DANNY LENNON: Professor Jacobs, welcome to the podcast.

DAVID JACOBS: Thank you very much. It's very nice to be here.

DANNY LENNON: Yes, and there's lots that we could get into, but I suppose, as a good starting point, to give people listening some context, could you maybe first speak to perhaps the origins of how you came to start thinking so deeply through these, I suppose, meta level questions about nutrition science, and what drew you to that in the first place.

DAVID JACOBS: I think I'd like to start with my work on whole grain foods. We could go a little bit further back, if you're interested in the relationships with Ancel Keys and that work, and a little bit before I started really getting into nutrition. But starting in 1994, there was a question asked to me as part of a consultation with General Mills, the cereal company and flour company, about whether whole grains were better than refined grains. I had done quite a bit of work kind of on the edges of nutrition, and especially with respect to serum cholesterol, but I had not done that kind of thing. And so, we did a project and found that whole grain in the literature was related to reduced cancer rates in a series of case control studies, and the power of that single nutritional

variable was pretty remarkable. But still, if it seems too good to be true, it probably isn't. So we had another study, the Iowa Women's Health Study, which was about 40,000, women aged about 62, and they were followed at that time for about nine years. So we could look prospectively at, especially vascular disease, which was my main interest, not cancer, at whether the consumption of whole grains was related to future disease. We only had death in these women, so we did not have non-fatal events, but it turned out to be very strong, and that was published in 1998. And by that time, I had become a true believer. And in 1999, we published a paper showing that in the Iowa women, the relationship was actually extending to a wide variety of different conditions, not just vascular disease.

So then I got on to a talk series of people going the rounds at different meetings, and really understanding the nature of grains, and grain as a food, so if you think for example of a wheat kernel, or an oat kernel, has an endosperm, which is the center of the seed, and the center of the seed contains mostly starch, and that is what the new growth is intended to live on. And then it has a brand and a germ. The germ is where the plant embryo sits, that has various things in it that are needed to support a new life and get it going. And then it has the brand and the brand contains all kinds of things that plants have that the animal kingdom does not have, which is biochemical function and protection. So the issue that was raised by many other people was, was it the fiber, I mean, why was it that if you just ate the endosperm as a human food, that health didn't seem to be as good. And I had some pictures electron micrograms of the – it's called the aleurone layer, which is kind of between the bran or the edge of the bran right on the endosperm, and pictures of the different phytochemicals that were sitting in those cells right there. And they just were an amazing array of color, we want to think of it like that. And one of my colleagues was saying that – he

used the term co-passengers. So when you eat the fiber, you eat the whole grain, you get all these phytochemicals.

I came to believe that it was the summation of the phytochemicals that was really what was important in eating whole grain food. So that was the beginning of my introduction into this kind of nutrition. And from there, I formulated the concept of food synergy, which I don't know how novel it is, it may be that the word is somewhat novel, and saying that the constituents of food act in concert, they're like an orchestra. So there were examples of supplemental studies where you would eat, for example, the big one is the alpha carotene beta carotene study, trying to raise beta carotene in smokers to prevent disease, and it actually caused disease instead of preventing it.

And so, the idea was that eating a great deal of one of these apparently beneficial constituents in isolation would be harmful. And somehow or other this concert of the orchestra must have checks and balances, they have powerful weapons, powerful weapons against plant diseases, herbicides and bactericides and so on. They could get out of hand. So in order for the plant to be alive, it had to have some other thing that would keep those things in balance. And so, that led to the idea that the different constituents of plant food act in concert, same thing with animal food, but the animal kingdom, in my teleologic view, gave up the ability to make a lot of these kinds of chemicals, in exchange for mobility, big brains, and that kind of thing. That food synergy, it's a little bit difficult to actually show that within a food, but it turns out that it works very well for dietary patterns, and looking at meal combinations, and, in general, what people eat. We show now over and over again, and many, many other people show it too, that those patterns that are kind of plant centered, whether they're vegetarian or they're just limiting meat, seem to be associated with less

disease in the future. I think that answers the question.

DANNY LENNON: Yeah-no, that actually sets up things perfectly for a number of topics that we wanted to get into that you've just raised throughout that initial answer. And I think at this juncture, it would be remiss of me not to mention that your work was actually introduced to me by Alan a number of years ago, and since then, through reading that work and having discussions with Alan about that has been incredibly informative for how I see some of this stuff. And so, with that, I think I'll hand over to Alan maybe to open us up with a preamble to what topics we maybe want to explore, and then off the back of what you said Professor Jacobs, where you think we should start with this Alan.

