

Diet Doctor Podcast with David Ludwig (Episode 12)

Dr. Bret Scher: Welcome to the DietDoctor podcast with Dr. Bret Scher. Today is my pleasure to be joined by Dr. David Ludwig. Dr. Ludwig is a pediatric endocrinologist at Boston Children's Hospital with affiliations at Harvard and he's the director of the New Balance Foundation Obesity Prevention Center. He's also the author of "Always Hungry".

And Dr. Ludwig has great experience both as a clinician taking care of children and seeing the epidemic of obesity and type 2 diabetes affecting children and also he's very involved in research and sort of helping us understand the problems and complexity of nutritional research and helping change the paradigm of how we can fund and design nutritional research studies to make them more worthwhile so we're not relying on poor epidemiologic studies and we're not relying on industry funded studies as well.

But trying to bridge that gap of industry in the sense of food production but not biased industry with a stake in the outcome combining with research to really help us answer this question. The questions of, "Is a calorie a calorie?" or the carbohydrate-insulin model. How does that affect us as individuals in the free living world and how does that affect our health?

And ultimately how can that affect our policy to help us stem this epidemic of diabetes, obesity, chronic health disease and help us reverse that course? Now David is a source of reason in today's society with so much polarity, with science being more like religion, with people so steeped in their own beliefs that they're not willing to see the other side, David tries to help bridge that gap and say, we're all fighting for the same thing, we all want to improve health.

How can we foster this conversation so that we can have a more reasonable debate, a more reasonable understanding of the situation to find a solution? So I hope you get that from his message and I hope you appreciate it as much as I do. Enjoy this interview with Dr. David Ludwig.

Before we get to the interview with Dr. David Ludwig I just wanted to give you a quick update. We filmed this interview at the very first weekend of November and two weeks later his study was published in BMJ.

So when you're a researcher you're not supposed to talk about your study until it's been published. So unfortunately during the interview we reference the study a few times, but can't get into any details because it hadn't been published yet. But now

that it's been published I want to give you some of the details about it so you have that in your brain as you're listening to this interview.

Now in my mind this was one of the best studies done to look at the quality of calories and how it affects energy expenditure. What they did was they took 164 adults with body mass index of 25 or greater and they had a two-week running period where they all had the same diet, all lost the same amount of weight.

Then he randomized them to one of three groups, 20% carbohydrates, 40% carbohydrate or 60% carbohydrate, keeping the protein fixed, so the only variables were the fat and the carbs, but here's the best part; they supplied every single meal to the participants over 100,000 meals and snacks costing more than \$12 million.

And that's what I think one of the biggest strengths of the study, because it takes away one of the largest variables in nutrition studies which is what do the subject actually eat? We can recommend whatever we want, but what are they actually going to eat? With this study they supplied the food, so we know exactly what they were eating. And it's a great example of the way nutrition studies should be done.

Well, what did they find? They found that the group that ate the lowest carbs, the 20% carbohydrates, compared to the highest, the 60%, the lowest carbs expended somewhere between 200 - 260 cal more during the day, their energy expenditure went up without more exercise, without more physical activity.

Their energy expenditure went up. And if you look at the subset that had the highest baseline insulin, they went up by over 300 cal per day. So the conclusion is pretty clear. The quality of calories do matter and it does make a difference in your energy expenditure.

Just 300 cal a day can make a tremendous difference in overall weight loss. So in my opinion this was one of the best and most well done studies to look at this question with a pretty clear answer. Right now with those details now we can go on with the interview with Dr. David Ludwig.

Dr. David Ludwig, thank you so much for joining me on the DietDoctor podcast today.

Dr. David Ludwig: Pleasure to be with you.

Bret: Now as a pediatric endocrinologist you have had a front row seat to this evolving tide of obesity and diabetes and as an adult doctor I see it and it's awful. But as a pediatrician it must be heartbreaking to see this evolution of this disease just take off in front of your eyes.

David: Well. Indeed it is. This is a generation that has excessive weight more of it from earlier in life than ever before and the consequences to both body and emotional well-being can be tragic.

Bret: Right.

