Episode 408: Cardiometabolic Risk, Lipoproteins and Metabolic Disorders With Dr. William Cromwell

Child: Welcome to my Mommy's podcast.

This podcast is sponsored by BluBlox glasses. Did you know that Blue light damages our eyes and leads to digital eye strain when it comes from artificial sources? Symptoms of digital eye strain are blurred vision, headaches and dry watery eyes. For some this could even cause heightened anxiety, depression, and low energy. I personally noticed that when I was exposed to blue light after dark, I didn't sleep as well and felt more fatigued the next day. BLUblox are the evidenced backed solution to this problem and made under optics laboratory conditions in Australia. They have over 40 styles and come in prescription and non-prescription so there is a pair for everyone. I also love that BLUblox is also giving back by working in partnership with Restoring Vision in their buy one gift one campaign. For each pair of BLUblox glasses purchased they donate a pair of reading glasses to someone in need. Really awesome company and really awesome mission. Get free shipping worldwide and 20% off by going to blublox.com/wellnessmama or enter code wellnessmama at check out.

This episode is brought to you by Beekeeper's Naturals. They're on a mission to reinvent your medicine cabinet with clean, effective products that really work. Every year we decide to be more healthy this time of year. And to do that, we need to start by supporting our immune systems, especially right now. That's why they've created a whole hive of products packed with immune loving essentials, so you can feel your best every day. One of my favorites is their Propolis Throat Spray, which is an easy daily spray for just general immune support and is also very soothing for sore scratchy throats. Propolis delivers natural germ-fighting properties and antioxidants to defend and protect our bodies. Theirs is sustainably sourced and it's made with just three simple ingredients. You'll never find refined sugars, dyes, or dirty chemicals in their products ever. When you're ready to upgrade your immune system and your medicine cabinet, check out Beekeeper's Naturals and discover all of their clean remedies that your family will love. You can save 15% on your first order by going to beekeepersnaturals.com/wellnessmama.

Katie: Hello, and welcome to "The Wellness Mama Podcast." I'm Katie from wellnessmama.com and wellnesse.com. That's wellness with an E on the end. It's my new line of personal care products. And I would really recommend you check out our whitening toothpaste and completely natural hair food hair care. Those are all available at wellnesse.com.

This episode goes deep on something called cardiometabolic risk, understanding lipoproteins and metabolic disorders. I'm here with Dr. William Cromwell, who is the chief of the Lipoprotein and Metabolic Disorders Institute in Raleigh, North Carolina, and who is one of the foremost experts in the world on these topics. And I feel like this was an important topic to really tackle, as we are still seeing rates of things like diabetes, heart attack, and stroke all continue to rise. And there are special considerations for this especially for women. So, in this episode, we go deep on what cardiometabolic risk is, how this ties into insulin resistance and what we need to know about that, the specific testing that's helpful in evaluating long-term risk, and the lifestyle factors that we all have control of that can affect our long-term risk and whether or not we are likely to get things like diabetes, heart attack, and stroke. And he has some very specific metrics that he checks, as well as

some comprehensive reports that take all of these into account. And I think you'll learn a lot. I know I did. So, let's jump in. Dr. Cromwell, welcome, and thanks for being here.

Dr. Cromwell: Hi, Katie, it's my pleasure.

Katie: I'm so excited to chat with you and your area of expertise is one I think that is so important and necessary right now. And I'm so excited to dive in and share your knowledge with the audience today. To start broad, I'm gonna have some very specific questions, I think, and really excited to delve into this with you. But to start broad and kind of define some of our terms, can you explain a term that you use often, which is cardiometabolic? Explain what that is, and what cardiometabolic risk is?

Dr. Cromwell: Sure, happy to. I think your audience is familiar with the components that we weld into cardiometabolic risk. So, cardiovascular risk includes heart attack, stroke, as well as bypass surgery stents procedures to open clogged vessels. So that's cardiovascular risk. Diabetic risk entails not only the propensity to develop diabetes, but it's the metabolic state that leads people to the formal diagnosis of diabetes. Some people call it dysglycemia or difficulties with glucose metabolism. And what we now know is that those two entities are not separate. They're actually highly interrelated. So cardiometabolic risk entails both traditional factors, emerging factors, and the metabolic milieu that collectively put people at risk for developing diabetes, heart attack, and stroke.

Katie: Got it. That makes sense. And when you explain it like that, it makes sense that these things are all related. But I feel like often when they're talked about, at least in news articles and health articles, often they're kind of separated into their own silos. But from what I've read of your work and researching for today, like, you make a strong case for these things are extremely intricately connected. Is that right?

Dr. Cromwell: That's exactly right. It's really, I think, not a really new topic. But as you said, I think very appropriately, it's been siloed. The heart disease patient has been thought of as their own entity, the diabetic patient has been thought of as their own entity, but the work that I actually integrated this goes back some number of years. Some of your listeners may be familiar with the work of Dr. Gerald Reaven, back in the '80s. And he was one of the first people to propose that there was an integrated pathology called the insulin resistance syndrome. And people call that syndrome X or the metabolic syndrome. And it was his work that really led us to understand that there's some common soil that grows both heart disease and diabetic risk.

