

Personalised Diets

Chair: Julia Wheeler (JW)

Participants: Giles Yeo (GY), Tim Spector (TS)

JW: Hello and welcome to the Cheltenham Science Festival @ Home, and in particular to this event. We are in association with EDF Energy, and thanks to them for supporting the festival. My name is Julia Wheeler and I'm absolutely delighted to welcome two scientists who come to this subject, personalised diets, from very different angles. How wonderful, because that's what makes a brilliant science event. Welcome, Dr Giles Yeo, welcome, Professor Tim Spector.

Giles is a geneticist at the University of Cambridge who specialises in genetics of obesity. His research looks at the influence of genes in our relationship with food and our eating habits. His book is *Gene Eating: The Science of Obesity and the Truth About Diets*. Tim Spector is Professor of Genetic Epidemiology at King's College London. He's Founder and Director of the Twins UK Registry, which holds genetic and other information on 13,000 sets of twins. His latest book is *Spoon Fed*, which is out in the summer, in August, and in it he says almost everything that we have been told about food is wrong. What a great place to start, really.

Let's come to the genetics. Giles, in your book, one of the first chapters is wonderfully titled 'are our genes to blame when our jeans don't fit'. Tell us how much genetics feeds into our relationship with food and obesity, and so on.

GY: Let's put it this way, like you said, I'm a geneticist by trade and every single human trait and behaviour will have a genetic influence. The trick, however, is to determine what role the environment plays. So actually, when it comes to body weight, and in particular, food intake, there is actually a huge genetic influence. So people think, 'body weight, it's all about eating less and moving, that's about it.' That is the physics of it, so therefore it's true, it's one of the fundamental laws, but we now know with regards to the genetics of bodyweight is that by studying the genetics of bodyweight, of which obesity just happens to be one end of the spectrum, we are by definition studying the genetics of how our brain controls our feeding behaviour. So, when people actually talk about the genetics of body weight, it's actually talking about the genetics of how we behave around food. Some people find it more difficult to say no to food than others, and so therefore eat more over a period of time, and so therefore there are some people who are skinny, who are average sized, and who are large.

JW: Tell us about how you've been able to research what you call those brain pathways?

GY: In order to do brain pathways, clearly a lot of the neurocircuitry, the neurocircuits that actually come to understanding the control of food intake, have had to be done in animal models. By its very definition, the last I checked, we can't legally remove my brain, look at it and put it back in. Yet. A lot of the neurocircuitry has been worked out with animal models. Although, certainly over the past year, I've begun to work with brain donor samples, post-mortem brain samples, in order to try and map feeding circuitry into the human context. Undoubtedly, when people talk about neurocircuitry, how our brain controls food intake, a lot of the initial work, the baseline work, was done in animal models, in particular mice.

JW: One of the big differences between us and animals is that we can take in information and act upon it, it perhaps changes our views and so on. How much are those brain pathways influenced, I mean, can you even tell this, from what we've learned?

GY: Clearly a mouse is a mouse, it's a little fuzzy thing with whiskers and a tail, and we are very, very different. So, I guess it depends what question you're asking. Can we look at things like hunger, can we look at things in terms of food seeking behaviour, can we look at proxies of what we might-, anthropomorphised, in terms of how, actually, humans-, clearly, you have to be careful about that. There are going to be elements, certainly with regards to hunger, food seeking behaviour, that we can actually infer from animal studies. You are absolutely right that clearly a mouse isn't going to be influenced by social media, and a mouse isn't going to be influenced, necessarily, by advertising in the way that we are. Those are going to be different inputs, different neural circuit inputs that come in, and so therefore those are going to be different between humans and mice.

JW: Tim, as I said at the beginning, you start from the point that, pretty much, everything that we've been told about food and diet is wrong, and how we have to unlearn that.