ALAN FLANAGAN: I think one kind of interesting finding that launches off, that perhaps is an example of food synergy, if I recall, David, there was an analysis of the Iowa Women's Health Study, where you matched the participants for the same amount of fiber, but looking at that fiber derived, I believe, the majority or 75% of that fiber from whole grains, and the other same absolute level of fiber intake matched but 75% from refined grains. And actually, there was a difference in outcomes, and the lower risk in the whole grain group. And so, I think that's a really kind of operative example of food synergy, because you're going beyond, you've matched them for fiber intake, and this kind of, there's clearly additional benefits potentially being derived from the whole grain itself. I wonder then if you could kind of elaborate on how this is relevant for a number of different exposures, and how, for example, it's relevant for even conducting research. I know you brought in this concept of like a top down approach, for example, so how does this then translate for relevance, particularly when we have epidemiological findings, and then we have an RCT comes along, tests an isolated nutrient, has a null finding, and people go, ah,

the observational research is wrong, and we get into these conflicts.

DAVID JACOBS: Right. Well, so the concept of top down is kind of like doing a puzzle, and it's often very difficult to take, say, a jigsaw puzzle or puzzle to get pegs in the right place and a board or something like that. It's hard to do it forwards, but it's easier to take it apart. If you start with the finished product, it's easier to see how are you starting with the finished product, you would get to a board which you could then reconstruct. And another way to think about that is that if you do have a highly synergistic, or maybe not synergistic in the mathematical sense but just lots of things going on, and you have to have all of them in place to see any effect, a technique is to start with the whole and start taking pieces away from it. So that was kind of what was in my mind with that term top down versus bottom up.

Another thing is that I'm an epidemiologist, and epidemiology has lots of nutrition studies on nutrients or in single foods, and those are very difficult to interpret and seem not always to give you an answer, which is repeatable across different formats, including animal studies and clinical trials and so on, and so on. And also, when you look over time, and if you're asking people about what do you eat, that quite often, the individual components, whether it's a single food or a single nutrient, are not very repeatable from time to time. But the overall pattern turns out to be quite repeatable. So that means that we can ask people about what pattern they eat, and that becomes a personal characteristic. And that personal characteristic seems to apply over a period of 20 years or more. When I think of my own self as a child, my diet was much different than it has been as an adult. So there was a point where I changed, but I think that the change over the past 50 years has been a lot more subtle than from childhood into young adulthood, and in middle age. So in general, the idea is that you had better approach,

understanding, nutrition, or understanding the science in every way that you can, and one way that had not been looked at a great deal was from the top down, taking the whole diet, the pattern, seeing how that worked, and then seeing whether you could break that apart to understand questions such as, okay, that's all fine, but should I eat yogurt.

ALAN FLANAGAN:

Yeah, one of the interesting things, I think, for anyone that has done nutrition dietetics or biomedical undergrad is with the top down pyramid flipped on its head, so to speak, reductionism was at the bottom of the pyramids. And this is something that obviously is kind of the – is oppositional to the biomedical model, in which reductionism is championed. It's kind of the goal of understanding at a molecular level. I know you've written before about this difference between nutrients and drugs as exposures, but I wonder if you could elaborate for listeners, like, what are these essential characteristic differences that make reductionism, fine if you're studying at statin, but not great if you're studying a dietary pattern or even yogurt.

DAVID JACOBS:

I am a little bit chagrined to say that I, in my, say, studies of particular biochemicals circulating, say, collagen biomarkers that I've written about, do tend to be reductionist. But, of course, epidemiology is fundamentally top down in the sense that if the ideal study gathers data for 30 years and then sees who gets sick based on something very early on. That's a very – that's sort of the whole body and looking holistically at the person. But still, when we do go in and try to understand the body, we have not figured out how to do better than reductionism. So we look at the biochemicals one at a time, if we look at omics, genomics, proteomics, whichever massive array, we're still picking out single items, and then trying to identify pathways. The pathway is a little bit closer to holistic. It's sort of saying this is one kind of thing that goes on in the body, you asked about nutrient, the kind of defined