Katie: Okay. So let's go a little deeper on that because I think that makes complete sense. And I think it's something that's maybe not talked about nearly enough, as it should be. Most people listening, probably at least have a passing understanding of what insulin resistance is. But for anyone who doesn't, can you explain what is going on when insulin resistance happens and then how that is kind of like a slippery slope into a higher risk factor for some of these conditions?

Dr. Cromwell: Yes, absolutely. So, first of all, this is extremely common. Estimates of frequency are that about 60% of the U.S. population harbors a genetic predisposition to insulin resistance. And what we're referring to when we say insulin resistance is that insulin is produced by the pancreas. And insulin works primarily on three tissues, liver, muscle, and fat cells. And the effect of insulin under normal circumstances is to regulate both glucose and cholesterol metabolism. And the insulin resistance state, what's happening is the body's making plenty of insulin. But those particular cells, liver cells, muscle cells, fat cells, are resistant to the insulin signal.

An analogy would be when you're asking your teenager to take out the garbage. And it may not happen right away with the first request, and you might have to repeat the request once or twice or three times. And what's happening is you're having to repeat yourself in order to get the intended effect. And similarly, when these tissues are resistant to the signal of insulin, the body repeats itself, the pancreas produces more and more insulin in order to achieve the desired effect. So this is the beginning of peripheral insulin resistance. And this insulin resistance state is usually present for several decades before people get into more commonly recognized expressions of insulin resistance, such as elevated glucose, elevated blood pressure, increasing body weight gain around the center part of the body. All of these manifestations of insulin resistance occur over time, but the insulin resistance state itself has been present for quite a long time before those things manifest themselves.

Katie: So what would be some way someone could know if they had insulin resistance and if this was a problem for them?

Dr. Cromwell: Well, it's a good question because early on in Dr. Reaven's work, he identified that the earliest objective manifestation of insulin resistance was disorders of cholesterol and triglyceride metabolism. So when we think about cholesterol and triglycerides, these are fats that are in our blood. They're used either for the purpose of cell membranes, making hormones, or in the case of triglycerides, storing energy for a rainy day. We absolutely have to have these fats or we would not be alive. And so, there is a very elegant, integrated pathology in which the body normally manufactures and transports cholesterol and triglyceride throughout our body. The earliest objective manifestation of insulin resistance is when triglyceride levels rise. And that is due to an increased production of particles that carry triglyceride called very-low-density lipoprotein or VLDL.

So numbers of VLDL particles are going up, specifically numbers of large VLDL particles are going up, and the lipid expression of that is triglyceride going up. The other things that are happening as that goes on is that there is an increased number of low-density lipoprotein particles, LDL particles. And those particles are particularly small in size. So there's an increased number of small LDL particles. And then the third thing that happens as this triumvirate, if you will, is that HDL goes down, both HDL cholesterol and the number of high-density lipoprotein particles they're carrying that cholesterol. So the earliest objective manifestation, which is often overlooked, is this lipoprotein disorder, which predates increases of insulin levels in the blood, predates increases in glucose. And so what you have is this kind of slow evolution of insulin resistance.

As the cells become resistant to insulin, glucose levels begin to rise. And they typically rise into the upper limit of normal range, say 80 to 90. After a while, when the cells are not able to maintain normal physiology, we get into a pre-diabetic state where glucose is getting into the 100 to 110 range. And the body can compensate with increasing insulin production to maintain that level for a very, very long time. So people are in the mildly elevated glucose state often for decades before they ultimately transition to diabetes.

Katie: That's fascinating. And it makes me wonder because obviously, cholesterol has gotten kind of a bad rap in at least a lot of the mainstream medical publications I've seen over the last decade. And there's kind of this widespread acceptance that you don't want high cholesterol. But you've said, you know, cholesterol is essential. And that's it's a building block of the body. So, it would seem that obviously, that cholesterol in and of itself is not inherently bad. And you mentioned the ratios and the levels. But you also mentioned triglycerides. Is it more helpful to track triglycerides than just general cholesterol or what can people know if they're getting lab results for some of these cardiovascular factors?

Dr. Cromwell: Well, you know, that's a great observation because the whole cholesterol controversy is twofold. Number one, as you said, cholesterol is necessary for life. So, it's not a bad thing. We're programmed to make cholesterol and all of our cells need it. But what's actually happening is that cholesterol does not cause vascular disease, and there's not a good cholesterol, and there's not a bad cholesterol. And it turns out the cholesterol are carried inside lipoprotein particles. And I want you to think of a lipoprotein particle kind of like a tennis ball. It has an outer spherical shell. It's hollow in the middle. And in this particular case, a lipoprotein particle is a sphere that is hollow in the middle. And these are what actually get the letter names. Low-density-lipoprotein, LDL is a particle. It is not cholesterol. Now, it turns out that these particles carry cholesterol, but it is the particle itself that interacts with the artery wall and other areas of the body to specifically increase risk of vascular disease, heart attack, and stroke.