TS: Yes. I think the more I got into this research, and because I'm not a lab scientist, I'm a clinician and I'm epidemiology, and so I've come into this from a different route over the last 12 years, and restarted more as a, sort of, informed clinician. All that time ago, realised that most of the things I took as gospel truth ended up, really, having no real basis scientifically, it wouldn't stand up if you presented those facts today. Like, there is a standard amount of calories that everyone needs a day and it's quite easy to work that out, and everyone is 2,000, or 2,500. Those studies are based on tiny amounts of people 30 years ago and haven't really been updated. The fact that we can actually work out how much fat is the optimum amount for the average human on the planet, and how much sugar, the fact it's quite alright to be eating five to six times a day, healthily. You realise, also, that most of the information we've been given, not only does it not stand up to scrutiny, but it's also heavily influenced by the food companies that either directly change our brains to advertising, as Giles has been saying, or are directly funding the research, which promotes their point of view, which there isn't really an alternate scientific answer.

That's why we associate things like it's fine to have fizzy drinks, as long as you exercise. That's fine, because you can balance these two out. It just so happens that the fizzy drinks companies funded 90% of all the research showing that kids really do well when they do exercise. The more I dug into it, the more I saw that there was this real mismatch between what any decent scientist would say is good evidence and the messages that are getting across, that are being mainly driven by industry. Also, the silly need of governments to try and get some guidelines in place to feel they're doing something for the public health good.

JW: Let's leave the government and the food industry side just for the moment, we will come back to it. Fats, carbohydrates and proteins is something that we all learnt at school, but actually the cutting-edge science of that has changed. Should some of us be eating more protein, some of us be eating less carbohydrate, and if so, Tim, is there any way to know whether we are the people that should be the fat ones, or the protein ones, or the carb ones?

TS: This is a debate that has actually been going on for over a century, and the fact we're still talking about it means we haven't really progressed in our mentality and the science. You've got the whole of humanity and you're saying ok, there are just three types of people. There are whites, blacks and Asians, and everything is in those three categories. Within those groups, there are healthy people, there are unhealthy people, there is a huge range of humankind in them, and that's exactly what we're doing to the complexity of nutrition, which has at least 50,000 known chemicals in it, probably many more, within these three categories that we are combining into this nursery school level lesson to say there are only these three things. To any modern scientist, it's completely ridiculous to talk, even, in those terms. There are some good fats, bad fats, average fats, and the same goes for

carbohydrates. There is a huge difference between fibre and just having sucrose and fructose. Proteins, we always think of proteins as a big bit of steak, but actually peanuts and mushrooms are equally good for you.

So, I think just the fact everyone has simplified this into this baby language, we're really struggling to actually understand what's right for ourselves, and when we see a packet it's dumbed down into these signs, how much fat, how much carbs, how much sugar. It's completely meaningless, and it's just there as a marketing exercise. If that particular country is marketing as low fat is good, then the packet says 'low fat' because they've tweaked it to add in a bit more fake soy, or something, to increase the ratios, and we buy it. That's nonsense, you've got to look beyond that, everyone has got to understand, in the same way that we can do basic maths and read and write, more about the food we're eating, and realise it isn't just about those three things and it isn't just about calories. It's all about quality, it's all about understanding.

GY: Part of the main issue here, obviously, in why it is still so simplified, is because, from a personalised perspective, it's been difficult to study what a single person should eat or shouldn't eat. A big part of the problem is because when you look at a public health scenario, people are looking for easy answers, because it's easier to do it on a public health scenario. Which is perennially always going to be in tension with personalisation, which is going to be the way that things are. Now, there are going to be reasons why I might be more responsive to, let's even just use the three categories, the protein, versus carbs, versus fat, maybe someone should be on a higher protein diet, or someone responds badly to fat. One of the fundamental problems with nutrition research is we still cannot do the basics very well at scale. What are the two basics? Can we measure food intake and what we're eating, and can we measure energy expenditure? What's interesting is, yes, you can take a human being and put them in a lab and measure those things very precisely and accurately, but that's one person, or two people, or ten people. Can you do it over 1 million people? That's the thing. If I asked you, 'What did you have for breakfast yesterday?' and you go, 'Porridge,' then you go, 'How much butter did you put with it?' 'A little bit,' 'How much sugar?' 'Maybe,' and then you say, 'Well, what did you have for dinner two weeks ago?' Suddenly, you can imagine how nutrition research becomes mired in imagination and opinion.

So, I think we need to be able to, first, measure our food intake better and our energy expenditure better at scale, before we can come and actually tackle the specificities for what we're doing, and therefore our personalisation.