nutrient or defined food versus drug. So nutrient is something that is found in food, I mentioned beta carotene before, which is highly prevalent in yellow, orange vegetables and fruits. In the alpha tocopherol beta carotene study, the syllogism was, if beta carotene is good for you, then a lot of beta carotene ought to be better for you; smokers have low levels of beta carotene, therefore, we'll give them a whole lot and they'll get better. So that would be a drug because nutrients, the single compounds do not come in isolation ever, except in a supplement, or in a drug. Looking at nutrients in amounts that are isolated from their natural presentation in foods, and usually in much larger amounts than you would ever get from a food or from a whole diet, that is kind of the dividing line between drug and nutrient or a food constituent. And so that if you can't take the item apart, if you can't take the diet apart, then you're stuck with top down. I think that's why your question about nutrient versus drug is highly pertinent to this question.

DANNY LENNON: One of the things that had just came up as you were talking through some of those answers, in particular, when we think about dietary patterns and how consistent they may be, particularly, if we will look at certain cohorts of people or certain demographic regions, that whilst nutrition epidemiology gives us a lot of really useful tools, probably more so than anywhere else to work out some of these diet disease relationships, that narrow variability and intake is one of those challenges to try and overcome, particularly, when we look at this concept of making sure we have appropriate exposures that we're comparing, and it's something we've discussed on this podcast before. I'm wondering, can you just maybe talk about that as a challenge to doing good epidemiology, of looking at the exposures, looking at the kind of exposure contrast, and then this issue of narrow variability that can often happen within diet, and dietary intake.

DAVID JACOBS: The issue of narrow variability was brought up years ago, when people were thinking that dietary fat was predictive of breast cancer. And you could see wide variability across cultures, which is confounded with many other things. And then within a given cohort, you had less power, because you just didn't have examples of people eating within a single culture, you didn't have examples of people eating one very low fat and other people eating very high fat. So the ability in epidemiology to discover an association in part depends on the range of the variable, and if the range is more narrow, then you can't see as much. Diet patterns are also restricted, but the correlation that I'm talking about is consistency within person. So epidemiology works better if you have a single characteristic which characterizes the person for their whole life. If you think about their Framingham score, and what happened in the early days of cardiovascular epidemiology, with cholesterol and blood pressure and smoking, they had measured those things once between age I think 35 and 64, and found 10 years later that they predicted disease. So why would that one measurement predict, you know, why wouldn't it just be some random number, and if I came back and had measured you tomorrow or next year or four years ago, it would be completely different?

So that kind of correlation within person says that people follow along some kind of a consistent track, if it's less and less consistent than to get the average exposure, say, the average dietary pattern intake over many years, you would have to have quite a few measures and average them. So the variability in epidemiology is a complex topic. If there's not too much variability within your sample, you may miss an important effect; but if people are too variable within themselves, then you don't characterize them very well, and you will not see any outcomes as well.

ALAN FLANAGAN: One of the things that this is useful for, as you've highlighted, is epidemiology, this

concept of, by nature, it's looking at things from a top down approach. But what are, do you think, the kind of challenges of, for example, to look at a dietary pattern, it's going to be a score based, using some form of index. And so, what kind of challenges do you see for the top down approach in epidemiology, rather than say, oh, we've got this range of – saturated fat is the only thing we're looking at. You're looking at this, for example, a plant based diet score or a healthy eating index type score. But challenges are kind of there from an epidemiological perspective in deriving and achieving this kind of relative estimate of consistency in a person over time.

DAVID JACOBS: When you talk about complexity, one of the reasons that people went to nutrients is to simplify, because there are many, many foods and, well, it turns out there's many, many constituents of foods also. I don't know which are more, the number of foods or the number of constituents. But the thinking was, anyway, in the early days in nutrition, that there were 55 nutrients. So the word nutrient is actually reserved for those 55 things which were judged to be essential for life. And the early founding fathers and mothers thought that there were other things that we might eat, but maybe they're not nutrients, they're just filler or empty calories, things of that type have been used.

ALAN FLANAGAN: Well, so this idea of using, because with the top down approach, using, say, for example, various score based or indices for epidemiology, because I think what you were saying was, okay, the reductionist approach was, in itself an effort to simplify. With the food based approach though, you can have, let's say, for example, we use a healthy eating index, and it's scored out of 100, it still has the potential perhaps to miss capturing some of the synergistic effects of foods, if it's kind of crudely like vegetables, for example.