So, thought of in this way, if you have many of the particles that are injurious to the wall of the artery, LDL particles, the more you have for the longer time, the more risk for heart disease you have. The way cholesterol fits into this is that cholesterol is what is being carried inside the particle. And we use cholesterol because it's a cheap, easy measure to approximate if we have a lot of the types of particles that we're worried about, for example, LDL. Not to go too deep in the weeds, but the reason this is controversial is because the amount of cholesterol in a particle is highly variable. Two people can have either a lot of LDL in their particles and cholesterol in their LDL particles, or they can have very little cholesterol in their LDL particles.

And why that's important is at the same level of cholesterol. Two people can have very different numbers of LDL particles. Some people can have a lot of LDL particles, some people can have very few LDL particles. And what we now know after many decades of research is, it is not the cholesterol measure, it's the number of particles which is strongly related to risk of disease. So, put another way, if two people had high particle number, one person could have a high LDL cholesterol, one person could have a low LDL cholesterol. If you have a high particle number, your risk of heart disease is high. In one situation, it's identified because the LDL cholesterol is high. In another situation, it would be totally missed because the LDL cholesterol is not high.

And so this is where the controversy of does cholesterol have a strong relationship to heart disease comes in. Many people have questioned how strong is the relationship between cholesterol and cardiovascular disease? And if that was the whole story, it's just your cholesterol level, then it would be very controversial. But when you look at it through the lens of how many particles are carrying your cholesterol, it's not very controversial at all. Because what we can say is that if you have high particle number for a long time, your risk of heart disease is elevated regardless of your cholesterol.

Katie: That's really interesting. So, this might be a controversial question then but then how do, for instance, statins come into play on this? Because I've heard personally from people who have had elevated cholesterol and been given statins, and to my knowledge, never been told by their doctor that maybe they should consider things like their diet and like any insulin-related factors and how much sugar they're consuming. If it's not too controversial to tackle, how does that come into play, and is that actually the solution in light of kind of the metabolic explanation you just gave?

Dr. Cromwell: Well, it's a great question. So, I think what we wanna do to clarify the situation is to go back to first principles. And the first principle is what's actually happening in the body when we're insulin resistant, that puts us at risk for heart disease, heart attack, stroke, and diabetes? And the answer is, it's all about lipoproteins and not the cholesterol or triglycerides themselves. So let's go back to what we talked about a couple of minutes ago. In the insulin-resistant person, you have an increased number of large VLDL particles, an increased number of small LDL particles, a decreased number of large HDL particles. And that is what is putting people at risk for diabetes, heart disease, and stroke. When we find that, when we find the insulin resistant individual, we have an opportunity to intervene with lifestyle appropriately directed to improve insulin sensitivity. And as we improve insulin sensitivity, many things happen. One thing that happens is that glucose levels begin to fall.

Another thing that happens is the number of bad particles or atherogenic particles that would increase risk of heart disease, likewise, go down. And so what we'd like to do is to find this common soil that grows heart disease risk and diabetic risk as early as possible, and intervene with lifestyle measures that have been proven to improve insulin sensitivity. In doing that correctly, in doing that well, many people will find improvements that lessen their need for medications, such as statins. It doesn't mean we don't have to use them. But the real common soil, the root cause is insulin resistance. And the better we improve insulin sensitivity, the fewer medications we need and the more effective medicines will be if we have to use them.

Katie: Gotcha. Okay. I love that you brought up the lifestyle side because I say this a lot on here. But at the end of the day, I think we are each our own primary healthcare provider and that we have the responsibility to take ownership for our health first. And I think the best outcomes happen when you have educated patients working with educated doctors and patients who are willing to actually do the work in the time when they're not visiting the doctor. And so, you mentioned lifestyle. I'd love to go a little deeper on understanding how we can track the insulin resistance equation and start improving it because you mentioned that if you can improve that through lifestyle, you see a reduction in these risk factors. And that makes complete sense in light of what you just explained. What are some ways we can start tracking and improving those things?

Dr. Cromwell Sure. Well, the best way for us to identify what I've already described is called the insulin resistance score. And this is specifically using nuclear magnetic resonance spectroscopy or the NMR lipoprotein insulin resistance score. That has been shown in a number of well-validated trials, including Women's Health Study, the Multi-Ethnic Study of Atherosclerosis, Cardiac Prevent, the Diabetes Prevention Program. When you have that metric, which is a multi-marker, which ranges from a low of less than 25 to a high of 100, the LPIR score is significantly independently predictive of transition to diabetes at any glucose level. It's independent of waist circumference. It's independent of body mass index. It's independent of insulin level. It's independent of triglyceride. It's independent of the triglyceride HDL ratio.

The LPIR score is a critical variable to identify insulin resistance. And what we know is that at any given glucose level, the higher the LPIR score, the greater the risk of diabetes. At any given glucose, the lower the LPIR score, the less the risk of diabetes. And if we look at one of the landmark intervention trials, demonstrating that people at risk of developing diabetes can have that significantly reduced by diet and exercise, this would be the diabetes prevention project. The most important variable that is associated with improvement and avoiding progression to diabetes is improvement in the LPIR score.

Katie: Okay. So what things correlate with improvement in that score? I'm curious because I know, like I track labs regularly for fun, and I've seen things that impact. But although it seems that one is not what I'm familiar with. And on general labs, I'm familiar with, like the hemoglobin A1c, and I'd often just measure things like fasting glucose out of curiosity. I'd love to hear how those relate, if they do, and what are some of the things we can do, each of us individually to improve that score or any of these labs?