TS: Yes, but we're being driven down that route about the calorie because it suits the food manufacturers to put on their packets 'this is low calorie' and people will buy something that's 1% lower calorie because it says 'low cal' on the packet. They actually end up eating more of it, as often is the case. The whole essence of the calorie is a complete myth for exactly the reasons Giles said, there is nothing wrong with a calorie, except you can't measure it. Even nutrition professionals cannot measure their calorie intakes.

GY: I mean, you can measure the calorie from a physics point of view, but it's very difficult to measure how much we actually get out of a single food absorbed into us.

TS: It's also hard to measure, on a practical level, over a week how many calories you're ingesting. Even the stuff on the packets is plus or minus 20%, which makes a huge effect. Plus, there isn't a clear link between calories in and calories out that it makes any meaningful sense. There was a Horizon TV programme recently that is still talking about this 20, 30 year old concept that you can just eat a meal and then go to the gym and work out exactly how many calories you're going to burn off.

GY: Both of us were on it, Tim!

TS: I know we were. None of us would have been on it, probably, if we knew what the beginning sequence was like! That's so ridiculously old fashioned, it made a mockery of what we were saying as scientists about the cutting-edge research. All one took from that study was that you can just look at a calorie count on a menu and then work out how many minutes on a bicycle you've then got to cycle off and you're fine. If that was correct, we'd all be skinny. It would be very simple to work out, 'I just need to cut down by half a banana a day and I'll be skinny.' You know, because it's so easy to calculate, you work it out. That's why it's just obvious nonsense, but we've been brainwashed with it all the time.

JW: If this isn't the right thing to do what should we be doing, in terms of thinking about our personal situation, Tim?

TS: I think we've got to move from this idea that it's all about macronutrients and calories and talk about quality of food. So, what effect is this food going to have on my body? Once you start to do that, and you also start thinking about the way you're eating, not the mode of eating, the fact that we've been indoctrinated to snacking and things like this, and you start experimenting yourself with what works for you. You throw out all this brainwashing nonsense and you start thinking, 'Ok, I'll eat this food, which is high in fibre, lots of variety, lots of plants, not much ultra-processed stuff and I'm going to experiment with eating at intervals that suit my metabolism better, I'm not going to be eating six times a day like the average person does. I'm going to leave large fasting intervals, which will help my metabolism.' People start to make their own experiments and work out what's right for them, until the studies like we're doing, with apps and things that can help your personalisation are readily available for everyone, which they're not yet, we have to wait for that.

JW: Giles, genetically, is it easier for some people than others to not only look at what they should be doing, but actually to follow through on what they should be doing?

GY: Undoubtedly. Like I said, before people start @ing me, it's undoubtedly true, only because, as I said, every single human behaviour and trait, including the ability or the willingness to follow rules, regulations independently, what have you, are going to have a genetic influence, but also, obviously, a huge environmental influence as well. Whenever we're talking about the genetics of feeding behaviour, which is what we're discussing here, we obviously have to take into account our biology, undoubtedly, we have to take into account the kind of food we're looking at, but also we have to take into account the environment we've been brought up in, and crucially, our socioeconomic class, our privilege. Our privilege, and privilege comes in three flavours, it comes in time, it comes in cash, it comes in literacy, food literacy, rather than ABC, what's high in fibre, what's low in fibre. As you slide down the socioeconomic scale of privilege, all three of those privileges go away. So, I think that is also very important to actually take into account, but yes, genes have got to play a role, we're trying to find out as much as we can about the genetic aspects of each of these different behaviours.

I happen to be a food intake person, but there are a lot of my colleagues, for example, who are studying the genetics of the ability to want to gamble, or the ability to actually take positive pieces of information and actually integrate that. There is a lot of complexity out there to think about, in addition to just simply putting a pizza in the oven.

JW: You talk in your book about having taken a test. Tell us, one, Giles, about your view on tests as a whole in terms of personalised diets-

GY: Genetic tests, yes?

JW: Yes, and also your own experience and what the results were.

