

## Harvard - Interviews - Joanne Manson

**Jonathan:** You have done some of the most expansive research in the history of preventive medicine. In terms of women and diabetes, what have been the things that you've just consistently throughout your career seen?

**Joanne Manson:** What has been so striking to us is that type 2 diabetes is a highly preventable and modifiable disease. We have found that it is very strongly linked to lifestyle factors and that with relatively straightforward lifestyle modifications there is a market reduction in the risk of developing type 2 diabetes. And I think that this is good news for women as well as men. It does suggest that heredity is not destiny, that even if you have a family history of diabetes and you have risk factors for developing diabetes there is a lot that can be done to reduce your risk and we can really largely manage our risk of type 2 diabetes, but it does require attention to lifestyle factors.

**Jonathan:** That's so encouraging because we've seen statistics, we've talked with other researchers who estimate that currently one in four to one in three Americans are diabetic or pre-diabetic. That's a potentially fatal condition. So, let's assume one in three or one in four. What could that be if these lifestyle interventions took place? How much better could we make things?

**Joanne Manson:** We found in our large-scale study population of women that there was actually a 90 percent lower risk of developing type 2 diabetes in the women who were exercising regularly, having a high-quality diet, maintaining healthy weight and not smoking. So, lifestyle factors like that were very strongly related to the risk of type 2 diabetes and diabetes is the pandemic of our time. It is a very common health condition and it's been increasing over time, but the good news is that it appears to be largely preventable. And it's important to get the word out about ways that people can reduce their risk of developing this disease.

**Jonathan:** One of the most shocking when you say it's largely preventable. I think maybe people don't understand where we used to be in terms of diabetes. Some of the statistics I've seen are type 2 diabetes used to be potentially one in every four thousand people. I mean it was like this person has a very different thing. So, we're looking at a 100 to 200 thousand percent increase. Has there ever been any other medical condition

to your knowledge that has gone from being that rare to as common as type 2 diabetes is today?

**Joanne Manson:** Aside from infectious diseases that will suddenly become epidemics. It is highly unusual for a chronic disease to increase in incidence and prevalence in this way.

**Jonathan:** So, while it has increased so much for example diseases, like cancer, so horrific and catastrophic without a clear path, at least not as clear of a path. So, have you seen any other disease that is both so prevalent and so preventable at the same time.

**Joanne Manson:** I would say that of the chronic diseases that are common in the United States and throughout the world. Type 2 diabetes is one of the very most preventable and it appears to be the one that unfortunately is going in the wrong direction. Many of the chronic diseases such as heart disease and stroke have been decreasing over time, but type 2 diabetes has been increasing. And what is particularly concerning is that it's becoming pandemic globally. There are market increases in the incidence prevalence of type 2 diabetes throughout the world and there is no signal that this is decreasing this that this trend is going to abate.

**Jonathan:** And when you say you use terms like pandemic, I'm not sure the viewers understand. Like are we talking in some of these developing countries or in any country are we talking double, triple, are we talking a 30 percent increase? Can you give us an approximate quantitative example of what pandemic means?

**Joanne Manson:** So already there are about 400 and 20 million people around the world with diabetes and it's projected that in another 20 years 22 years there could be more than 600 million people globally with diabetes and it's potentially even closer to 640 million 650 million so we're talking about very large numbers.

**Jonathan:** My math is not precise here but a number like 640 million I believe that was the total population of our planet like a century ago, that's a huge number

**Joanne Manson:** We are getting very close to diabetes being 10 percent of the global population over the next few decades and this is tremendously concerning because diabetes is such a serious disease it's associated with many other health threats it has personal costs in terms of the patient the people who have diabetes are spending a great deal of time managing their disease, it impairs their quality of life. There are also societal and healthcare costs associated with the disease. So, it's very important to address this problem.