Dr. Cromwell: That's a great point. So, actually, what you're teeing up for a conversation is the fact that most commonly people are using a metric of glucose to assess their risk of diabetes or where they are in a progression toward diabetes. American Diabetes Association, for example, would categorize fasting glucose as normal at less than 100, borderline or pre-diabetes at 100 to 125, and diabetic if you were 126 or higher on multiple occasions and a normal physiologic state, which means not on medications that would upset your glucose and not being ill. Now, the challenge with that is, glucose change is a very lagging indicator of risk of diabetes. As I said earlier, it is very common for the insulin-resistant person to have a compensated state of elevated glucose, say 100 to 110.

And the question you can ask is, well, what is your individual risk for developing diabetes at any particular glucose level? What we know is that there is a wide range of individual variability at the same glucose. For example, at 105 glucose, some individuals can have a 15% risk of diabetes over eight years. Other people at that same glucose could have a 45% or 50%, risk of diabetes over eight years. So, 15% to 50% is a huge individual range. And how would you discern where an individual is at a given glucose? That's where you can integrate fasting glucose and the LPIR score. And by knowing those two together, you can get a much more precise estimate of eight-year diabetic risk. And what would be very interesting to your listeners is that this is very gender-specific. Women and men have a very different impact of insulin resistance at the same glucose,

with women having a much broader range of diabetic risk and a much higher range of diabetic risk as insulin resistance scores increase versus their male counterparts.

Katie: Interesting. And that seems like this is something that's coming more to the forefront of the conversation, which I think is really important because it seems like for a long time, studies were done a lot more so with men, which I get. It's easier to study men, there's less hormone fluctuations, but I love that we're now seeing data specific to women. And it seems like things like this are incredibly important to know, especially for the majority people listening being women. Is there a time and a place for things like fasting blood sugar, just as a metric, since that's one that we can all kind of do at home? Or I asked somewhat personally curious as well. I've had the chance to wear a continuous glucose monitor recently, which I've just found fascinating for the data of seeing how my body responds to different foods. But I was also able to see my fasting glucose every morning, which is about 83, which I think is in a good range. But I'm curious, like, can we use that data to our advantage, even if it's not necessarily as much of a gold standard as that LPIR test that you mentioned?

Dr. Cromwell: You know, well, you can use that. And, you know, as a single metric, fasting glucose is something that will give you a directional sense over time as it rises. It will give you the directional sense that you are moving in a direction of potentially increased risk. But this is what we wanted to address specifically so that everybody could have available to them not only in fasting glucose, not only in LPIR score but also eight-year diabetic risk assessment that is gender-specific. And so, this is where we started precision health reports as a company that brings forward precision cardiometabolic testing and reporting for individuals so that people can know exactly where they are for their diabetic risk, for their cardiovascular risk in light of insulin resistance, metabolic syndrome, LPIR score, lipoproteins, and glucose.

And so, armed with this information, you asked question a couple of minutes ago, what can you do if you happen to find someone who is insulin resistant, has increased risk of diabetes over an eight-year period of time? This is where therapeutic lifestyle intervention has shown marked reduction in risk. One example, if you look at the Diabetes Prevention Program, which was a randomized trial of 3,000 individuals at risk of diabetes, who underwent lifestyle change and weight loss, there was a 60% reduction in transition to diabetes, which was twice as good as the decreased risk observed individuals who were treated with a drug called Metformin. So that was an observation some years ago. We now know that that can be tuned to specifically get even better results, in many cases, with carbohydrate restriction, with intermittent fasting, with other approaches that are tuned to specifically address insulin resistance and improve insulin sensitivity.

Katie: Gotcha. Okay. So can we go through some examples of that? I'm just thinking off the top of my head from research I've seen and also from having gotten the chance to track some of these metrics in real-time on myself. I would guess some of the building blocks of that equation would be things like exercise and protein consumption, reducing refined processed carb and sugar consumption. I found for me, actually like sunlight was an important hormone signaling factor that over time has been helpful. And also not one for everybody, but sauna use seems to correlate with improvement in some of these risk factors over time. But when you have someone coming in who is at a higher risk, what are the factors that you have them address first?

Dr. Cromwell: So it's a great question. So let me start with the tail of that question and work backwards. When someone comes in to see me, what we put a great emphasis on is understanding the individual factors that make their risk of heart disease, diabetes, stroke, what it is. From a diabetic standpoint, it's looking at their LPIR score, and their glucose, and their eight-year diabetic risk. On the cardiovascular side, as your listeners I'm sure are aware, there are a number of different guidelines that give physicians and practitioners kind of a general roadmap of how you would assess risk. You start with major risk factors, you look at lipoprotein levels, but there are some 17 plus additional risk enhancing factors that people may or may not be familiar with, that also fit into the individual assessment of their risk. At the end of the day, when we find individuals who have the insulin resistance syndrome or the metabolic syndrome, we have found individuals who have that common soil, which over time put them at risk for diabetes, heart disease, and stroke.