David: Of course there has been a lot of attention to type 2 diabetes in adults, but children are now getting type 2 diabetes. This is unprecedented. When I was training as a pediatric endocrinologist type 1 diabetes was 90% and occasionally I'd see a case or two of MODY, some of these rare genetic causes of diabetes. But at least among adolescents type 2 diabetes is about a third in minority populations. Type 2 diabetes can be half or more new onsets.

Bret: Yeah.

David: You know think about it that it's one thing for an adult who's gaining excessive weight to develop type 2 diabetes at age 50 and then suffer heart attack, stroke or kidney failure at age 60, and that's bad enough. But if the clock starts ticking at age 10, we're talking about a profoundly different situation.

Bret: Yeah. I read that the diagnosis of diabetes at age 10 has a worse outcome than the diagnosis of leukemia. I mean that kind of puts in to perspective as to how serious this is. And I mean we can point to a number of different reasons as to why this happened, but it seems like the primary one is processed foods, sugars and just too much of it.

Now, a lot of people focus on the sugars themselves and some people focus more on sort of the glycemic index. Now not to put you in a box, but you seem to be more of the glycemic index camp. Is that true? Or tell me a little more about it.

David: But that would be a bit too much out of the box. But stepping back a little bit more, there's certainly no consensus that sugars or processed carbohydrates, whichever side of that box one is in, is in fact the cause. At least there's no consensus among the conventional nutrition community.

The basic teaching is that all calories are metabolically alike. The main problem is obesity and we just have to get people eat less and move more, they'll attain a healthy weight and the problem will take care of itself.

Now, that's of course disregarding much evidence that food independent of its calorie content affects our hormones, metabolism and even the expression of our genes in ways that would importantly influence not just the likelihood that we would succeed

with weight loss, avoid obesity, but also risks for type 2 diabetes, cardio-vascular disease, even cancer at any given body weight.

Bret: So for those of us who are in this camp of understanding that it's more than just eating less and moving more it's almost mind boggling that the sort of mainstream dietary community does not embrace that. So that's when we have to look to the science, and say, "What does the science say?"

And you and your group did a study to show that calories do matter and so, you probably know the details better than I do, but you had 21 overweight patients, and you had a running period where they had a 10% weight loss, and then you had different iso-caloric regimens that they were eating and you provided the food for them, and it was based on their percentage of carbohydrates and you found that the lowest percent of carbs had the highest increase in their resting energy expenditure by 325 calories per day.

That seems conclusive. The type of food you eat affects your resting metabolic rate and it's iso-caloric so it's not simply calories in, calories out. So why doesn't a study like that change the paradigm?

David: Well first off, no single study is conclusive and definitive, and we can talk about that in a moment. But let me provide the broader context. On the one hand obesity treatment has focused on so-called calorie balance. Eat less, move more, doesn't matter how you do it and that is the primary focus both for public health, as well as treatment in the clinic.

An alternative paradigm which we've been developing along with others is called the carbohydrate-insulin model. Now it focuses on carbohydrate and insulin, because you need a name for something, but it's not a single nutrient, single hormone hypothesis. It proposes that we've had it backwards.

That overeating doesn't cause obesity over the long term, that the process of getting fat causes us to overeat. Now, that's a little hard for the mind to hold, but think about it, think about what happens in pregnancy. A woman typically eats a lot more. She's hungry, she has food cravings, she eats more, and the fetus is growing.

But which is coming first? Is the overeating causing the fetus to grow? Or, is the growing fetus that's taking up extra calories triggering the mother to be hungry and to eat more? You know of course the latter, we understand it. The same is true for an adolescent in a growth spurt. You know, you and I no matter how much we eat, aren't going to force our bodies to get any taller, unfortunately.

It's the process of getting taller in that adolescent in a growth spurt that's causing him or her to eat hundreds or sometimes thousands of calories more than what otherwise would be the case. So that's obvious in those situations.

Why not consider the possibility that a rapidly growing fat mass that's been triggered to take in too many calories could be the cause of excessive hunger and the overeating that follows? That's the carbohydrate-insulin model.

We focus on carbohydrates because they've flooded our diet in the last 40 years, during the low-fat years, carbohydrates especially the processed kinds, sugar, but just as much or perhaps even more so, the refined starches, raise insulin, and insulin, I call insulin the miracle growth for your fat cells just not the sort of miracle you want happening in your body.