**Jonathan:** You mentioned there's a tremendous amount of personal costs. I think sometimes we say, 'Oh I have a diabetes diagnosis but there's metformin or here's insulin and I'm good'. Can you help people understand how you're not OK now because you've got a metformin prescription? What are the personal costs of diabetes?

**Joanne Manson:** Well diabetes has an enormous personal and human toll in terms of it requires a lot of time and effort to manage the condition. Many people will be constantly thinking about what's happening with their blood sugar, is what they are eating or doing in terms of physical activity affecting their blood sugar, do they have to modify a medication because of their physical activity, are they going to have a complication such as vision loss, a nerve disorder or neuropathy as we call it, kidney disease or some of the large blood vessel conditions such as heart attacks, stroke and other vascular conditions. Amputations used to be more common, fortunately they are less common today, but it is still at risk. Diseases of the blood vessels in the legs, as well as the heart and the brain, terms of stroke. So, these are very serious health consequences of diabetes.

**Jonathan:** My grandfather, actually the way this film is actually starting out as a dramatic re-enact, one of my earliest memories is I was in a hospital hallway corridor and I heard my grandfather cry out from a hospital room "Don't let them take my leg. Please don't let them take my leg" and what had happened is he, the diabetes complications, he had gotten sepsis in his leg. And then my mother respected his wishes and 24 hours later he died. And so, people say 'oh diabetes is manageable', what happens if you mismanage diabetes?

**Joanne Manson:** If diabetes is, um...ok. If diabetes isn't well managed the risk of complications will be higher. And this includes the complications involving vision, the

retinopathy and other eye disease complications, the kidneys, the nerve problems as well as the cardiovascular disease heart disease or stroke. Now the good news about preventing these vascular complications, both the small blood vessels and the larger blood vessel complications, is that there's evidence that lifestyle modifications go a long way in that regard as well. We've recently published a paper in one of the cardiology journals suggesting that men and women with diabetes can markedly reduce, 50 percent to 70 percent lower, the risk of developing cardiovascular complications if they're attentive to healthy lifestyle practices such as having regular physical activity, heart healthy diet, not smoking and, or changes of that nature.

**Jonathan:** So, with that I want to ask you this one; actually, I'll do it in two parts. So, it's my understanding that there is a very quantifiable way that we diagnose type 2 diabetes. A numeric scale, above this level you are, now if you're on one point below you don't have diabetes if you're one point above you do. What do we call it when someone is above the diabetes threshold and then changes their lifestyle, high quality eating, high quality living, exercise and then they fall below the pre-diabetes level? Because I'm sure you've observed that happening. What has happened and what do you call that patient?

**Joanne Manson:** We used to say that once you have diabetes you always have diabetes because it is a marker for having some predisposition to developing high blood sugar levels especially if there isn't attention to the management of the condition. However, we now know that people can get into a very normal blood sugar range and in some ways, you can consider the disease going away. However, there will be the risk of the high blood sugars coming back if there isn't attention to managing the condition, attention to diet, regular physical activity, healthy weight and risk factors of that nature.

**Jonathan:** So, if you have cancer they say a cancer goes into remission and there's but saying I'm cancer free is a different thing. And the word cure of course we have to be very careful with, but on a spectrum of cure too we don't know what they'll do. Kind of where are we in the ability to handle this disease?

**Joanne Manson:** I think that anyone who does develop a blood sugar that is high enough to be classified as having diabetes should be aware that they have a predisposition to this condition. If they don't manage their blood sugars through lifestyle

modifications or through medications if need be, it is very likely to recur without attention to these risk factors. And it can be a genetic predisposition it can be a propensity to develop that you have insulin resistance which can manifest itself as having a higher blood sugar level. So, it's really a marker of risk. And it's best to try to stay vigilant about managing risk factors.