So, the things that you've already touched on that are critically important from a carbohydrate level, it is the type of carbohydrate and the quantity of carbohydrate. Refined carbohydrates need to be severely limited. Quantive carbohydrates fits into an interesting conversation regarding how much carbohydrate restriction is necessary in order to improve insulin sensitivity. There are data out there for individuals who want to go on a more aggressive carbohydrate-restricted approach, which would be a keto approach. There is a modest carbohydrate restriction, which would not necessarily put you into a ketotic state, but would definitely limit excess carbohydrates. And that would be something in the order of 50 to 75 grams as a maximum carbohydrate intake per day.

There's also the incorporation of intermittent fasting, which itself has a huge opportunity to improve insulin sensitivity over time. And as your listeners I'm sure are familiar, the intermittent fasting concept is one where you limit calorie consumption to a window of time per day. And by so doing, what you're allowing the body to do is to be fed during, say, an eight-hour window, and the rest of the time and the body needs calories. It must recruit calories from existing energy stores in the body, such as our fat cells. And that's what promotes an improvement in insulin sensitivity. By combining restriction in refined carbohydrates, emphasis on naturally occurring lower glycemic index carbs, such as leafy greens, low glycemic index fruits, non-starchy vegetables, limiting total carbohydrates, say to 50 to 75 grams per day, and then adopting a window of eating say eight hours from noon to 8:00 pm, or shorter window if necessary. The combination of those factors on a sustained basis really improve insulin sensitivity from a diet perspective.

Katie: That makes sense. And I love that you brought up intermittent fasting or time-restricted eating. I've seen those changes in my own labs. And that's something I now practice. I'm a big proponent of not doing the same thing every day. So I don't eat in a six to eight-hour window every single day, but I do most days. And then I also eat in a longer window and spike calories occasionally just to signal the body that it doesn't need to downshift metabolism. But I love that you brought that up because I think it's such a valuable tool and easier than just basic caloric restriction for a lot of people, because you're still able to eat food, but just in a shorter window. So it feels a lot less depriving to many people. And like you said, as well, with carbohydrates, it's very much about the type and the amount.

And I know I've seen from tracking my own levels, I don't think it's that carbs inherently are bad at all. In fact, I'm finding the more I work out, I actually need certain types of carbs, where I don't feel good after a really intense workout. But in general, on average, in America, we know we're eating too many carbs, especially processed carbs, which so easily convert, essentially, like the body treats just like sugar. We're eating so many of those and we're not moving as much as we should be moving to need that much fuel. So when you think of it in a fuel perspective, we're over fueling and not using the fuel, so it has to get stored somewhere. And that leads to that equation that you mentioned. But it was fascinating for me, I think there are very personal aspects here... But to see, for instance, things like sweet potatoes did not really spike my glucose at all, especially when I ate them with protein and other vegetables, whereas things like white rice would immediately skyrocket my glucose.

And I think there's an individual aspect there. But that was a really helpful thing for me to see and really kind of brought home the things I had seen in research, I got to see them in real-time in my own body. How can people know if their lifestyle changes are working to decrease the risk of diabetes, and heart attack, and stroke?

Dr. Cromwell: That's a great question. So, what you really need to track are the metrics that are most closely associated with insulin sensitivity, decreased transition to diabetes over time, as well as decreased cardiovascular events. And that boils down to a couple of things. First, we go back to the LPIR score. There are many metrics that overlap with the insulin resistance state. And I've mentioned a few of them before. Glucose is one, increase waist circumference is one, high triglycerides are another. High triglycerides and low HDL together as a ratio is another. Some people look at insulin levels. But when you take all of these things into account, and you put them into a predictive model, and you ask the question, since they overlap with each other, what happens, if in research terms, I adjust the relationship of the LPIR score with diabetic risk? If I put glucose in the equation, does the LPIR continue to significantly independently predict diabetic risk? And the answer is yes.

Okay. Let's add something else. If I add waist circumference, does it continue to predict? The answer is yes. If I add body mass index, does it continue to significantly independently predict? And the answer is yes. We can continue doing this by adding insulin, a metric of insulin and glucose. Some of your people will remember HOMA-IR. At the end of the day, it is the LPIR score, which is the single most predictive and instructive element to understanding your improvement in diabetic risk. On a cardiovascular side, it's really not your cholesterol levels. It's the number of particles that are carrying your cholesterol. And that can either be measured as an LDL particle number or as a test called Apolipoprotein B as in boy. ApoB is the protein on the outer surface of these atherogenic or injurious particles. And by tracking your response for either particle number or ApoB, you have a much more discriminative test of are you meaningfully reducing the risk that would be attributable to your LDL and atherogenic lipoproteins. So those are the types of things that can tell you immediately, at the most discriminative level, how am I doing as I'm improving with diet, exercise, therapeutic lifestyle change.

Katie: Fascinating. Okay. And you touched on the waist circumference a couple of times. And I'd love to just explain this a little bit deeper. Because this is another great thing I think people can measure at home and

don't necessarily think to measure and track but it is correlated... There is a correlation here between waist circumference, I believe, and also like things like waist to hip ratio and health. Am I remembering that correctly?