GY: Yes, so I did this for a major newspaper who wanted me to trial out one of these genetic tests that are everywhere. They come in different models, I won't mention any of them, they come in ones where you can buy a little watch thing, in which it actually blinks red or green depending on what food you're near, or something like that, along those lines. I think here is the issue, it might be surprising to hear this from a geneticist, but these tests, at the moment, are a waste of money. They're a waste of money not because the companies that are testing them are lying to you, they're not. They are taking published information about whether or not a specific change in a gene here is associated with a given behaviour, you know, should you be eating carbs, or protein, or something like that. The problem is, these studies are done over millions of people using imperfect data. So yes, on a population level you can say, 'This particular genetic change would influence a flavour, my preference for sweetness,' for example. The problem with it is taking that individual change and making an individual prediction on me, for example. It completely ignores the complexities of my life.

So, for example, when I took this test, obviously they took my DNA and they had my birth date, so they had my age, they could figure out my sex, and they knew my DNA. That was all the information they had, they didn't know how rich or poor I was, what ethnicity, maybe they could work that out, or anything else. So, a lot of these genetic companies are trying to make the data do what they cannot do at the moment. That's my opinion about these genetic tests for now. At some point, integrated into a more holistic, biological framework, so what your parents are doing, your microbiome, your zip code, your postal code and what you do for a living, that may begin to actually provide some useful information. Not for now, don't waste your cash.

JW: Tim, you've been experimenting on yourself in certain ways, and also on your son. You talk about those experiments in your book, tell us what you discovered through doing that.

TS: Yes, I guess for the last six years or so I've been doing self-experimentation, and that's involved going on various diets and seeing what effect it had on me. Some of this I wrote about in the last book, *The Diet Myth*, and one of them was the idea to go on a McDonald's diet for ten days, only eating McDonald's. I'd just finished the cheese diet and didn't face it, and my son was the obvious choice to replace me because he loved McDonald's and he was hard up as a student, so I was paying for his food. He did it, after five days he phoned me up and said, 'Dad, the novelty is wearing off,' he was studying genetics at the time and he said, 'It's affecting my grades and things, I really ought to stop.' As a good father I, of course, said, 'No way, you're going to carry on, we're going to publish this in *The Sunday Times*.' So, he did get a publication, at least, out of his genetics degree, but not, perhaps, as they'd wanted. He'd lost up to 40% of his diversity in that time, his gut diversity, so he got a massive loss of that probably due to the lack of fibre plus all these hyper-processed chemicals and the lack of variety in the diet, I think, in that time. That was much more than anyone had thought possible.

We've tested him every year since then, this was a few years ago, and he still hasn't regained all his microdiversity in that time. I think that's very interesting, because there haven't been many longitudinal studies of this, although it's clearly anecdotal. So, my experiment is to be generally healthy, so I'm right at the top of the diversity tree, and he's right at the bottom, and every time he wants money he reminds me of that. It's an interesting story, and the person who is on a junk food diet in the UK, we have the highest rate of people on processed foods in the whole of Europe, close to 50% of all meals are ultra-processed in the UK. This is an appalling indictment, really, on our public health system and the economy of food, and the fact that it's cheap and everything else. This

suggests that once you're in this rut, your microbes are going to take a very long time to recover, even if you do have the odd kale smoothie, because it's very hard to change that.

I've now also discovered, I did tests on personalising my own-, so you'll say, 'What should I eat?' ok, so generically, eat for my gut microbiome, that's what I talked about a lot in *The Diet Myth*, but then there is nuance on that, it's not just everyone having exactly the same meals. Should I be eating more fat, or more carbs in a broad sense? How safe is it for me to have pasta rather than rice, or whatever? We started this big study called the PREDICT study, which is going to be published in *Nature Medicine* in a few weeks' time, with 1,000 twins and 100 people in the US as a validation cohort. We gave everyone identical meals, basically, and looked at their responses. Like me, everyone had a different response to fats, to a high fatty muffin or a sugary drink, a glucose tolerance test, basically no two people were the same once you looked across the board of about three meals. Nobody is average, and that was the number one message we got, even identical twins were never exactly the same, and often were quite different. One would have a big lipid response when you gave them a fatty meal that lasted for six hours and the other would clear it quite quickly.