**Jonathan:** So, let's use a very specific example let's say from 20 to 30 years old a person, a very healthy lifestyle. very normal blood sugar. A catastrophic family event that happens at age 31 and their lifestyle habits so to hell. So, from 30, 31, 32 bad lifestyle habits. So, from 33 to 35 they have diabetes 35 they have an epiphany, they changed their life back to their lifestyle habits over the next 10 years they just resumed the lifestyle habits they used on has that person cured their diabetes?

**Joanne Manson:** We tend to say that the diabetes is very well managed and that it's really so well under control that they don't have any signs of a high blood sugar anymore. But there's evidence that they have a predisposition to developing the condition and for their blood sugar to go high and this may be due to insulin resistance or having a genetic predisposition. So, it's particularly important to stay vigilant about lifestyle factors and if they're doing that for all intents and purposes they have their diabetes completely under control.

**Jonathan:** If you were going to explain to a fifth grader, what diabetes is, what has happened that has caused diabetes? Because then my next question is going to be like well what is happening when you make lifestyle changes to reverse that.

**Joanne Manson:** We're talking about Type 2 diabetes?

**Jonathan:** I'm a fifth grader. What happens in the body to cause type 2 diabetes.

**Joanne Manson:** The main problem with type 2 diabetes is what's called insulin resistance and its difficulty driving the sugar that's in the bloodstream into the body's cells in order for that sugar or glucose to be used as fuel or as energy. So, the sugar stays outside the cell usually insulin is necessary to drive the sugar into the cell so it can be used as fuel but there is resistance to the effect of the insulin so the blood sugars

building up outside of the cells leads to a high blood sugar level and also the cells inability to make use of the sugar for fuel.

**Jonathan:** Beautiful, so it sounds like a non-diabetic body will, if your blood sugar rises, a non-diabetic body will react to bring blood sugar down, if blood sugar drops too low the body will, whether it's trigger hunger or something else, it will do things to balance your blood sugar for you. But when you have a diabetes diagnosis you're essentially just really kind of manually having to do that.

**Joanne Manson:** Ok, let me say one other thing about it. So usually if the problem is only the insulin resistance the pancreas which is producing the insulin in the beta cells of the pancreas will be able to make more insulin and then there'll be enough insulin in the bloodstream to drive the glucose into the body's cells. However, people who have diabetes they may start with this insulin resistance but eventually the pancreas cannot keep up with the demand for insulin. So, they may have also an element of some decreased ability to synthesize the insulin and this can lead with the not having enough insulin available to drive the sugar into the cells for fuel.

**Jonathan:** Beautiful, So the body...

**Joanne Manson:** I think it's too technical, but I don't know if...

**Jonathan:** Oh no, that's fine, we have editing it's good. So, the body insulin, blood sugar goes up, body releases more insulin to bring blood sugar down and it does that within a range that is healthy. Diabetes diagnosis seems to indicate that the body's ability to maintain that blood sugar balance has broken now, thus, elevated blood sugar over time.

**Joanne Manson:** Right. So often what happens with type 2 diabetes is that the pancreas can no longer keep up with the body's demands for insulin to drive the sugar into the cells to be used for fuel. It starts out having some resistance to insulin and requiring higher amounts of insulin and eventually what often happens is that the pancreas can't keep up with that demand for insulin.

**Jonathan:** What is the relationship? Does obesity predispose you to diabetes? Does diabetes predispose you to obesity? Is it a causal or is it a correlation? What is the relationship?

**Joanne Manson:** It actually can work in both directions that obesity can increase insulin resistance and the requirement for insulin to drive sugar into the cells for fuel and also a high blood sugar can cause some damage to the pancreas, can decrease the synthesis of insulin and can also exacerbate the problems with the insulin resistance. It's actually, it's really complicated.

**Jonathan:** If I am overweight. Do I, and if I do, why...have an increased likelihood of developing diabetes? O

**Joanne Manson:** Overweight and obesity are major risk factors for developing diabetes. We now also know that the fat tissue, the adipose tissue, is a major source of producing inflammatory molecules. So, people who have excess adipose tissue often have a high inflammatory state and that is itself a risk factor for insulin resistance and developing type 2 diabetes. Some of the inflammatory markers are have been shown to be linked to an increased risk of type 2 diabetes.