Dr. Cromwell: You know, what's really interesting is that what we're trying to get our arms around, pardon the pun, is intra-abdominal fat, visceral fat. And so having increased fat in the center of our body, under the skin around the organs of our intestines and whatnot, this visceral fat is very, very metabolically active. And as visceral fat increases, that is a strong correlate to insulin resistance. So, one way to do that is to simply use a tape measure, and start at the top of the right hip bone. We call that the iliac crest. So put the tape measure right above the top of the right hip bone, and parallel with the floor, use your tape all the way around the body and see what the waist circumference is. The measurement at that point in the body is strongly associated with increased visceral fat, which is highly metabolically active and highly associated with insulin resistance.

Katie: Got it. Yeah, that makes sense. And I think that it's important to have that differentiation as well, like you said, with between visceral fat and other types of fat. And with just a tape measure, that's something people can keep track of easily at home and have that health metric in their pocket to understand.

Explain a little bit more about how people can figure out their LPIR index like you've talked about. Is that a test that you perform in your office? Or, like, I know that you work with people directly on this. How can people start to learn that?

Dr. Cromwell: So the LPIR score is actually a test performed by LabCorp. And the test that would be ordered is called an NMR, nuclear magnetic resonance. NMR LipoProfile. An NMR LipoProfile test is actually what gives the LPIR score. The LPIR score itself is a meaningful metric. We take it one step further, precision health report. We actually integrate the LPIR score with the other factors that are necessary to understand metabolic syndrome, insulin resistance, eight-year diabetic risk, and cardiovascular risk. So that's the way that that information is available.

Katie: Got it. Okay. That makes sense. And then yeah, like we've mentioned, that these other factors and lifestyle interventions that seem like, in general, even if someone doesn't know for sure that they would be at an increased risk of any of these things, those general lifestyle changes seemed like they would be beneficial relatively across the board, right? Like, we should all be probably exercising and eating the right balance of macros, and all those things, even if we're not at high risk for diabetes.

Dr. Cromwell: I think you're absolutely right. Just one comment about exercise because we haven't unpacked that yet. There are many ways that exercise improves insulin sensitivity. But if we're asking the question, what principle of exercise seems to have the best effect? And that would be high-intensity intermittent training or HIIT, right? So that would be an activity that you are able to sustain over time. And once you get to a warmed up target heart rate, what you would want to do is periodically increase the intensity for a short period of time, and then go back to your baseline level of exertion. So this could look like, for example, if you are on a treadmill, and you've warmed up, and you're at your target heart rate, well, say every two minutes, pick up the pace for 30 seconds. And at the end of that 30 seconds, go back to your baseline and pace for two more minutes. At the end of that two minutes, pick up the intensity for another 30 seconds. And after 30 seconds, go back to your baseline intensity for two minutes. So that's sort of intermittent higher intensity activity, specifically, causes muscles to become more insulin sensitive. So that would be something that could be adapted into activities, either walking, running, jogging, bicycling, other activities that people might be involved with.

Katie: That's a great point. Are there any other exercise specific things to know that are really helpful? Like, I know it seems like anecdotally, from what I've seen, definitely high-intensity training, you're right, that seems to have a measurable difference both in things like body composition, my sleep patterns, but then also my lab results. And I concentrate a lot on high-intensity training like Sprints, and sprinting bike rides, and also like resistance strength training with weights. And found those, in general, seemed much more helpful than just extended cardio. But are there any other good general guidelines when it comes to exercise for reducing our cardiometabolic risk?

Dr. Cromwell: I think you're spot on. And I think some people get into a little bit of a rut where they get on a treadmill, for example, or an elliptical and they're kind of at a constant pace doing the cardio thing. And the challenge there is you're really not optimizing the metabolic changes necessary for insulin sensitivity. The other thing is, I would caution people to make this a progressive change over time. I think a lot of us are very enthusiastic and we want to adopt something, but we may not have the cardiovascular conditioning to jump right in with both hands and both feet. And so I think we wanna take this as a progressive opportunity. So first thing is involve yourself in a variety of activities, as you said, not just one activity. Second, try to make sure that your activity pattern is one that you're doing at least five days a week and you're trying to maintain your activity for 20 to 30 minutes at a time. And then once we're there, then begin to incorporate these opportunities for intermittent higher intensity within the context of that 20 to 30 minutes activity session. And that's gonna be I think, easier to onboard and more sustainable and less frustrating for people.

Katie: That seemed like really good guidelines. What about...? We've touched on it a teeny bit, but I'm curious if there are specific sleep factors that come into play when it comes to cardiometabolic risk. And I ask because sleep is another thing I track relatively carefully. And I've read the studies that, for instance, you know, one night of really impaired sleep can affect your blood sugar the next day drastically, even just from one night of impaired sleep. And I see differences when I get lots of deep sleep and get to bed early, for instance, like before 10:00 in my sleep levels, and also in my glucose levels the next day, and also long-term lab results. Is there data that you know of, or specific considerations people should take into account when it comes to sleep?