We showed in this that the role of genetics still had some role in the way you metabolise sugars, but zero in the way you metabolised fat. That was actually quite revolutionary to understand that. Our gut microbes are much more important in how we digest fat and our gut microbes are much more varied than our genes between all of us. We have a much richer set of genes in our microbes than we do in the genes in all our cells. So, I think what I've discovered is you can't say, 'Just do what I do because it works for me,' everyone is different. That's really the new era we're heading into which, as Giles said, it's hard to transition. You can see why Public Health England hate this kind of stuff, because it's pretty hard to write rule books like this.

GY: But that doesn't mean we shouldn't try. That, I think, is the thing.

TS: No, it doesn't. It doesn't mean, as you said, that we should just trot out the same old rubbish that we've been doing for 50 years that says avoid fats, have starchy foods, try and have a little bit more of this or a bit of that, that's been failing so badly. We ought to educate people, not treat them like idiots, and this needs to be done at school and in medical school, as well. I'm medically trained and I only got two hours on nutrition, I think it was, but you speak to the guys now, they're not getting very much more, and they've forgotten it by the time they're qualified. We're still in this really bad vicious circle where nutrition is seen as not a real science and it's not given the priority it should do, whether it's in school, medical school, or in the grant world, as well.

JW: You say that it's an unglamorous part of science, you touched on the microbiome there and the fact that even in twins they can be very different. Is there something that we can all do to feed our own microbiome? I'm thinking about the diversity side of things, would that be a universal, really, that everybody can buy into?

TS: I think so. I mean, there is a small genetic component to which microbes live in your gut, but compared to other conditions, it's relatively small. It's probably, who knows, about 10%, or something. So, most of it is diet related and environmental related, and so the good news is you can change that, which means you can effectively change your genes, because your microbes are basically a collection of trillions of genes that are all chemical factories. So, if you feed them right, they'll grow and they'll produce chemicals that go in the right direction and will interact with your body and make you healthier, and so we can all do that. Because of this individuality, it's very difficult to say whether this one microbe is good for you and it's going to be good for everybody. We know that's not true, in Africa they can have opposite effects in the environment. What we've learned so far is, there are some general rules that probably work for 95% of people, and that is

having good microbiome diversity, which is increased number of species, is associated with health in virtually every disease we've looked at so far. It's associated with a good immune system, it's associated with less weight gain and a good metabolism and a good response to food. That should be, until we know more about the individual microbes, and we are learning more and we will be publishing soon on 20 or so microbes that we think are ones to watch, that we can maybe use in the population. Until then, diets that improve your diversity of microbes is where we should be heading, and that should help everybody.

JW: Giles, let's talk about metabolism. As far as we know, is there a genetic link which dictates our metabolism?

GY: When you mean metabolism, you mean the rate at which we burn the calories?

JW: Yes.

GY: It's a very good question, you will note that when I started this conversation I said it was all about the genetics of food intake, why didn't I mention metabolism? Undoubtedly, there is going to be a genetic component to metabolism. A scientist Claude Bouchard did this work in which he housed twins in a place for, I forgot how long, a month or so, fed them exactly the same. How many months?

TS: Two months.

GY: Two months, fed them exactly the same thing, and what he found was that in twin pairs, they would gain roughly the same amount of weight, whereas if you actually looked at different twin pairs, they gain a whole range of different weights, ok, and they were all fed exactly the same. Clearly, there is going to be some form of genetic influence about metabolism, so why am I not speaking about that? I think for two different reasons. The first is measurement error, and it's always easier to measure eating than it is to measure energy expenditure. Why? Because eating is a physical act, there are grams you can measure of something, it's imperfect, but we can do it. Energy expenditure is one of two things, you either measure it in terms of heat or you measure it in terms of CO₂ to O₂ ratio. That, at scale, is very, very difficult to measure. At scale, in millions of people. That's the first thing, so I think there is a measurement error. The second problem is effect size. So, a Mars bar, other candy bars are available, is 240 calories. Now, if I'm motivated, I can probably finish a Mars bar in 60 seconds or less, but it will always take me, on average, half an hour trotting around on a treadmill to actually burn off these notional 240 calories. So, my point is, we are going to be very efficient at keeping the calories in us and not burning them as quickly to keep ourselves alive. So, for those two different reasons, the genes are there to be found, but because of measurement error and effect size, food intake is always going to swamp out the energy expenditure, the metabolism side of things, but that doesn't mean there isn't a genetic impact on metabolism.

