



Prof. Christopher Gardner
**DIETFITS Trial 2018:
Low-Fat vs Low-Carb Weight Loss Diets
and Effect of Genotype and Insulin
Secretion**

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DANNY LENNON: A very welcome to the show, Professor Christopher Gardner. Thank you so much for joining me today.

CHRISTOPHER GARDNER: Thanks for having me Danny.

DANNY LENNON: It's my absolute pleasure. I am really looking forward to this discussion; and today in particular, we are going to be focusing on the very recently published DIETFITS trial which you've been overseeing, which is super impressive to look at and has obviously created a lot of buzz afterwards just because of the implications of the study. So maybe just as a starting point for people, before we get into the nuts and bolts of the methodology and some of the results, what was the real purpose of setting out on this track? What was the question that you were trying to either tease out the answer to or contribute to at least by this study design?

CHRISTOPHER GARDNER: Sure. I am going to start out in a funny way. I am going to tell you what it was not designed for. It was not designed to see if low carb or low fat were better. So really this goes back to a 2007 study we published with 311 overweight obese women, we compared Atkins to Zone to Ornish to a health professional's diet and after a year there were a couple of pounds' difference between each group. The only significant

difference was actually between the two low carb groups, between Atkins and Zone. But what was way more interesting was instead of looking at averages, we started plotting every person out on a graphic, that I brought to some meetings, and people were much more interested in the individual variability within the diets than they were in the very small average differences between the diets.

So we looked into it a little more and for the sake of time I am just going to say that we and some colleagues found what looked like a genetic predisposition, a three-gene pattern of SNP single nucleotide polymorphisms. It looks like one would suggest a low fat genotype, another would suggest a low fat genotype, and a third would be neither of those. So we were going to do a new study and test to see whether this sort of genetic signature would help predict this variability. And we had another metabolic link or hint and that was insulin resistance which is measured in a bunch of different ways and we wanted to get some really great glucose insulin data, and we thought that might predict it. So we got 609 people, randomly assigned them to low fat or low carb. For a year, collectively they lost 6500 pounds, pretty cool. However, in both groups, the amount of within group variance was from 60 pounds lost to 20 pounds gained, so then that's in a 80-pound range of different response to the same instruction, when in fact the average difference between groups, the average is 12 versus 13 pounds – one pound difference.

So the between group difference is meaningless and the within is super interesting and mind-bogglingly fascinating and yet neither are genetic predictive marker, nor a metabolic predictive marker. Explain that difference.

DANNY LENNON:

Yeah, there's certainly a lot to dig through there. So plenty of follow-ups on that. So just at this point, just so we have kind of clear for people, we are saying that you've looked at this or set out to look at these two particular types

of diets but relooking at the effects of does this certain genotype and separately that does someone's insulin secretion to any of these things help us predict whose types of diets, low carb or low fat is going to be potentially better. So the first thing that kind of popped out to me when looking at this particular study which I think were quite novel and a bit different typically when we see these crazy debates about macro nutrients is that there was a strong emphasis on diet quality in your study. So both the low fat condition and low carbohydrate condition, the kind of counsel and recommendations you are giving had a strong focus on diet quality. So, can you touch on first the kind of thought process behind this and how it was kind of different to maybe some other research, and then secondly more so what kind of parameters did you use to classify a diet as "healthy"?

CHRISTOPHER GARDNER:

I am going to start on a really selfish note. So I've done this long enough to know that when you finish a study of a diet that somebody is a big fan of, you are almost sure to be attacked at the end if they didn't get the result they wanted. And so I wanted to be fully prepared to publish this and go to a meeting and have Dr. Low Fat and Dr. Low Carb come up to me and say, "So what is it, did you really do everything you could to make this the best low fat and the best low carb diet you could?" And we did. That's what we told the health educators. So the way this intervention was delivered is participants were supposed to come to 22 evening sessions, led by dieticians and at every step along the way the dieticians were teaching both low fat and both low carb, they didn't want to look anybody in the eye and say, sorry you got assigned to the crappy diet, too bad you didn't get the other one.

What they really wanted to do is look at them authentically and say, you know there's this debate, it's been hard to answer, we want to give both diets their best shot, we want to give you, we want to give every participant their

best chance, so we are making this the best low fat and the best low carb we can. And so let me get to that second part of the question where you said, "How did you define that?" So we told everybody that no matter what group you go to, Dr. Keto, Dr. Paleo, Dr. Vegan, Dr. Mediterranean, you name it, they are all down on added sugar and refined grain, which both happen to be low fat but that's crappy low fat. So we said, we want low carbers and low fatters to avoid those kinds of non-nutritious low fat carbs, and we want everybody in both groups eat as many vegetables as you can. Now, if you look, there's almost no fat in vegetables, there's only small amounts of protein, and so veggies are mostly carb. But we told the low carb people to eat as many vegetables as they could.