DAVID JACOBS: Right. So what defines a food and what defines a category, that's a challenge. What should you

count as a positive and as a negative, if you look at all the varietals of onions or apples or whatever, they're all certainly different from each other. They're more alike within, say, the category of apple or within the category of onion, than they are between apples and onions or apples, onions and meat. So, for the score, which we developed, in the CARDIA study, we have 46 food groups, and in the Iowa study, the same score, we used only 34 food groups. But score is like the healthy eating index, tend to reduce the categories more than that. So that I think that they did not necessarily give clear answers to what to eat, just because they're not specific enough. But the challenge really is, it's a statistical challenge, what's your metric, how do you decide what a food is, how do you decide what a nutrient is – the nutrient is a little bit easier to get at, because you can take a food table, say you have 6000 or 25,000 food items, and you actually have subjected each one to laboratory testing for whatever it is, you can subject it to testing for a nutrient. So you could get the amount of carbohydrate, for example, you could do functional testing, which is something – if you take a bit of apple and you say, what does it do to the proliferation of a cancer cell, does it inhibit it or promote it, that would not be a food constituent, that would be a food functionality in an in vitro setting, where you could do things like that.

So those things, although tend to be very highly specific, and the nutrients, in particular, operate in the context of only being delivered in combinations, where the combination was developed somehow through evolution. It was good for the life of the food being eaten of the plant or the animal, and it was good for the eater in coevolution. So that made me think that if I'm going to pick on some combination, it would be better to pick on a combination of foods. Well, so then I have to decide if I had onions, or if I have yellow, orange vegetables or fruit, whatever, I have to decide operationally what to include in each one of those categories.

And then you get in epidemiology, you get into the question of how do you capture food intake. And so, we do that typically with questionnaires, some of the questionnaires are more superficial, some of them are better. The nutrition community has gotten itself mired down almost irretrievably in detail, and it turns – so you know you just have to, you have to say it right, you have to do it right, and some kind of a middle road where you say, yes, apple is an entity, apple is something that we know and we can ask a person how often they eat apples and how many. And we don't, I mean, we could, but we don't have to ask about Honeycrisp versus Jazz.

So that issue of deciding what a food is, and what's the fundamental unit, also a gram weight versus energy intake, for example, coffee provides no energy, it seems to be a very important food, it's seed derived, and it's extracting from the seed all kinds of interesting chemicals, like caffeic acid, ferulic acid, it's just extracting that from passing hot water over the seed. Would you do better to eat the coffee seed? I've never heard anybody address eating the coffee beans, although you can get candy coffee beans, I guess. But the question about figuring out the epidemiology or even figuring out what diet you're going to use in a randomized clinical trial has to do with a question of what is a food, how do you distinguish one food from another.

ALAN FLANAGAN:

There's one part that I think is quite interesting in this, conceptually, for epidemiology, which is, if we're happy to call the apple the exposure of interest, for example, and look at that in the context of a dietary pattern, one of the biggest criticisms of nutritional epidemiology is confounding, oh, there'll be inherent confounding. But coming at an analysis from a top down perspective, more top down perspective will account for that, because your exposure of interest is either the kind of dietary pattern or the method of analysis that you use to kind of classify different kinds of dietary

patterns, and the characteristics of those patterns, so you get the exposure of the pattern, and the food group combinations kind of somewhat obviating the potential for the issue of confounding to be a limiting factor.

DAVID JACOBS: Well, at least, my theory is that you reduce the food to food or the nutrient to nutrient confounding by making dietary patterns. I give the example of this score that we develop, a priori diet quality score, which, as I mentioned a little bit earlier, in Iowa, was based on 34 food groups in CARDIA that I've been working with more recently, it is 46-food group. But we've just published in the past few months, three papers showing that that score is related to reduce cardiovascular disease, to reduced incident of diabetes, mostly type 2 diabetes, and to better maintenance of kidney function. So that score actually we have maybe 20 food groups that are rated positively, so that would be fruit, it would be yellow vegetables, it would be green vegetables, other vegetables.