Fat cells don't do much of anything until they're told what to do by hormones, and insulin is the most potent anabolic hormone. Promotes fat cell store, calorie storage at fat cells, it inhibits release of fat from the fat cells. States of excess insulin action consistently lead to weight gain, such as mutations, that lead to overproduction of insulin or in type 2 diabetes where insulin has started, weight gain consistently occurs.

The opposite is also true, states of inadequate insulin action such as type 1 diabetes. A child first coming to attention who because of an autoimmune attack on the beta cells can't make enough insulin, that child will have invariably lost weight before treatment whether he or she is eating 3000, 5000 or 7000 calories a day.

Now if you don't have diabetes the fastest way to change your insulin levels is with the amount and type of carbohydrate you're consuming. But beyond carbohydrate, protein, the types of fats we're eating, micronutrients, fiber, the state of our gut microbiome and non-dietary factors like sleep deprivation, stress and excessively sedentary life. All these things affect fat cell function and determine whether the calories we're eating are shunted a little bit more towards storage rather than oxidation.

All you have to do is store a few grams of extra fat a day to mean the difference between staying lean and having a substantial problem with obesity after 10 years. So going back to the study, we brought people's weights down to stress out their body adapted mechanisms. These were people who had high body weight at baseline.

Brought their weight down by at least 10%, and then we randomly assigned them to either an Atkins type low-carb diet, a high-carb diet with 60% carbohydrate or something in the middle kind of a 40% fat, 40% carb Mediterranean diet. And everybody got each of these diets for a month and we measured energy expenditure

both resting and total energy expenditure by a method called doubly labeled water. We found that despite the weight loss, on the low-carb diet there was no decline in the total energy expenditure at all.

We know that typically your body adapts to weight loss by becoming more efficient, that makes losing weight harder and harder. But there was none of that adaptation on the low-carb diet, a potentially tremendous advantage to losing weight.

On a high carb diet, energy expenditure plummeted by more than 400 calories a day. That difference of 325 calories would translate into 35 pounds perhaps of weight loss without any change in calorie intake.

Bret: So that's the difference between being lean and being obese, right there.

David: Potentially, a big part of the difference. And if you get changes in hunger, if you get lower hunger and fewer food cravings on a low-carb diet has been reported in other studies the effects could be potentially even larger. So, this was a study that was published in JAMA, certainly got considerable attention.

You know itself has limitations it's just one study that needs to be reproduced and then a group from the NIH published a sort of rebuttal, a counter attack, on this hypothesis and on this study, reviewing other studies of diet composition and energy expenditure, claiming that there was no effect. And this meta analysis by the NIH group was used to claim that they had literally-- the term they used was "falsified" the carbohydrate-insulin model.

Now if you look at the studies that were included in this meta analysis, virtually all of them with just maybe three exceptions, 20 or more studies were two weeks or less. So the folks in the low-carb movement are immediately going to understand that when you cut back carbohydrate especially into the ketogenic range and some of these studies did, you need to allow the body to undergo an adaptive process.

You've cut off carbohydrates which is the main source of fuel for the brain, but yet ketones have not yet reached a steady state. The classic starvation studies by Cahill and all and others show that ketones with complete fasting was starvation. Don't reach steady state until about two to three weeks afterwards.

Bret: And how long was your study?

David: Ours was a month.

Bret: A month, alright.

David: Ours was long enough to see these adaptive changes. But almost all of the other studies published didn't. And so if you've cut off carbohydrate but you're not yet adapted to that high fat diet, what's going to happen? You're going to feel tired. You know physically tired, mentally a little sluggish, we have a name for this, it's called the keto flu.

Very well described, there are dozens of papers showing that it takes several weeks, and if you conduct your study during that short period of time of adaptation, you know of course you're not going to see the full benefits of a low-carbohydrate diet, in fact you might see some adverse effects.

But I would make the comparison to a scientist wanting to study the effects of intense physical training on a sedentary population. You take a group of 45-year-old men who are overweight, sit around all day watching TV, and suddenly you're giving them 6 hours a day of physical activity boot camp.

You know they're running track, they're doing calisthenics, they're engaged in contact sports 6 hours a day. And then you measure them three days later. What're you going to say?

Bret: They're going to feel awful.