Dr. Cromwell: You're absolutely right. And it's critical. We know this in a couple of ways. Number one is, there's a lot of data from individuals who we call hyper-vigilant. This includes our first responders, fire, police, military, people who live in a state of hyperresponsiveness for periods of time because that's just what they have to do in order to do their jobs. These individuals who are oftentimes sleep deprived or sleep disrupted, have problems with insulin resistance. And what's happening in those situations is the counter-regulatory hormones that are released, cortisol, epinephrine, and norepinephrine tend to give us that fight or flight response on an ongoing basis. And as we have disordered sleep, as people are hyper-vigilant, they find themselves in this situation where there are greater and greater exposures to cortisol, epinephrine, norepinephrine, which wreaks havoc on our glucose metabolism on our cardiovascular risk. Contrary, individuals who are able to get a much better quality of sleep for seven to eight hours that are not in this hyper-vigilant state, are able to really tamp down their cortisol back into the normal circadian rhythm where they're not having spikes of this at inappropriate times. And the result of that is to facilitate improvement in glucose metabolism, as well as cardiovascular risk.

Katie: That makes complete sense. And I feel like you've made such a compelling case for the details of how the things that in general people kind of hopefully know are good for them are drastically important for reducing risk of these problems, which are really the biggest killers other than cancer that anyone is facing at this point. Like heart disease is a massive killer every year. And it's also an area that, like you've explained, we have a lot of control of a lot of these variables. We have the ability to impact our long-term risk in a pretty drastic way. And I love how well you've explained that and I'm curious, especially, like, someone who's done

so much research in a specific area, like you, I love to hear a little bit of, like, what is your typical day look like or what are some of the factors that you are consistent about to keep your risk low?

Dr. Cromwell: Yeah, well, you know, it's really trying to practice much what we've talked about. I do tend to take advantage of the fact that when I'm busy during the day, I'm not eating during the day. And so, I have windows of time that I try to maintain. As you said, it's not very structured every day. It's not four hours every day but it's a four to six-hour window on most days. So, I have intermittent fasting as part of my lifestyle just because, you know, I'm busy as most people are during the day and I just kind of go, go, go. I don't stop for breakfast. I don't stop for lunch. Which means that 5:00 or 6:00 in the afternoon begins my eating window. And I usually go up to 8:00 or 9:00. So I've got about a four to six-hour window on most days.

I'm very cognizant of wanting to eat whole foods that are minimally processed. I joke, if I can identify it, if you can pick it off a tree, pull it out of the ground, catch it in your lawn, or shoot it, then it's good to eat. There's no cellophane tree so I try to avoid that the processed things, I try to stay away from unrefined carbohydrates. I like a balanced diet and I like leafy greens. So, that's kind of my common thing. As far as exercise, I like to swim. And so swimming becomes something I try to incorporate a few days a week. I'm a martial artist and have been for years. I've got a Taekwondo school that I've run for 20 years. And so that keeps me going on other days. And so, it's really kind of a combination of those factors that I try on day in and day out basis to make kind of my normal routine.

Katie: Love it. Yeah, I think it's very much a marathon, not a sprint. And it's the things you do over the long-term consistently that seem to make the difference, and what a metaphor for life that is. A few questions I love to ask as we get toward the end of our time, the first being, to go through a couple of things that people either don't know or most misunderstand about your area of expertise. And this could be a recap of... Because we've gone already so deep into a lot of different topics. But I feel like there is so much misinformation when it comes to this realm. So, what are some of those things people need to be aware of that are often misunderstood?

Dr. Cromwell: Well, let me give you a patient case as an example. And this is a fellow who came to see me two weeks ago, and I think it encapsulates a lot of what we've talked about as well as what can commonly be misunderstood. So this is a 42-year-old young man who came to me to establish a doctor-patient relationship. He had moved from Texas, and his concern was he wanted to know if he was at risk of diabetes or heart disease. Now the reason he was concerned is his mother was a diabetic and his father had a heart attack at the age of 67.

So, when you look at this gentleman, his blood pressure's 132 over 86, a little up and not terrible. His waist circumference is 36 inches, that's not 40 or more, which is what the guidelines say would be an indicator of potential risk. His triglyceride was up a little bit at 188. His HDL cholesterol was down at 36. He did not have any medical problems that had been diagnosed. He was on no medications. He was not following any particular diet. He exercised a couple of times a week with no chest pain or cardiovascular symptoms.

So when you look at this guy, you would say, "Well, you know, a little borderline across the board." But here's the rest of the story. He had four of five criteria for metabolic syndrome. His glucose was 102. So he's in the early pre-diabetic state. His triglyceride is over 150 at 188. His HDL cholesterol is less than 40 at 36. His systolic blood pressure is over 85. His systolic was 130 and his diastolic was over 85. So he has four or five features of the metabolic syndrome right there. When you put this in a metabolic syndrome severity score equation, he's actually at the very high-risk range of metabolic syndrome.

When you look at his insulin resistance score, even though he had a glucose that was only 102, he had an insulin resistance score of 85, which is very high. And his eight-year risk of diabetes is 35%. Very high for somebody who only has a glucose of 102. When you look at his LDL cholesterol, the bad cholesterol, 128, which isn't very high, but his LDL particle number is over 1,800, which is extremely high. So when you put all this into a cardiometabolic paradigm, this is an individual who has very high risk of diabetes, very high risk for stroke and heart disease. And yet, when you look at his conventional factors, there's no one thing that makes him jump at you as being problematic. And so what people I think need to understand is that cardiometabolic risk is actually frequently much more profound than would be expected for these individual factors, which are just a little bit over the line, but collectively put somebody at much greater risk. And this is what we are seeking to give people visibility to with precision health reports.