And so that was the foundation. No added sugar, no refined grain – not that they all followed that but that was the instruction, and as many vegetables as you can. And then once you've got that, then we are going to help you choose low fat or low carb foods, we want to make sure the ones we are helping you pick is in a box of brownies that says low fat on it or a bag of chips that says low carb on it. That's gaining the system. Don't do that. So you got to – we want you to go to the farmer's market, cook more at home, stop eating in front of the TV or any kind of screen, stop eating in your car, basically eat more mindfully and less mindlessly while you are choosing whole foods that are either low carb or low fat. So that's the essence of it

DANNY LENNON:

Yeah. And I think that's really something that struck me immediately from reading the paper and I think it's similar to I think the 2014 paper that you published as well where there was this kind of focus on diet quality and it's something that is very valuable particularly to people listening who are maybe dieticians or nutritionists or coaches, because it kind of parallels well with what we are trying to instruct people to do in the real world. And it's kind of this nice dovetail with the kind of

metabolic ward studies that we see but now we want to layer in, well, what would happen if we give people certain recommendations that we are likely to give. And so off the back of that, another thing that was part of your study was how you came up with getting people to a certain level of either fat or carbohydrate restriction and what type of levels are those in the diet they came to. So how did you set the restriction for fat and carbohydrate and what degree of restriction actually ended up being there with most of the participants?

CHRISTOPHER GARDNER:

Okay, so picture, part of this is science and part of this is selfish again. So Danny, at the end of the day, if you pull off a big study and most of the people quit, nobody is really going to listen to you. So they have real human beings signing for this. You don't want to give them an outrageous goal that no one can achieve and they will never finish up on, and plus you do really want to help real people. So, we said, the whole point of this study from the beginning is that we think we could help find which diet is best for whom; and to prove our point we have to randomly assign you to both diets, which means we might assign you to the wrong diet. This might be the worst diet for you and yet we assigned it to you. And if it is not the one that fits you, you are going to have a harder time adhering to it than the person next to you who maybe it was the right diet.

So, we don't have a set number that we are trying to achieve for low fat or low carb. If we did, then a lot of people wouldn't ever hit that one number. I know a lot of nutritionists, myself included, who couldn't really hit a specific number meal after meal, day after day. So instead, and get ready, this isn't really going to roll off your tongue but I am going to say it anyway, so our approach was limbo-titrate-quality. So the limbo part was in the first eight weeks, depending on what you got to sign to, try to get down to 20 grams of carb or 20 grams of fat and look at your baseline diet, we will teach you what that means, this is a huge

difference. You have to throw away a lot of stuff and your covers in your fridge, you have to shop all over again. You are really going to have to exclude some things, so this is going to be a massive change in all of your diet. It's not just one group, both groups, we are expecting to make a big change. But, to be perfectly honest, we made up that number, it's not a scientific number, it's more to psychologically anchor you at a much different level, much lower level, make you really appreciate that you are going to do something for yourself and you are going to test this out.

And after eight weeks, if you've done it, and most people said they did – we weren't actually tracking this part very closely – they said they got there. We said, "Can you stay there another week?" And some of them said no; some of them said yes. So, either that week or a couple of weeks later we'd say, okay, now it's time to titrate. So go ahead and add 5 to 15 gm pack per day and do that for a week. See what happens. And most importantly, check how hungry you are feeling. We never asked anybody to count calories or cut back on calories. We only asked them to cut back on high fat or high carb foods. So they weren't counting calories, they were just focusing on certain foods and food groups to avoid. And at the lower level, some of them were hungry. We said, you are not done yet then, because if you look us in the eye, and you say I can do this for a while but not forever, then you are not done yet, because then the study will end and you will quit, because it's a diet and it will come back on and we will have to start all over again.

We want you to look us in the eye after you've done this titration and find this point that works for you. What is the lowest level of fat or the lowest level of carb that you could foresee doing forever? And within your group you won't all get to the same number. We actually think some of you are more predisposed to one diet than the other, so we are never going to give you a number. We want you to get the

lowest you can get after anchoring you to 20 gm, and then we want you to feel like you are not on a diet anymore, you are on an eating pattern, and this is potentially your eating pattern for the rest of your life. And if you listen to all of our plugs for quality along the way, then you will be choosing a highly nutritious, high quality diet that is low in fat or as low as carb as you can get. And you will help define for the American public whatever realistic healthy low fat and healthy low carb diet is, and we will present the average and we will show everybody that there was also a range, there wasn't one number but collectively as a group of 609 people you help define what that range is for real people and what the average is.