David: They're going to feel tired, their muscles are going to be sore, they're going to have decreased physical abilities. If you concluded at that point that physical training worsened fitness you would be doing the same thing that these very short-trimmed low-carb diet states are doing, that they're missing the boat.

So we need longer studies... our study and the only 2 or 3 others to date that are of a month duration show benefit to the low-carb diet. I say we need longer studies and we've just completed one. We'll be presenting the first public... we'll be unveiling the results of the study to the public at the obesity society meetings in November, we'll be doing so in November 14th.

And, this is a study that actually cost 12 million dollars, it was done with philanthropy. NIH, unfortunately doesn't typically fund nutrition studies of this size. And the after weight loss same design as an initial weight loss phase, in this case we studied three diets parallel, so you just got into one diet either 20%, 40%, or 60% carb controlling protein and the test phase was 20 weeks.

So four times as long as our JAMA study and ten times or more, as long as most of the studies that were in that NIH meta analysis. So this study will be of sufficient power and duration to put the carbohydrate-insulin model to a definitive test.

Bret: That sounds fascinating.

David: We look forward to showing those results very soon.

Bret: You're just teasing me now, I can't wait to hear those results.

David: And they'll also be in press, they'll also be published soon as well.

Bret: Good. Yeah that's always a problem too. When a study is presented at a conference but we don't have all the details and then the media starts publicizing it about these amazing results but the devil sometimes is in details. And I like that it will be published shortly after.

David: We're actually hoping that they'll be simultaneously published.

Bret: You said a few things in there that I wanted to touch on. One it is funded by philanthropy. Now that's a big problem because, not a problem that it was funded by philanthropy, but a problem that it needs to be funded by philanthropy, because if you have a drug trial no problem getting funded.

Even some studies probably showing calorie in calorie out, or trying to show that that's the paradigm could be funded by industry, because Coca-Cola said just exercise more and drink your coke and you'll be fine. But funding first studies like this is got to be hard to get, and that's part of why they're not being done because it's such a challenge and expensive to do it correctly. So was that one of your bigger challenges? Getting the right funding from the right people?

David: That's terribly short-sided and as you point out not that any drugs study will get funded, but if you are a big drug company and you have a new agent that you think that is going to be useful for just one obesity related complication, you can routinely get funding in the many hundreds millions of dollars to take it to phase three clinical trial.

You know you can count on one hand the number of nutrition studies addressing a specific dietary hypothesis over a hundred billion dollars. And it's terribly short-sided because we're investing a fraction of a cent for every dollar of diet related disease that the United States and the, you know, the rest of the world suffers.

You know, we do want the funding infrastructure to be skeptical of new ideas, that's the scientific method. Very few new ideas will ultimately prove valuable, because the state of science is an accumulation of many years of study and so the next study statistically isn't going to change the paradigm. So we want some skepticism, we just don't want to suppress new ideas, and that's the problem because we clearly need new ideas in obesity and diet related disease, where based on the latest evidence

seeing prevalence rates that are continuing upward the current mind set of eat less move more has failed.

And yet there is an attempt, it seems like an attempt by folks who are in the leadership of the nutrition community to really prematurely falsify, dismiss new ideas, such as the carbohydrate-insulin model with data that are plainly not up just enough. I mean if the folks on this side of the debate were to publish studies of that quality we would be shut down immediately and yet these poor quality studies are being used to falsify the model.

So that's not in anybody's interest. We don't want to claim victory or insist upon defeat prematurely, in fact this is a little too binary. We want a more nuanced discussion, recognizing that we have a public health crisis that the current mind set has not solved, and whether the carbohydrate-insulin model is 90% right or 10% right, we need to understand what we can learn from it and not attempt to dismiss these new ideas so fastly.

Bret: And that's why nutrition science starts to look more like religion than science, and that's a problem.

David: Well that can be true on both sides to be fair. On social media, just like the calorie in calorie out folks can be close minded. The low-carb community has its own dogma, its own accepted ways of dialoging. I think both sides should really tone down the rhetoric and not to make this ad hominem.

On Twitter it's just all too common to accuse our opponents of being intentionally pigheaded, and I don't think they are, I think they may be wrong but by promoting ad hominem attack and I've been on the receiving end of ad hominem attack. Ad hominem attack is always a distraction from the science. Let's stay focused on the science, the public health issues, deal with your frustrations.