There's quite a few items for the vegetables, nuts and seeds, I think, get two-food groups, coffee and tea as beverages get a food group, and those are all good, and then we have another 13 that are adverse; and we have 13 that we couldn't decide and said, well, to fill up the whole diet will give you a 46, but only the 33 counts. So you can look at all that, and one thing that that score does is it forces people to eat from a variety of our food groups, because you can only get four points for a food group. We put people into five categories, either quintiles or for foods that are not eaten very much, a zero group, and then quartile. And if you're at the top of that for a positively rated food, you would get a score of four, and if you're at the bottom of that, for an adversity related rated food, you would get a four. But in order to get a good score, you have to eat and get good points from a variety of foods from either eating or not eating. And then you still have some of your diet leftover, so you can look

in the other 13 food groups what you're choosing.

So that works quite well. It's a chore for people to understand exactly what it is. It's a more in depth statement than the alternative healthy eating index DASH diet, some things like that where the people have tried to simplify it into sort of 10 easy steps or something. The point I was going to make is that for dairy, we coded dairy as a high fat or low fat. And so you get, generally speaking, you get more points for low fat dairy. If we're wrong about that, and actually, fermentation is the issue, you know, the yogurts and cheeses are going to be good for you, the liquid milk, maybe the butter is not going to be good for you, we would have to reformulate the score in order to give people credit for that. Right now, they're eating yogurt, yes, it's good, if it's low fat; eating yogurt that's full fat would be rated bad. And in terms of that particular score, you would lose points for that. I actually think that, when I go to the grocery store, most of the yogurts have zero fat. That means you've taken out all of that dairy stuff, which contains saturated fat, but contains some other things as well, and you have replaced it with some kind of carbohydrate, and that seems to be a really bad idea.

So that's something where you could see kind of tweaking the score at the level of saying, what if we formulated it a little bit differently, but we get a different answer. And we think about that, we haven't actually done that, but we have – we do think about it. So going back to your original question, how you formulate the score is everything, in terms of what you're going to figure out epidemiologically.

DANNY LENNON: To bring things in a slightly different but related area, one of the concepts I did want to ask you about was when we have large datasets, and we're looking at analysis of that data, but particularly you've written about when this data is being gathered over ecological units,

and how we have to be very mindful of how that data analysis goes. And I think you gave a really good example of referencing Mahshid Dehghan study with the PURE study where they concluded that high carbohydrate intake was associated with higher risk of total mortality, and off the back of that, they were kind of giving this recommendation to maybe reconsider dietary guidelines. And I know you wrote quite eloquently about that issue and how that relates to this concept of data that's collected over ecological units, and how we go about that data analysis. I was wondering, could you maybe just go into that for people and riff a bit on the idea?

DAVID JACOBS:

It comes back, in a way, to the issue that you raised about variability between cultures and within cultures, and if you did not look across cultures, which Ancel Keys did in the Seven Countries Study, and which Salim Yusuf did in the PURE study, you can't see those extreme differences, you don't even get a hint about them. But when you only look within study, you may still see some very strong relationships, but you're not necessarily seeing how the relationship is nonlinear and bends at the edges. So my issue with the Seven Countries Study is not having measured diet in individual, which was based on an understanding in 1960, as I said, that nutritionist being mired in complexity, and feeling that you really didn't learn anything if you didn't know all of these details, which by the way, we didn't really know how to put together, so we're going to put it together just as a nutrient. On the other hand, in the PURE study in their diet papers, they have not shown it by cohort. So the between – you just have to be very careful interpreting that between cohort differences are very interesting, and within cohort differences are very interesting, and you shouldn't be ignoring either, but you shouldn't just collapse them. I wish in the Seven Countries Study that there have been more individual data, and there is actually in some of the cohorts, some of that's been

published. And on the other hand, I wish in the PURE study that because they do have a substantial amount of individual diet data on every person, they have all these different cohorts, I wish they would present it by cohort, so that you could look for cohorts and situations such as particularly low economic development countries that are just completely different.

ALAN FLANAGAN: Yeah, one of the – this is actually perhaps pulling in some of maybe your earliest work, but if I remember correctly, did you work on some of the modeling on intra-individual variation in blood cholesterol levels, and how that meant that it could make associations where blood cholesterol is mediated which impacts by say, diet, it could make associations more difficult to detect at a population level.

DAVID JACOBS: That actually goes back to a paper that was published in 1979.

ALAN FLANAGAN: Yeah.