JW: Tim, one of the ways that people often think about personalising their diets is by supplements, and I mean by that vitamins. Vitamin D is very topical at the moment because of COVID-19, and perhaps that has an effect on people's reaction to it, but also vegans take B12 and so on and so forth. Vitamins is one of the things you say in the book you've changed your mind about in recent years.

TS: Yes, so my clinical specialty is rheumatology, and very early on I specialised in osteoporosis. The number one drug that everyone gets in a bone clinic is calcium and vitamin D, it's just your standard, you can't really get out of the clinic without it. For 20-odd years I was happily prescribing this and writing papers about how important it was, I led the team that discovered the genes for vitamin D in the blood, it has a genetic component as well, interestingly, which means that some people are

genetically higher than others. They may not need as much, we tend to forget that. I was a big fan of it. Really, I guess, the last ten years I've started looking at it, questioning it, studies about vitamin D really working in osteoporosis started to come out and all the data, really, in the last five to ten years has been negative. There is no benefit at all once you do a clinical trial. So, all the data observationally associates things like vitamin D, or vitamin C, or fish oil, or whatever it is, with being healthy and not taking it and being unhealthy. Or, even levels in the blood. But that doesn't mean it's causal. It just means it's an association, that once you get ill maybe these levels go down, or you don't eat right, or whatever it is, we don't really know, and that seems to be across the board. As soon as you do a large, massive randomised trial, and they've done some huge ones, particularly in the US, they see no effect of these minerals, supplements, on the outcome.

There is no evidence that they do prevent against fracture or bone loss to any extent, which is the cardinal one everyone knows, you know, it must work, the sunshine vitamin, everyone loves it. Yet, the government still promotes it and tells everyone to have it every year because of the association studies. Now they're promoting it for COVID on the basis of association studies that show that people in intensive care units have low vitamin D levels. It is just complete nonsense. It's a billion dollar con every year, the vitamin industry. We think of it as a small industry, but it's pretty much as big as the pharma industry now, with marketing people and sponsoring all kinds of research, so all the information we see is biased. Basically, I can hardly think of any real examples where it has been shown without any reasonable doubt to work. Vitamin D and fish oils are marvellous examples, they're the two commonest drugs, medicines people take, and they spend a fortune on every year. As soon as I mention something negative about it I get so much negative press, I get my email inbox filled up, I get my Twitter account-, you know, I get crazies after me saying that I'm in the pay of the pharma industry, it's like a religious cult. Giles must have had this as well.

GY: I did. So, I did a Horizon investigating the supplements industry. What is interesting is what Tim says is right, now I only learnt this when I actually did this documentary, is that because vitamins are considered 'food', meaning that I find it in an orange and what have you, they're not regulated like drugs. In fact, they're not regulated at all, when it actually comes to vitamins. Whereas, if you're saying a drug, paracetamol, whatever, it helps with my fever, there have actually been clinical trials to show that paracetamol lowers my fever, and so therefore you say, 'Oh, ok.' Whereas, no one has actually done this with most vitamins because they're considered food. If you look at the side of the packs of supplements and vitamins, they don't say 'this will cure your-', whatever it is they cure, they say 'this contributes to normal', which is a word gymnastics, as far as I can understand, in order to try and associate it with something. The vitamins, supplements industry, that's a whole other Cheltenham talk!

JW: Giles, I wonder how concerned are you as a scientist about the whole funding model? I should imagine you have to be careful in what you say here because you are funded in a particular way, but reading both Tim's book and more generally, there does seem to be something systemically problematic about the funding coming from people who have, potentially, vested interests.

GY: Ok, so I think it's very tricky. Just FYI, I'm paid by the MRC.

JW: What's the MRC?