Yeah, people aren't always going to understand. I mean look at the history of science; some correct ideas have taken decades or centuries to finally be proven. You know, let's have a little maturity here just because you may be right and the world might not recognize it, but that's not going to help the cause to attack the other side.

Bret: You're definitely a voice of reason in a world that likes polarity, because polarity sells, it gets clicks, it gets views.

David: You know, there's nothing wrong with polarity. Actually we need more vigorous debates that clarify the polarity. One of my other problems with the conventional paradigm is it keeps morphing. You know, every time a new finding comes up it morphs in a way that tries to account for that finding without having to reassess the

basic principle, the basic assumptions of that. So yes we need to shine a bright light. Let's have debates that really clarify the polarity but let's not make it personal.

Bret: Right, now, I like something else you said, that maybe the carbohydrate-insulin model is 90% right or 80% right.

David: Or 10%, right.

Bret: Right, like it doesn't have to be in all or none and some people still put it into that camp that, well, if it's the carbohydrates and insulin, then calories don't matter. Well, calories do still matter, if you have 10000 calories on a low-fat diet you're still probably not going to lose weight, you're going to overeat.

Whereas if you have 800 calories on a low-carb diet you're still probably going to affect your resting energy expenditure and your metabolic rate. So I have a personal problem saying it has to be one way or the other. But yet some people who are very prominent in this field still think it's one way or the other. How do we address that and explain that it is not so black and white?

David: We have remind ourselves that science shouldn't be religion. You're talking about one of the most complex, multifactorial clinical challenges we have, which is body weight regulation, we know that it is affected by genes, but also by diet, physical activities, stress, sleep, family dynamics, community, the food supply, political and policy decisions. We can all look at one little piece of the elephant and delude ourselves into thinking that we have the full picture.

Some humility is in order here, and as you say it's not that carbohydrate-insulin model acts in defiance of calorie balance. In fact I've tried to make that point in the recent review that we wrote for JAMA internal medicine. It's simply reinterpreting the first law of thermodynamics in a way that's more consistent with the evidence around biology.

I mean of course humans aren't toaster ovens. We respond dynamically to changes in calorie balance, and unfortunately that has been well demonstrated in the laboratory, it's neglected in public health and in the clinic.

Bret: Right, and that gets into the issues of how to design a study to measure this. Is it real world, free living people? Is it in a metabolic chamber? Is it only measuring doubly labeled water?

David: It's all of it.

Bret: Right, we need a little bit of all that, right.

David: Of course, we need to understand. Now the problem has been that we've jumped to effectiveness studies prematurely where you put large numbers of people on different diets, you give them some typically very low intensity nutritional counseling, and then tell them to go follow it. And if you're lucky they will change their diet moderately for a few weeks or few months but almost invariably by a year all groups are eating pretty much the same.

Not surprisingly their weight and their other health outcomes are pretty much the same, but can you conclude then that diets don't matter, and it's just a question of compliance? No, that's very sloppy thinking. We would never do that in any other area, biomedical research.

Imagine you had a promising new drug for cancer it could potentially wipe out acute leukemia in children. You gave one group the drug, prescribe on group the drug and you gave the other group placebo. But it turned out that the kids in the treatment group never got the drug at the right dose at the right time.

They may be have gotten the wrong instructions, or maybe many of the families couldn't afford the drug or there were some mild, transient side effects that good counseling could've gotten them through, but didn't. So it turned out, that you know, that the drug wasn't taken as intended, and there wasn't a statistically significant difference in cancer outcomes.

Would you conclude that the drug was ineffective, or that the study was a failure? We need a better quality study to ask these basic questions. We make that mistake in nutrition. We've skipped over mechanisms, and especially efficacy. What happens under ideal circumstances? Prematurely gone to effectiveness, what happens in the real world, especially when this real world antagonizes healthy behaviors?

If we find out that a lower carb diet is going to be really optimal for a third or half of the population, or two thirds of the population, then that knowledge will help us design behavioral interventions and environmental interventions that will help them become more effective. It's not like, you know, you have to understand that smoking cause lung cancer before you could go beyond just telling people not to smoke to developing environmental policy, environmental base policy actions that actually helped people not smoke.