**Jonathan:** How do we help people to see that one, regardless of how your body looks, you're an amazing person and we need you to not develop diabetes?

**Joanne Manson:** I think that there are few things that can be said. First, regardless of body weight there are lifestyle modifications that will lower the risk of developing type 2 diabetes. So, for example being regularly physically active and it doesn't take tremendous amounts, it doesn't require running marathons, even 30 minutes a day of moderate intensity exercise walking, cycling, that type of activity will go a long way in reducing risk of type 2 diabetes. Also, the quality of the diet is a very important factor. So, having general lots of fruits and vegetables and whole foods as opposed to refined sugars and a lot of refined and processed foods will be very good in reducing the risk of type 2 diabetes. Having a diet that is higher in unprocessed foods avoiding the refined and processed foods and a diet such as the Mediterranean type dietary pattern has been linked to a lower risk of type 2 diabetes. So healthy fats, healthy carbs, lots of

vegetables, fruits, whole grains as opposed to refined grains. These are dietary patterns and changes that can go a long way in reducing the risk of type 2 diabetes.

**Jonathan:** Let's talk about those specific high-quality foods. So, vegetables, non-starchy vegetables. How powerful or even therapeutic are non-starchy vegetables both in the prevention of and possible management/treatment of type 2 diabetes.

**Joanne Manson:** Well there's evidence from the epidemiologic studies that men and women who have higher intake of fruits and vegetables and who are choosing whole grains and higher fiber foods over the refined carbs do have a lower risk of type 2 diabetes. Also having nuts and unsaturated fats as opposed to saturated or trans fats have been linked to a lower risk of type 2 diabetes. So generally, it's higher quality carbs and the unprocessed and whole grains and whole wheat type of carbs fruits and vegetables and avoiding the processed foods and also having the healthy fats the unsaturated fats the polyunsaturated olive oil fish the omega 3 fatty acids these are the types of fats that have been related to lower risk than the saturated fats and particularly the trans fats have been linked to a substantial increase in risk of type 2 diabetes.

**Jonathan:** So, you just listed, you know, 15 different things basically. If you told someone who has diabetes, or a severe risk of diabetes just eat more this thing. If you had to pick one thing what would that be?

**Joanne Manson:** I would say probably vegetables, nuts, legumes and foods of that nature would be the ones to have more of and less of the refined carbs and trans fats, saturated fats.

**Jonathan:** (inaudible) Sometimes people will ask...you know, I'm overwhelmed, I'm so busy I'm so tired I can only make one change. What one food group if I'm just going to make like just eat more of this one thing. Just do this and of course you'll want them to do more over time but, they're only going to do one thing today.

**Joanne Manson:** I would say that having a handful of nuts as opposed to having cookies and pastries that are high in refined sugars would be the way to go because nuts have protein they lead to satiety, they've been linked in a number of studies to a

lower risk of type 2 diabetes and they're very much part and parcel with the Mediterranean diet and that would be one important change that they could be made that many people would find very acceptable.

**Jonathan:** Beautiful, beautiful, and this is a question that I get asked personally often a lot that I'd love your help with. We always hear fruits and vegetables, fruits and vegetables, eat more fruits and vegetables. If I were to eat five additional servings of grapes per day versus five additional servings of green leafy vegetables. It seems like just mathematically there's a big difference. Can you talk about, should I just eat five more servings of grapes per day because that's a lot more palatable for a lot of people than eating more green leafy vegetables and possibly talk about the difference? Help people understand that if that's what you're comfortable talking about.