And the second thing is what I just described is highly amenable to therapeutic lifestyle intervention. By doing the types of things we've talked about with diet and activity, you can make a huge improvement. It doesn't mean he won't need medication at some point down the road but I would much, much prefer to properly identify his individual cardiometabolic risk, give him an opportunity to adopt the lifestyle change we talked about, and then follow the most meaningful factors, his LPIR score, his particle number over time, so that we can get an accurate reflection of where he is and what residual needs he may or may not have for medication down the road.

Katie: Gotcha. That makes sense to have a more complete picture like that and not to focus on... I think there's a trend as we've learned more about some of these different lab markers that we can get into like hyper-focus on one in which we touched on a little bit. And it seems like this more comprehensive approach gives you a much better picture over time. I'll, of course, make sure that there will be links in the show notes at wellnessmama.fm, for people to find out more specifically about that, and to be able to get those precision health reports from you guys. Because that seems like such a valuable tool, especially for anybody who is seeing any of these symptoms or has, you know, family history or increased risk factors. Other question I love to ask at the end of interviews, if there's any advice that you have as parting advice you wanna make sure to leave with our listeners today?

Dr. Cromwell: Well, I think we're in an age now where people are much, much more knowledgeable about these diseases, in general, and about themselves, specifically. And I think you made the point early on that we are our own healthcare advocates. And I think that's wonderful. I really wanna encourage people to make sure that, number one, they continue to learn from you and from others. These different levels of understanding of

insulin resistance, it's simple things they can do that can make a big difference. Tape measure around the area we talked about right above the right hip bone. Central adiposity as we call that is their waist circumference up. Look at their blood pressure. Is their systolic 130 or higher? Is their diastolic 85 or higher? Look at their glucose. Are they in the upper 90s to low 100? That's not a place which is a safe zone.

That's just a place where we frequently have been having problems ongoing for a while, and it's just now getting to a place that might get noticed. Whenever any of these things are beginning to show up on the radar screen, the first thing I would do, as you've already talked about is what are the things I have control over? How can I optimize my diet and my lifestyle? How can I adopt healthy eating patterns? How can I consider adopting intermittent fasting or window of time eating along with reduction in processed carbohydrates? How can I up my activity level and begin to incorporate these principles of intermittent higher intensity? And as you're doing those things, you're doing all the right steps to get to that root cause of insulin resistance and metabolic syndrome, which can be so importantly assessed and intervened with therapeutic lifestyle.

Katie: And lastly, is there a book or a number of books that have had a dramatic impact on your life? And if so, what are they and why?

Dr. Cromwell: That's a great question. I would say at a personal level, it may or may not surprise your listeners, it's the Bible that has had the single biggest impact in my life. And it has given me an understanding of myself and the values that I hold dear. And it also gives me the way to see the world through the lens of others, not myself, and putting others as more important than myself. I think that's a principle for living that resonates with what's important to me and how I try to see my patients and others. So that's the first.

And then at a medical level, going back to a couple of things that are kind of old, there was a publication back in the 1950s by Gofman and Lindgren, which actually was the first description of human lipoproteins. It was the case that we knew that cholesterol was part of plaques that gave heart attacks going back to the late 1800s. But it wasn't until the 1950s that we understood how cholesterol got there. The options were either it was made locally or it was somehow transported to sites that caused heart attacks at some point. And the work of Gofman and Lindgren clearly showed that there were these entities that we now called lipoprotein particles that transported the cholesterol.

They were the ones who identified that some particles were likely to hurt us, LDL, some particles were likely to help us HDL. And they were also the first to show in 1952 that it was number of these particles, not the cholesterol inside of them, which was strongly related to your risk of heart disease. So we knew back in the '50s, that lipoprotein particles, not the cholesterol was really where the action was. It took us many more decades to get to the point of understanding that and using it to good effect.

Katie: Wow, that's a new recommendation. I'm excited to check that one out. And thank you so much for being here and for going so in-depth and so specific on this. Like I said at the beginning, I think this is an area of increasing importance as we see all of these diabetes, heart attack, and stroke risk are also on the rise. And

I love that you're bringing a comprehensive approach and giving people tangible lifestyle tools they can use to start improving those risk factors and knowing that they're improving those risk factors. So, thank you for being here today and sharing your expertise.

Dr. Cromwell: Oh, my pleasure. And a shout out to you as well because I think these types of podcasts are really what we need more of so that people can understand, at a little deeper level, not only what's going on, but as you've said, more importantly, what can they do to take control of the factors in their own health?

Katie: Absolutely. Well, thank you. And thank you all, as always, for listening and for sharing your most valuable resource, your time with both of us today. We're so grateful that you did. And I hope that you will join me again on the next episode of "The Wellness Mama Podcast."

If you're enjoying these interviews, would you please take two minutes to leave a rating or review on iTunes for me? Doing this helps more people to find the podcast, which means even more moms and families could benefit from the information. I really appreciate your time, and thanks as always for listening.