Bret: Right, proving that first in an ideal trial then figuring out how to move that to a real world scenario.

David: Those are separate questions, separate scientific facts that get confounded all the time.

Bret: So one of the things in your study that you did was that you actually provided food rather than saying go eat. Is that what you did in your upcoming study as well?

David: Yes, the recently completed study which is called the Framingham State Food study, we did it in collaboration with the Framingham state University where we could recruit students, staff and faculty and local community members and feed them through the college kitchen, the commercial food service.

So we took advantage of the synergies that the food service knew how to make tasty foods financially efficient and in large volume. We controlled the quality of those foods and so we were able to test a mechanistically oriented hypothesis. If people actually eat different ways, do you get a difference in metabolism?

Bret: Yeah, that shows sort of a new way of doing these studies... not a new way but a way that should be done, and I remember you wrote something about that on Twitter about a sort of a new paradigm on how to incorporate research and industry, bring them together to help find the answers and that takes money.

David: Right, although we're in this case bringing industry and not with a risk for conflicts of interests. It's very different to pair up with the food service provider who has no vested interest in one particular diet, but can serve high quality foods much tastier than a metabolic kitchen in a hospital.

That's one thing to pair up with them. It's another to pair up with Coca-Cola to do a study as to whether sugary beverages are a good way of preventing dehydration in children.

Bret: Yet that happens all the time. Those types of partnerships and funding and you know...

David: Yeah, so we do the-- NIH has really I think dropped the ball in terms of adequately funding high quality nutrition research of a sufficient scale on power to definitively address questions that have bedeviled us for centuries. So it's really been up to philanthropy to step in and fill that gap.

And I think that if there are any other billionaires out there please come find us at Harvard and we will do our best to give definitive answers to some of these long term challenges.

Bret: Well so along those lines there was a philanthropy funded study run by-- well not run but sort of spearheaded by Gary Taubes, a very publicly anticipated study with--

David: NuSI.

Bret: With NuSI.

David: Okay so we were funded by NuSI. This is one of their three initial major studies. There was a study, a pilot study, it was actually a non-randomized pilot study done through the NIH and several collaborators that was published in AJCN and despite some spin it actually showed an advantage to the ketogenic diet...

Bret: See, that's what I wanted to talk about.

David: ...by both doubly labelled water and metabolic chamber, the ketogenic diet had a metabolic advantage. It wasn't huge but it was statistically significant in a pilot study that's not powered to get a precise estimate and it was non-randomized in a way that biased against the low-carb diet.

Why? Because everybody got the standard diet first for a month and then they were all in a non-randomized way put on to the ketogenic diet, but the experimenters miscalculated energy. They wanted it to do it a weight stability, they miscalculated and the participants were at substantial negative energy balance.

They were at about 300 or more calories a day, they were losing weight systematically. So this is why you randomize; to cover mistakes like that. In this case without the randomization on a conventional diet their average weight was substantially higher than their weight was on the ketogenic diet, and so of course that's going to bias you in terms of total energy expenditure. Despite that, and despite other biases the low-carb diet still came out advantageously and yet I think it's in a masterful display, a spin that was dismissed.

Bret: Right, the lead investigators said that it disproved the carbohydrate-insulin model like you were saying.

David: If you look at the registry, that study was specified as an observational pilot study, a pilot study can never prove or disprove a hypothesis, that's the nature of it. It's designed to assess study methods and to come up with broad effect estimates that give you then definitely test. So that NuSI study was, if you reinterpret it and we did, and we think that if you take into account the biases then you get a benefit of the low-carb diet in the 200, 250 calorie a day range.

And that's quite consistent with what we got in our JAMA study and we'll be able to compare that to what we got in our new Framingham study. The third study that NuSI funded was the diet fit study from Stanford published in the Journal of the American Medical Association or JAMA recently.

And that study found a non-significant, non-statistically significant, very small non-significant advantage to a low-carb as compared to a low-fat diet, but the low-fat diet, the people on that diet were told to greatly reduce or eliminate all processed foods but specifically refined grains and added sugars. As a result the glycemic load that's the best determinative of how your blood sugar and insulin will actually change after a meal, that's the product of glycemic index and carbohydrate amount.