DAVID JACOBS: Getting to be ancient history. But that was my excursion into what is now called either regression dilution bias or errors in variables models. In epidemiology, we assume that the independent variables are fixed. So if I'm to take the diet, say diet pattern score, or saturated fat, I assume that we know what each person's value is, and then the random variable is the long term outcome or the time to event. And in the errors in variables models, you say, well, I don't actually know exactly what that person had, what was the person's cholesterol, what was the person's diet. And so, what I wrote about in that article, without knowing this stuff that I now know, 40 years later, about how to deal with those models is that there was some of this extra variance and that you could actually show it in that paper that if you looked at change over a certain period of time, you could see the associations in the observational diet, which was the association in that case, for change in Keys' score versus change in diet. So

that's a technical, statistical or epidemiologic issue in detecting relationships.

ALAN FLANAGAN: There's a kind of relevance to, I think, in one of your papers, you mentioned the Keys' equation, for example, and how, because of the nature of the equation, the saturated fat: twice the cholesterol raising effect of polyunsaturated fat, with lower cholesterol and then the addition of dietary cholesterol to give full effect of saturated fat, and you have this kind of, as a result, again, nutrient focused orientation, as we think about nutrition and cardiovascular disease, I mean, dietary recommendations are focused on saturated fat and cholesterol for a long time, less so on dietary cholesterol now, but you see again this importance as it relates to dietary synergy, food synergy and dietary patterns, because you see variables like the polyunsaturated to saturated fat ratio play out in epidemiology. And so, I wonder whether, in fact, some of the nutrient focus in terms of knowledge that we do have is we're still able to detect it when we come at nutrition from this top down dietary pattern oriented focus.

DAVID JACOBS: One of the early things that I did was to ask the extent to which serum cholesterol responsiveness buried by the, how closely were individual people characterized in terms of their serum cholesterol response to diet, how closely were they characterized by the Keys' score. And so, I actually had over 50 Ancel Keys' dataset, and many people had been in a lot of his feeding studies. And so, I showed that the responsiveness within person ranged from about half as much as he said to about one and a half times as much as he said. Martijn Katan wrote a paper on the same topic with his feeding studies, which were also very numerous later on, and he had a different – my take was this shows that, yeah, there's a little bit of slippage in the system, but basically, on average, Keys was right, and people might be a little bit less or more responsive, but not that much. So I was saying, the concept of serum cholesterol, and this combination of saturated

fat, polyunsaturated fat and cholesterol, somehow adjusted for energy, was a valid concept. And Martijn's paper focused more on the opposite side of that coin, which was, well, there were some people who were pretty far away from being right on to the prediction from that.

So that's one part of this issue of the limitation of a single score, based on a few nutrients like that. It may or may not give you a sufficiently accurate answer. But my thinking now is that much more the problem with any score, so anything like, if you say low fat, eat a low fat diet, eat a low carbohydrate diet, do this specially to get more protein, what you need is a beta carotene supplement, all those kinds of single nutrient or not very diverse nutrient kinds of statements, miss a whole lot of the diet, and they miss nutrition – they miss distinctions, even within categories that are important. So the particular problem with the Keys' score by itself as a standard is that it doesn't consider all the other stuff in plant foods, especially. And our a priori diet quality score does consider the plant foods, and that, I think, is a really big deal. So maybe if people were saying, like Denis Burkitt was saying in the 1970s to eat your roughage, you know, if you had the right message that would include a lot of those plant constituents, maybe you would do better with that kind of a message. Needless to say, you don't do well with a low fat message, because they're very important distinctions between types of fat. You also don't do well with a low carbohydrate message, because they're very important distinctions between types of carbohydrates.

And I'm very skeptical about almost all the things that are called supplements, which I think are really drugs with less regulation, because again, an awful lot of them are single nutrients. Some of the supplements are actually whole plant foods, I don't know what to make of those; those are things that you can eat, which don't kill you right away, maybe help

you. But are they food – they're not quite on the usual menu. So Psyllium – Psyllium Husk is a really good example of that. We don't eat much Psyllium in our diet, but it does, we know, lower cholesterol quite a bit. The US dietary guidelines and many of the guidelines across the world now, really emphasize plant centered diet. But at the same time, they would also tend to say, but keep fat less than 35% of calories.

So I think that it's confusing and inconsistent and political. The big problem then becomes for the consumer becomes that we eat only food that's prepared for us by industry. So you can get a lettuce head that'll come from wherever it is, it's still passing, you're not growing it yourself, and probably not much has been done to a head of lettuce. Maybe there's some pesticides on it or some other things to keep it fresher. You can get a dinner tray kind of a thing, or you can get can thing, you can get highly processed things that are set up to maintain a long shelf life, and easy to prepare and so on, those things are probably much less healthy than foods that are closer to as grown. We depend on the food industry, and so, it becomes a vicious circle where the food industry is in business to make money, their business is to supply food, the food affects the health of the people that they're serving, and yet it's not sort of optimally prepared for health. So those are big issues.