DANNY LENNON:

Yeah. I think it's wonderful because so many times we've heard about how important for example adherence to any type of diet is. That's the main driver. If someone is not going to adhere to a diet, then regardless of the intervention, then it's not going to be successful. So, with that in mind, the fact that you've been able to take both these diets, but focus really on making good quality food choices, picking highly nutritious foods, having a good set of eating behaviors around that, and really pushing this as an eating pattern as opposed to a very restrictive diet is, I think, super useful particularly for long term retention. So a couple of things that popped up with that said is in terms of participant retention in this particular study then, what was that like in each of those groups, was that comparable in both types of eating patterns or was there a favor for one type that potentially has better adherence rates?

CHRISTOPHER GARDNER:

I am so glad you asked that question. It's pretty funny. I am super proud of this. You may be the first one who asked me that question. So I think it's either identical or it's off by one or two people. So, 304 and 305 people got randomized and 240 and 241 finished. So it's virtually identical. So now for various reasons,

that's a little moot and maybe lost on some of your listeners but from a scientific perspective for internal validity, I could not be happier. It really looks bad if – as you are probably hinting at there - if twice as many people dropped out of one group than the other, then you would have questioned how realistic that one was that people were dropping out of. But it was virtually identical.

DANNY LENNON:

That was such an amazing thing to see because I think that takes away again one of these potential things people already almost have ready to go to dismiss a diet that they don't like if it comes out favorable or it doesn't back up their dietary belief is that oh, there was no difference but our diet is superior for adherence. And we've seen that kind of talked about when people discuss some of the metabolic ward studies to see something like this at 12-month study with general guidelines given and similar retention levels is like you say, great for the science side but also great for some of the practical implications of that. So, with this, let's get into, again, just to kind of be clear with people, over some of the results from the study. What are the main things to take away in terms of the results you saw from not only the weight changes but then also if there was any kind of effect detected in those two different parameters genotype and insulin secretion that you looked at?

CHRISTOPHER GARDNER:

Yeah, so the genotype pattern didn't make any difference and unfortunately some of the reports on that just leaped to the conclusion that genotype doesn't matter. And that's not really fair. There are dozens and probably hundreds of genes associated with metabolism and weight and things like that. We only use three genes. There's almost an infinite number of other possibilities you could look at which means now there's an infinite number minus 1 that we might go ahead and test, but it's not really like that. We had a lead, we had some pilot data, we picked one, didn't work. We had that insulin resistance idea which is really

strong and powerful for some people, and that didn't work out for us. There could be other ways to measure insulin resistance and we are going to do a separate follow-up paper on that right now. But really, the two of them were pretty well done and looked at, and so those doors are closed for us.

And I think the larger implication has to do with this fascination with personalized nutrition – that if we just get your genome and your epigenome and your proteome and your microbiome, we will hand you a prescription and you will know what the best diet is for you. I think that maybe coming but it is not today. This is such a long process to find this sort of genetic or metabolic or other signature and test it to see if it works. You can't test it in 10 people and you can't test it for 10 days. You really have to go and try to apply this. And I am all for the plausibility of explaining that huge variability we got within each diet and I really think we owe it to Americans for the scientific and public health community to help explain that – what is all that variability due to. But we are not yet there for some of those claims for personalization.

DANNY LENNON:

Sure. And I think the complex nature of this is so important to bear in mind, particularly when you get over-simplified messages. So for example someone saying that sure different people might do different diets but if someone is insulin resistant then they must eat almost no carbohydrate in order to be healthy. I mean, all that like maybe there's something to that you will eventually see, but as of right now, we can't say that. And two, it's more likely that it's going to be an interaction of many of these different variables that will probably dictate the right diet for someone. So I think this is super interesting. So if we are seeing that based on this there was no real differences between those groups or really what we are seeing is there's no real predictive power in someone either having a low fat genotype or low carb genotype based on those particular three genes

that you looked at, and their insulin secretion as measured in this study doesn't seem to be predictive of a benefit for either particular one. So we know that the retention rates were some range group. So another question people might have is – did we see any differences in overall caloric intake between the groups? Was those simple recommendations to do one thing or another, did that correlate to differences in average caloric intake or are we seeing a similar pattern in each group there too?

CHRISTOPHER GARDNER:

It's a great question. Keep in mind that this is all self-report of diet and in and of itself that's just a hugely problematic field because people don't do that well at estimating their own diets, they overestimate, underestimate, forget and sadly sometimes they lie. But in the sense of if you under-report in the beginning, you'll probably under-report in the end, there's probably some internal consistency within the individuals. They basically recorded on average eating about 2000 calories before the study started and then they basically recorded in both groups cutting back 500 calories, not counting them, focusing on lowering fat and carb-rich foods but they both reported – and this is not statistically significant – they both reported this exact same – okay not exact, they both reported a non-statistically significant, therefore in that sense, similar deficit in calories.