That actually, went down as low as other clinical trials, low-carb or low glycemic load group were. And so what this means I think is that if you avoid processed carbohydrates you can do reasonably well on diets with varying macronutrients, relatively more carbohydrate, relatively more fat. It's different if you have type 2 diabetes but they weren't included it in this study.

But that's again consistent with the carbohydrate-insulin model. It's focused on the processed carbohydrates. It's not saying your fruits, vegetables, you know, traditional starchy tubers that might have been eaten in the Okinawa diet are the problem.

It's focusing on the processed carbohydrates that flooded our diet during the low-fat years and that raise insulin too much. So I think that in a sense all-- I don't have the liberty to give you the result of our study, but I think we'll see that there are consistencies among the results that the studies funded by NuSI.

Bret: And I like that you clarified not considering type 2 diabetes patients because in those people, the fruit, the tubers, that can be too much of a glucose load and insulin response for them. But for the general more metabolically healthy population then that's not the evil we're talking about so far.

David: Then clearly the world can't give up all carbohydrates, all grains, I mean with--

Bret: Why not?

David: We're getting 10 billion, there just aren't enough animals for 10 billion humans to eat. So, you know, you need grains to feed that many people. We're not hunter gatherers anymore. The question is what are those grains? Are they minimally processed, and can we also--?

Because you know this traditional, like the sourdough breads that were made with less finely ground flours and that were fermented over a long time, so a lot of that rapidly available carbohydrate got digested and turned into organic acids which are very beneficial, that's really different than wonder bread. And we can also be shifting to an agriculture that produces more healthy fats, you know, avocado, nuts, dark

chocolate. These are all delicious and very nourishing, and can also help to feed the world's 10 billion people.

Bret: So, with our current state of policy with the farm bill, and who they supplement and who they benefit, and with our current industry structure and our current medical community how do we get there from here? It seems like there are so many roadblocks. And you've been involve with policy and trying to affect things. What do you see as the necessary steps we need to start taking to get there from here?

David: First is what we're doing, we have to understand what the science tells us. About how the human body is designed and how to care for it and feed it, so that it doesn't all too often develop these metabolic breakdowns. You know in our 50's or 60's or as we discussed at the beginning of this session sometimes, you know, in a person's teens.

So we've got to understand the science including whether there's susceptibility, differences based on our genes or other biological factors, we're especially interested insulin secretions but that's another story.

So what's right for the general population, are there major subgroups that need to be specially treated such as people with type 2 diabetes which is highly prevalent. So it's a public health issue. And then I think we begin to look for collaborations of common interest. You know, one obvious place to look is the insurance industry.

They're spending a fortune, and increasingly a fortune. Unpreventable diseases; if the investment of \$10 in good nutrition or infrastructure change or policy could produce \$100 of economic benefit, lower medical costs, but also then to employer's greater worker productivity, less days, lost in illness to diet related diseases, I think you've suddenly counterbalance the power of Big Pharma and the food industry.

So we need to begin to develop alliances. They're going to help us create policies that earn the greatest common good for society, not just the special interest that inordinately have access to politicians and power.

Bret: Right, very good point. So people have proposed factoring in the down shame health cost of certain foods into the price of that food, I don't know how's that necessarily practical but that's the real mindset.

David: That's called the Pigovian tax, and it's well established capitalist principle. You know, you can't just create a product, that, let's say it produces a lot of pollution let's just make it very simple. You've got a pig farm that's creating massive lagoons of toxic waste; you can't sell those products really cheaply and then expect somebody else to deal with the environmental disaster of that waste lagoon.

Has this off to tax the case. So a Pigovian tax which is now used across the country with cigarettes says we need to have some of the long-term costs of that product such as taking care of people's emphysema or lung cancer included in the price so it doesn't fall back on the population. That's a capitalist idea of, you know, market responsibilities as you can get. But we do need more of that.

Bret: Yeah, and I agree. But when it's well done and the caveat out there is that there is so much epidemiology and observational studies that this type of tax I think would be based on and so many studies say increasing meat intake will increase your risk of heart disease and cancer. And those are frequently promoted by the school of public health at Harvard.