DANNY LENNON: So thinking about where we are right now, because some of the topics that we discussed here, for example, this very deep question of thinking about the exposure of interest within nutrition science, and you did extensive writing on this in mid 2000s, in particular, a couple of papers we've referenced, and Alan and I have often talked about your paper with Linda Tapsell for example, the 2007 paper, which gets into much of this. So I'm just kind of interested, because obviously, while writing about this is very interesting, it's with the express purpose of hopefully laying some

foundation for how we can do better nutrition science, and so, I'm just wondering, in those intervening periods of time, let's say, over the last decade, what is your kind of take of where we are with nutrition science now, has some of those messages been – have they been heated to some degree? Has there been an improvement in how we're doing nutrition science at a very broad level? And it might be a difficult question to even answer, where do you think we are and what progress has been made in recent decades with this whole field?

DAVID JACOBS:

Well, I think as an individual science, scientists try to do work, which adds knowledge to the world, I've been much less involved with health communication, and with the idea of actually getting people to change or to follow one thing or another. So my focus has been more on putting information out there. I have colleagues in my department, for example, one of my colleagues years ago, brought to the attention of a local city council that children could buy cigarettes from a vending machine, and that resulted in a city council ordinance that said that cigarette vending machines had to be behind the counter, and it had to be inconvenient and had to have an adult checking. That was an example of a really impactful interventional thing.

Another one is more recently, the Minneapolis City Council passed an ordinance that if, say a small "mom and pop" grocery store or shop, and usually in a food desert, in other words, a place where the socioeconomic status is lower, and it's just harder to get good food, partly because of the insurance costs are so high for supermarkets, so the ordinance said that, if a store said that they had fruits and vegetables, they couldn't have one rotten tomato and overripe avocado, and that was all, but they actually had to have some food and some healthy food that they were presenting.

So I haven't done that kind of work and others have been doing it. What I've been hearing, I

think it's very gratifying to look at the sequence of dietary guidelines reports over the past number of five-year periods, and see the movement towards plant centering, food centering and dietary patterning, people are unwilling to give up the old, and some of the older ideas which are maybe not as helpful, are still in there. The field as a whole, if I say something really extreme, like, just stop talking about nutrients and talk only about foods or talk only about dietary patterns, I do get pushback from my colleagues who say, well, nutrients are also important. And I also think that if you are going to do, say, animal studies, or in vitro studies, of course, pathways exist. And so, you can get back into that reductionism and study some of the foundations of how this holistic approach works, so you can pick it apart and put several of those things together and get a better picture of why it might be that an apple is healthy.

And so, I see a lot of movement in that direction, and also some desire to retain nutrients in messaging, and especially, nutrients where I think it's much more appropriate in doing the scientific studies that are the underpinnings that will help us in terms of the genomics and the proteomics and the other omics in terms of really getting a better understanding of how things work. But I think that the main thing at the point of purchase or at the point of consumption is still, its food base, and its dietary pattern based. So a simple term like a plant centered diet is really extremely helpful. I do see lots of places where human beings do not seem to be entirely rational, beyond the issue of agreement or disagreement, the distinction of what's political, what should societies decide versus what is, quote-unquote, fact. It's pretty hard to discern, and the internet has helped and hindered with that. But I guess, I do see some acceptance of a lot of these concepts. And so, I think they are incorporated in current thinking.

DANNY LENNON: Fantastic. Given that we're just up on the hour mark, we'll start wrapping up. And from my perspective, David, I want to say thank you so much for taking the time, first of all, to do this and come and talk to us. It's been extremely enjoyable to be able to pick your brain on some of this. And as I said at the outset, your work has certainly informed the way both of us think about a lot of these things, so I appreciate your work and for taking the time to do this.

DAVID JACOBS: I appreciate both of you, and the questions that you've asked me indicate that you've read this stuff that I've written, and thank you so much for doing that, and for this whole podcast series.

ALAN FLANAGAN: It's been a pleasure, David, thank you very much in a pleasure.

DANNY LENNON: It's been a pleasure.

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