**Joanne Manson:** Generally, the vegetables and salads would be a better way to go for lowering the risk of type 2 diabetes and also choosing a salad dressing such as oil and vinegar as opposed to having something that is extremely high in fat would be the way to go. People with diabetes don't have to avoid fruit. There are some fruits that tend to be associated with more of an increase in blood sugar. However, I would recommend that people test their blood sugar and see how their own bodies are responding to certain types of fruits. And there's no one size fits all answer in terms of which fruits to have. And many people do well having two or three servings of fruit three or four servings of vegetables a day more fruits and vegetables really the better. I know that that's commonly said and it's almost like a mantra. But it has been linked to a lower risk of developing type 2 diabetes and also many of the cardiovascular complications that are common with diabetes.

**Jonathan:** Perfect. You mentioned nuts you mentioned satiety and Mediterranean diet. Can we talk a little bit about nutritious sources of protein, like seafood or the Mediterranean diet? What is the role of nutrient dense proteins in a healthy lifestyle in your experience?

**Joanne Manson:** So, in terms of different types of meats probably the more Mediterranean type diet that is higher in fish or poultry would be the way to go. And that and there are several studies linking that type of diet but it's also a dietary pattern that is higher in fruits, vegetables, whole grains, olive oil, nuts and not just a seafood as

opposed to red meat. It's a whole dietary pattern and that has been linked to a number of studies to a lower risk of type 2 diabetes. There's also some evidence that processed meats may be associated with particularly high risk of diabetes so those would be foods to avoid. And there is increasing evidence that foods that are high in iron that iron itself may be a risk factor.

**Jonathan:** How, so if I just up to you at a dinner and said the diabetes epidemic is out of control. That word exists in medical literature, it's not used very much. Would you feel comfortable using the term diabetes? Do you think it is a useful term? Do you think we should help people understand what it is?

**Joanne Manson:** I think diabetes is a reasonable term because it emphasizes the very close connection between adiposity and obesity and the risk of type 2 diabetes. But it really isn't just obesity or excess body fat that's a risk factor. It is so much, the other lifestyle factors that are aggravating the problem and many people can improve their health and lower their risk of developing diabetes or having complications from diabetes from focusing on having regular physical activity, avoiding sitting, prolonged sitting, having a high quality diet without having a major weight loss and if they are trying to lose weight it takes only modest weight loss, even 5 percent 7 percent of body weight loss will substantially reduce the risk of developing type 2 diabetes. So, it doesn't require suddenly becoming thin or losing half of the excess weight. It can be even a modest weight loss that will improve health.

**Jonathan:** Can we do a dedicated answer to sleep then a dedicated answer towards stress management.

**Joanne Manson:** So, it's not only regular physical activity and high-quality diet that are important for reducing risk of type 2 diabetes there's also increasing evidence that having adequate sleep and managing stress are tremendously important in reducing risk. And one of the problems with having inadequate sleep is that the body has higher blood levels of cortisol and stress hormones that aggravate insulin resistance and actually increase the risk of developing type 2 diabetes. So, I think it's important for really everyone to be sure that they're getting enough sleep and especially those who are at higher risk of type 2 diabetes and other chronic diseases due to family history or other risk factors to try to ensure that they're getting adequate sleep. And this is often

seven to eight hours of sleep and doing certain things like avoiding a lot of exposure to light and having coffee and alcohol late at night and things like that that can really disrupt sleep. So, I do think that this is important for people to be aware of that the evidence is really mounting that having adequate sleep is important to reducing risk of type 2 diabetes.

**Jonathan:** People have been told to sleep, sleep is important, you hear that a lot. Is sleep therapeutic? People will go out of their way to exercise more, they'll go to the gym and spend all this money, but you tell someone to sleep more...how important is sleep?

**Joanne Manson:** I think that there is mounting evidence that sleep is on a par with being physically active that really getting enough sleep is a very important goal. And someone who is at increased risk of type 2 diabetes hopefully will have higher even greater incentive to ensure that they are focusing on getting adequate sleep.

**Jonathan:** Beautiful. So, we've talked about stress management, we've talked about sleep, we talked about physical activity, we talked about high quality eating...