If you looked at everything else, protein, carbs, fats, percent of fat, percent of carbs, percent saturated fat, grams of fiber, grams of fiber per 1000 calories, they differed significantly in every other factor other than calories. So now the caloric intake that's reported to them was similar and matched that they had the same amount of weight loss on average and the same type of distribution in both groups.

DANNY LENNON:

Yeah. And I mean, that's a huge thing to take away from this because we've already seen those like super well-controlled trials where we have a very specific number of calories and we

see similar weight loss between two groups, at least for people that are actually onboard with the energy balance equation and we are going to say, well, that's an expected result, right. That's what we are going to plan to see. Now, when we are seeing these kind of more free living conditions with just some general guidelines, these similar changes in bodyweight and that they are matching up with these similar changes in calorie intake once that focus goes onto good quality food, so I think it's all these pieces are really interesting, there's so much within the study.

So before we start wrapping up here, Professor Gardner, I want to ask a couple of formal things. First, what would you say you would give as your main kind of conclusions, takeaway, from this or the main takeaway points you are keen for people to bear in mind when they are trying to interpret this study?

CHRISTOPHER GARDNER:

Sure. I would love to give you at least three. The first one is going to be short. If you look at the distribution of weight change that we reported, about 10% of the people gained weight in a weight loss study and people kind of scratched their heads like "Wow, you did a crappy job with them, didn't you?" Really, a lot of people who signed up for this study, unbeknownst to us, but quite common in the real world brought lots of psychological and emotional baggage with them. That food was a comfort thing. It's the way they got out of some of their stress issues and they probably shouldn't have signed up for this study until they got through some of those issues or we should have had a psychologist onboard, not just dieticians. So they could work through that and focus more on the food than the issues that were getting in their way. So that's that end of the spectrum.

The other end of the spectrum was that people who lost 30, 40 and 50 pounds. Well, the average was 12 versus 13 in the two groups. Plenty of people lost 30, 40 and 50 pounds and

one of the most consistent themes we heard from those people had nothing to do with low fat or low carb. The way we framed this up is to suggest that those people told us we helped them change their relationship to food. And what that meant to them when they gave it back to us is they said, we listened to you when you said, don't eat in the car, don't eat in front of a screen, go to the farmer's market, cook more, cook more for yourself, cook more for your family, sit down, put the fork down once in a while and talk to the people that you are sitting with. So it was really, they started recognizing how mindlessly they had been eating and that separate from the low carb and low fat thing, had been this relationship with food which was pretty toxic and not healthy and we had helped them change that, regardless of whether it was low carb or low fat.

And then the last thing I will leave you with that I think would get more towards this personalization is that I think once you hit this foundational diet that's minimizing or eliminating added sugars and refined grains and maximizing vegetables, which I can't think of any health professional, who would disagree with, not one, no matter what crazy diet they are in favor of – no added sugars, no refined grains, lots of vegetables. After that, I think the key to this was hunger and satiety.

And so I think there's probably an active area of research we should get into about personalizing satiety. I don't have data for this Danny, so don't hold me to this, but my sense is that some people eating steel cut oats for breakfast and having lentils for lunch were more satiated than others and they quit sooner, they took them longer before they started their next meal and they weren't hungry on that approach and they cut their calories that way without feeling hungry; while others did that same thing and a couple of hours later they were hungry and they wanted more and they had to eat again; whereas another group was making sure they put avocados and nuts and

seeds and having fatty salmon in their meals and they didn't have to eat that much, they got satiated pretty quickly and so ended up eating fewer calories while others weren't satiated, some signals didn't go off in their brain and those fat calories with 9 calories per gram, they ate more calories than some of the other folks.

And so trying to eat to the point where they were satiated was different for some people on low carb or low fat, and that might be a really interesting area that any of your listeners can play with. Once they are eating mindfully, which combinations of foods are they using to not feel hungry and feel satiated sooner, I think that would be a really healthy approach to this, and we empower people to explore for themselves different types of diets, the Mediterranean or an Asian or a Latin American or some – and focus on taste, have at least something that you enjoy. You are going to eat for the rest of your life, you better enjoy it.

DANNY LENNON:

Wonderful. A brilliant roundup and with that I think that's a great point to leave that there. Professor Gardner I want to say thank you so much for your time today. It's been an absolute honor to be able to talk to you and also I want to say a massive thank you for the continued amazing work you are doing. It's really providing novel, interesting answers and questions in this area and it's very much appreciated from all of us who are reading it. So, thank you for all you do and I really appreciate taking the time out today to be on the show.

CHRISTOPHER GARDNER:

Great. Well, I thought you really asked some good questions in. I think you have a good sense of what's going on, so it was a pleasure to have this conversation with you.

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