That doesn't factor in sort of the reduced quality of the science. The studies we've been talking about so far are controlled studies, prospective studies, not these retrospective studies looking at societies with healthy user bias and confounding variables and with entirely too small hazard ratios that then make this broad sweeping conclusion. So my concern is if we do go in that route we're going to be facing a meat tax because of what this poor epidemiologic studies shows.

David: So I think you've just conflated two important issues. One issue is what the evidence based suggests, and you know, do taxes or subsidies that fairly balance the long-term costs on the prices on the product are those an appropriate policy measure when the science indicates? And I think that the answer is yes and it sounded like we might agree on that.

Bret: I agree on that.

David: A second question is why do you need to get an adequate knowledge base for action? So that is a whole another debate. And there are issues with observational research but there's also problems with clinical trials. Did you know that there was never a clinical trial to this day that shows reduction of lung cancer from cigarette from smoking cessation interventions?

There's never been one. Yet we all agree that it's a true cause and effect and it's a huge cause and effect. So why, despite attempts to find it, why has no clinical trial ever seen it? Those are the limitations of a clinical trial. You didn't get complete compliance. You got washed in and washed out, and you were looking at effects that take decades in some cases to emerge.

So just because a clinical trial doesn't show it or alternatively if it shows it, doesn't mean it's true, there are limitations in both sides, and I think it's become fashionable among the low-carb community to focus exclusively on the limitation of observational research and not those of interventional research.

Both have a place. You know, there are many questions that will never be answered by a clinical trial. You just have to understand good ATBI from bad ATBI. Just as we understand good clinical trials from bad clinical trials as we were discussing earlier.

Bret: Right, so smoking is considered good ATBI because the hazard ratio is above three, three and a half. As one of the reasons why and there's a dose response effect and you know this Bradford hill criteria that it meets. Whereas saturated fats, red meat, a lot of the nutritional ones don't even come close to that level of ATBI, yet the Harvard school of public health reports these studies over and over again probably overstating what they can prove. Does that bother you?

David: Well, I'm in favor of appropriate interpretation of all data. I also want to say that there's no monolithic Harvard school of public health.

Bret: Good point.

David: There are investigators who have a diversity of opinions including those who've published, explicitly stating that the prior recommendations on saturated fat were overblown and that saturated fat, in the context of conventional diet, doesn't increase cardiovascular disease risk.

You know I've got a secondary appointment at the school of public health and I'm on record in saying in the comparison between white bread and butter, butter is the healthier component. Even if you say that leads to many topics that'll be beyond our capacity today, but I do think that saturated fat in a context of high carbohydrate diet is a big problem. I think the ATBI consistently shows that, and I think those are true associations.

That doesn't mean that saturated fat on a low-carb diet is going to do the same thing, and in fact, I think likely, you have to be eating more sat-- you can vary the amount of saturated fat you eat on a low-carb diet, but it's inevitably going to be higher, but when you're not eating a lot of carbohydrate, that saturated fat has, Steve Phinney says, to use his metaphor, "goes to the front line of oxidation", and it doesn't stay around as long.

And you get compensatory changes in triglycerides and HDL and chronic inflammation. So I think we do a disservice of both directions including among the low-carb community of totally dismissing any adverse effects of saturated fat in a conventional high carbohydrate diet. I think that's a mistake.

Bret: Well, as usual I really appreciate your perspective and you really have a great way of seeing both sides of the coin and trying to bring them together to make a reasonable decision and trying to further the science in a way that will help answer

these questions, not that it has to be one way or the other but that we need true answer to help our patients and help us understand the complexity of this. So thank you very much for that.

David: Great, you know I just want to say it's wonderful that you as cardiologist are taking a deep dive on these issues. I think you'll be able to do so with a perspective and credibility that's oftentimes lacking and so congratulations on your work.

Bret: Thank you. I appreciate that very much. So where can people go to learn more about you and hear more about what your thoughts?

David: Well if you are, I don't know when is this coming out, but you can come to the obesity society meetings in Ashville in mid-November. We'd love to see you there for presentation of our data. Otherwise follow me on social media Twitter, Facebook. I'm @davidludwigmd and you can also find all of my links on my website which is doctordavidludwig.com, that's drdavidludwig.com.

Bret: Well, Dr. David Ludwig, thank you so much for joining me today, it was a pleasure.