**Joanne Manson:** We haven't really talked too much about stress management.

**Jonathan:** So, let's talk about stress management and a lot of people hear stress less. Okay, how? How do I do? So how important is it and how do you just stress less. It's not a switch you can flip in your body. You know how, do you do that?

**Joanne Manson:** It's very challenging to manage stress especially when people are concerned about their health and then to be told try to manage your stress and reduce your stress because that will lower your risk of developing a health problem you're concerned about or having a complication once you have a health problem is like telling people not to think about the elephant in the room. You know it's going to backfire, however, if there are ways for people to manage their stress. This can include being physically active which can be tremendously helpful having mindful eating and focusing on healthy dietary patterns as opposed to being overly focused on body weights or what the scale is reading and just understanding that they need some time each day just to

focus on their own needs and be sure they're not getting overly busy and too many demands on their schedule. I think that that can go a long way in managing their stress.

**Jonathan:** I love the paradox you just touched on about how the pursuit of trying to be healthy can cause stress which is extremely unhealthy. Can you talk just a little bit about, we use the term progress rather than perfection because that pursuit of perfection causes the stress, the stress causes more problems, blah blah blah blah. Can you talk a little bit about that? I'm trying to be healthy, so I get stressed and stress is unhealthy cycle and how to avoid that? Because even some people feel shame and that's really that's really stressful. Like, they are ashamed that they didn't eat perfectly, or they are ashamed of their body weight and that's not productive. That's stressful and if stress is a risk factor that's not good. So how do we how do we motivate lifestyle change without causing perfectionism which freaks people out, but we've made progress in the right direction.

**Joanne Manson:** One of the reasons we try to focus on how even moderate changes in physical activity and diet quality can go a long way is to avoid the problem where people are striving for perfection and they feel like they have to make a hundred and eighty-degree change in everything they're doing in order for them to be satisfied or to feel that they shouldn't be stressed out. It's really important to feel good about any changes in progress that's in the right direction and small changes will over time go a long way. So, one of the ways to avoid feeling stressed out is not to feel burdened by striving for perfection but to feel good about even the small changes in physical activity and diet and getting more sleep than perhaps in the past even these very small changes in lifestyle can go a long way.

**Unknown:** Tell me about how great the human body can be when all of that things are working together to keep you healthy.

**Jonathan:** Like you know, we didn't all use to be diabetic. We didn't all use to be overweight and for hundreds of thousands of years the human body seemed to do darn good job of keeping blood sugar and body weight under control. Have we lost sight of some sort of innate robustness that's there that we can facilitate if we just take these small consistent lifestyle modifications.

**Joanne Manson:** We certainly didn't evolve in the current environment. Bombarded with abundant food and constant messages. I do agree that it's an important point to make just having it all come together in a real epiphany kind of sentence.

**Unknown:** What excites you about how the body works. What got you into this in the first place? From a Joanne's standpoint, 25 years ago, like when I talk about film I well up and have so many ideas and so much things in the motifs and the colors and the feelings and the plot, like there's so much there. Can you encapsulate that into something that makes you get up in the morning about how the human body works?

**Joanne Manson:** As an endocrinologist I've always been amazed and fascinated by how well the body is able to regulate levels of hormones and minerals and enzymes electrolytes within a very narrow range just stays just where it has to be in order to maintain health unless something does go wrong the body is very skilled at maintaining that what we call homeostasis or equilibrium.

**Jonathan:** And is there any relationship, like, are you passionate about prevention because it can somehow maintain the integrity of that balance.

**Joanne Manson:** A major passion of mine is prevention and population health can have such impact in reducing risks of chronic diseases and improving well-being. For example, I often say that physical activity is a magic bullet for improving health. Physical activity itself has been linked to reduced risk of type 2 diabetes, heart disease, stroke, osteoporosis, cognitive decline, and many forms of cancer that is truly a magic bullet.