risk accumulation, is if you become obese tomorrow, you're not going to develop diabetes and heart disease the next day. The disease process takes time and each person is a little bit different. One person it might take three years, one person it might take 10 years, another person 15, and another person may never end up having some of those comorbidities. But the associations are super strong, and we do know that there is a lag time. We see this in epidemiological data, we see this in kind of the cohort data; and we even see this, if you've been a clinician or worked with clinicians, they will tell you, here's the natural history of this disease, here's the course it will take, here's the percentage of people who will exit the pool to disease, here's the people who will remain disease-free. It's kind of like smoking. If you start smoking today, you're not going to get lung cancer tomorrow. If you smoke for 30 years, your likelihood of developing cancer increases every year. But it doesn't mean you're perfectly healthy at year one, at year two, at year three, year four, you're just accumulating risk. And then there's also people who will smoke for 30 years and never develop a disease, but that doesn't mean that that behavior is "healthy".

So that's kind of the lag time piece, and then the other piece, I think we had talked about

this a little bit, is just having people have a better understanding of the risk, and quantifying it in a different way. So if we kind of take the discussion of weight and all these diseases is realizing your likelihood of developing any of these chronic diseases, heart disease, cancer, obesity, diabetes, etc. You have all these pieces that play into it. You have blood pressure, you have lipids, you have your fasting glucose, you have smoking, drinking, exercise, nutrition patterns, all those pieces. And then weight is one of those pieces. And in some diseases, weight has a better diagnostic prognostic value than in others. So for some cancers, weight is not predictive at all. For obesity or for diabetes, we know weight is very predictive. For heart disease, we know weight is very predictive. For other diseases, we know it's not. So just kind of starting to maybe bend that weight piece as here it is as a risk factor, along with everything else that is in your life, and here's how you track it. And so instead of having it, you know, putting it that way I think is an easier way to have discussion. That's pretty divorced of some of the more political discussions around it, and some of the social stigma around it, and I think it maybe is more useful for people.

DANNY LENNON: Yeah, because there is good points on both sides, so someone could make a very good point now, well, let's just look at people's metabolic markers, there's other things that are more directly related, let's say, to pre-diabetes or type 2 diabetes. But also there are many behaviors that person can follow that aren't around weight loss intervention. We don't the target weight loss but we can get them sleeping better, get them more physically active that are all going to play a role. But what I like about your discussion around this risk equation is that fits perfectly within that. You're just choosing to work on these other variables within that risk equation that change your overall risk, physical activity, lifestyle, sleep, stress, whatever it is, but you're just not choosing to say, we'll focus specifically on

weight loss. But one of the things that, I'm sure people have heard me mention this several times in the podcast before, that I think through with this, I come to diabetes as the example of being when we know that, let's say someone loses 10% of their body weight and that what that does to their risk of diabetes, is there anything outside of weight loss that you can change with all these other health promoting behaviors that can get anywhere close to that impact on someone's risk, now that's not me saying, we need to counsel everyone on weight loss, but there needs to be an acknowledgement that is there anything as potent I suppose as that.

BRAD DIETER: Yeah, and I think that's where part of it comes from is understanding the outcome. So for some patients, they may not have a huge care about what their risk of developing diabetes is. For some, it may be something completely different. But just acknowledging what the risks are, and just kind of saying this is this risk, this is this risk, we can do risk mitigation here, we can do risk mitigation here, this is a piece that you don't want to touch, totally fine. But just, here's the box where that risk is and just let's acknowledge and say this is here, we can work on it, if that's something that you really feel we could do. I kind of think about it like, an analogy that I'll draw is in athletes is their risks for different things add up. So if we think about risk of injury, perfect example would be, like, did you watch the NBA Finals this year at all with Kevin Durant, Game Five. Everybody kind of had this big reaction to it. And if you think about it, what he was doing is, he was doing the risk management in his head, and his doctors were, and he was like, okay, you've got a 2% risk of tearing your Achilles if you play in this game. And so he was kind of doing, okay, here's what I value, here's the risks that I know, and here's what I'm willing to do. And we do this with athletes all the time. And so he probably worked with his physicians, made the decision, and then we all know what happened. But it was like, he did a risk

assessment and then made a decision, and I think people should have that ability, but they should not ignore what those risks are.

DANNY LENNON: That's what I like because it fits them perfectly within whatever paradigm you want to choose and if we are, example, using health every size, then we can say, yeah, here's different risks but we're choosing not to focus on this because of reasons X, Y, and Z which are part of that philosophy, which is cool, we can focus on these others. As you mentioned the Kevin Durant example, it kind of reminded me of before I've mentioned good versus bad decision-making and how a lot of people have retrospectively tried and explained it, whereas that's just not the way decisions work. And that's a perfect example because, as you say, if there's a very low risk of reinjury, and the injury had it, I think, there was actually almost no chance of reinjury, it was another freak accident, it was Achilles, it was Game Five in NBA final – all these other variables that go into it, gets cleared by the team doctor. So if you lay all that out, you can only make a decision on if it's good or bad at that point, you can't wait to see the outcome. So in that case, you could probably say, mostly we would have agreed, yeah, he's got to play, it's a good decision. But then it's very easy afterwards for people to say, well, I made the wrong decision because he got injured. But that's not how decision-making works.

BRAD DIETER: Yeah, exactly. And I think that's part of the difficulty of health science, of dealing with a lot of these things is we have large population data, so we've got a good idea of how risk plays out on a large level. But on individual levels, we don't really know. So you can take the people who go, the thing that matters to me the most is my health. I'm going to make sure I always have a really lean body, my physical activity levels are always super high, my nutrition is always perfect, I'm never going to smoke, I'm never going to drink, I'm going to live in a HEPA filtered air in my house, I'm going to

drink filtered water, and then they get diagnosed with cancer at 36. It's like, okay, they managed all the risk but then there's the unmanaged risk. Then you've got the other side of the coin where you've got the people who will do everything wrong and live to a 100. And so, there's still a lot of this kind of residual unknown, but then understanding that, we do know some risks, here's how we should talk about it, and here's how we can intervene on it.

DANNY LENNON: Before we finish, one big question I'm intrigued to ask you, because I've been trying to ask some people about this recently, and it kind of actually directly relates to what we discussed with prevalence rates right now of obesity, prevalence rates of chronic diseases related to lifestyle, and with that kind of consistent uptick right now and all the challenge that proposes, are you more optimistic or pessimistic about us being able to do something about it?

BRAD DIETER: Both. And I think the pessimism comes from we haven't seen the worst of it yet, and it's going to get substantially worse before it gets better. So I think that's the pessimism. I think the other pessimism is we're going to biomedical-engineer our way out of this problem, either one, the problems are so intractable that we just can't figure out a clean solution for them or two it's going to take us so long that we will have been so far past the point of being able to address this with all these people whatever we find, that it's going to be too late. And I think that's pretty much shown true with most of what we've tried to do. Obviously, the Human Genome Project did not do what we thought it was going to do. The Cancer Moonshot project taught us a lot about the biology of cancer, we've made a lot of progress in the area, but we haven't solved that problem at a fundamental level. So I don't think we're going to biomedical-engineer our way out of it. The optimism piece, I think, comes from, if we start changing how we view the problem and start putting the resources in place, I think we can do a good job of kind of

managing the tides so to speak, and then slowly reversing the trend, because we have a population of very sick people now, we have a population of people that is going to become sick, and then we've got a population that's healthy and hasn't become sick. And so we have to manage the people who are currently sick, we have to figure out a way to slow the progression and manage the people who are becoming sick, and then we have to find a way to prevent the, maintain the health of this population longer – and how do we make, if only 30% of the population is going to be healthy now, how do we get that to 35, how do we get that to 40, and so that's kind of where the optimism lies, is I think, with very simple tools, but big powerful interventions, I think we can actually start to make some change.

DANNY LENNON: I think my optimism comes from the robots will wipe us out before it gets worse, but when you said you suspect it's going to get substantially worse, then it gets better. What is substantially worse?

BRAD DIETER: So cost, we're going to run into major economic issues, I don't think people are fully grasping in the next 10 years of what we're going to run up against financially, that's the first piece. We're starting to see it kind of break at the seams, but we still have – we're not quite to where it's mass hysteria yet, and it will not be pretty. That's coming down the pipeline for sure. The other thing of substantially worse is if we think about what makes a productive society of happy, healthy people, living together, being happy, building an economy, the more sick a population gets, the less productive they are and the more help they require. And so I think as we see a large percentage of the population become more unwell they're going to be less contributory towards society. And so, I think that's another big piece that we haven't fully grasped yet. We're starting to see a little bit of this in kind of a microcosm, in some of the countries that have had, you know, they had large families for a while, and now they've kind

of limited whether it was like in some of Asian countries where family size has really dwindled down and they just have a more aging population, and there's more young people taking care of their parents. We're starting to see some of that productive versus non-productive members of society and how that can start to impact some things. So I think we're going to start seeing more of that too.

DANNY LENNON: With the scale of the problem, do you think the solution is going to have to come from like a top-down level that's going to be rolled out as opposed to anything that people can do bottom-up, like, is it going to have to be policy rolled out at nationwide level, governmentally, that's going to be the end solution or what the alternatives are?

BRAD DIETER: I think it's a combination of both. I don't think like policy and rules and governance is really where there's going to be progress made, I think it's going to be how does the top who has all of the resources support the infrastructure. I think if we can get support from those people, if we can get buy-in from the government, and some of the policymakers, I think that's key, but I do think it's going to be a large effort on just kind of changing the structure of how we live, and it sounds really ambiguous, but I think it's going to be – I think the work is going to be done bottom-up, I think the resources are going to have to come from top-down. And I don't know if it's – it probably won't be one of those, like, snap your fingers and everything changes, it's kind of like our current situation we're in, it didn't just happen overnight. It happened quickly, but it wasn't like, hey, we rolled out this food plan, we rolled out this economic subsidy, we rolled out this guideline, we rolled out X, Y, Z, and just kind of society changed. Values started changing, companies started keying in on certain aspects of human behavior, and it's going to have to be the same way, and I think we're – I think we're starting to do pieces of that, it's just going to take a while for it all to coalesce, yeah.

DANNY LENNON: Brad, you've been super kind with your time as it is. So before I get to my final question, where can people find you on the internet?

BRAD DIETER: They can find me, Google me, I guess. Yeah, you can find me on Facebook or Instagram, I am on both those places. All of our coaching is done at Macros Inc., my website, where all my writing is on science driven nutrition, and those are probably the best places to reach me.

DANNY LENNON: Awesome. I will ask you a question that you've received before but as – at least this happens with me when I think about this question, my mind changes all the time, so I'm sure yours will. If you could advise people to do one thing each day that would have a positive impact on any area of their life, what would that one thing be?

BRAD DIETER: I would say, one thing I've been doing lately is telling people how grateful I am for them because I think, one, it's helpful for somebody else. I think a lot of people don't get a lot of appreciation. And two, the more you realize how lucky you are, I think it kind of changes your perspective. So whenever I'm having a bad day or a bad week, it's trying to go out of my way to tell somebody how grateful I am for them, and I think that's been really helpful.

DANNY LENNON: Awesome. Man, thank you so much for this, it's been awesome to spend some time and to be able to hang out.

BRAD DIETER: This is great, perfect.

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