GY: Sorry, by the UK Medical Research Council, I'm in effect government funded in order to do obesity research. I don't think there is a black and white answer to this. I think a couple of things, we do need to engage with the food industry, because they make a large chunk of our food. So, I think completely demonising them is unhelpful. That being said, Coca Cola or Pepsi Cola funding research on sugar and the effects of, you've got to be really, really careful. I think, first of all, a scientist

accepting that money, it has to be clear that the money comes from there, it has to be clear that you haven't been influenced in your publication, and people have got to believe you. It's interesting, once, I won't name the company, they asked me once to be-, a famous candy bar company asked me to sit on their scientific advisory board once, a long time ago. I'm no idiot, some people might disagree, I went to speak to my Head of Department and he asked me this question, which was very interesting. He says, 'Does it pass the *Daily Mail* test?' I said, 'What's the *Daily Mail* test?' If the *Daily Mail*, other tabloids are available, created a headline about you, 'Cambridge scientist funded by candy company', would your career survive? It was an enlightening moment and I turned down the opportunity. I think one has to be very careful and understand the benefits behind it, and make sure that you are absolutely not influenced by it at all, which is easier said than done, but I won't be black and white about it.

JW: Let me ask you, Tim, if I may, would your PREDICT study and your association with ZOE, would that pass the tabloid test?

TS: I think it's already passed it, because we've done lots of publicity and we're very transparent about it. I think there is a difference between doing real science, publishing in journals like *Nature*, where the company has actually paid for real research, rather than just marketing, in an open way, through grants to the university and things. So, I'm very happy to take the *Daily Mail* test. I'm an entrepreneurial academic, and basically no one else would fund that study that I wanted to do and good for these guys, they want to do it the hard way by spending millions of pounds to fund a study that was done in a fifth of the time that it would take standard grant writing and everything else to happen. So, I think we have to also embrace that side of it and realise it's very different to me-, you know, I wrote a negative piece about breakfast eating in the *BMJ*, saying that it's an invention by the food companies that we should all have breakfast and that there is this myth about it being really bad for you to skip breakfast, when actually the contrary is now true. Most people probably benefit from skipping breakfast, but it's personalised. Two days later I was invited to be on the advisory board of a breakfast cereal company, for potentially large amounts of money. That would have definitely failed the *Daily Mail* test.

Some people, and many in the nutrition world, don't have the benefit that Giles and I do of being in big institutions that are well funded, that give us security. They will be kicked out if they don't accept that money, and that's what happens around the world in many places, they're totally dependent on this industry money and they will then steer their research in that way. I think it's still very upsetting that in the UK, the people making up our nutritional guidelines, most of them have taken this kind of money, or are on advisory boards, etc. You can be as transparent as you like, it definitely still affects your independence and your ability to look at it from afar.

JW: So let's come back to the central question of this session, personalised diets. Giles, what are you excited about in that world that we can potentially look forward to in the next three to five years?

GY: I think the genetics, in terms of the way that we can actually look at our genes, the technology has come on leaps and bounds. So, we can almost now put to bed the looking at our genetics side of things, because we can pretty much look at every single gene in our body relatively cheaply. So that's exciting, we're now no longer just looking at a few hundred variations, a few thousand, even a few million variants, if we're able to look at all 3 billion. So, I think that is very, very powerful, and what is limiting us from fully leveraging at the moment is, A, computing power, but that will come up, but B, the measurement of the environment. So, what is going to be exciting to me is, as we become better at measuring the environment-, I mean, we walk around with these God forsaken

phones, I love my phone, you know, and take pictures of our meals and what have you, I am looking forward to the day when we can actually have a very, very precise measurement of what I've actually eaten, what someone has actually eaten, over a huge period of time, to then maximise the genetic information we're now able to get.

JW: Tim, same question to you and perhaps related to your PREDICT app, and so on?

TS: Yes, I think the experience we've had in the last two months of launching the COVID app, where we have 3.2 million people downloaded it now in the UK, probably the largest citizen science health project, shows how engaged people are now with their phones, and are prepared to interact with it in a way that wasn't possible just a couple of years ago. The PREDICT study, in a way, was a forerunner of that, we got several thousand people to log on there all their meals for two weeks, and then by doing blood samples and stool samples for microbiome and metabolites, etc, you'd get an algorithm and you can then see what food the algorithm predicts you will do well on. I think this combining of data on a big scale with all the aspects to it, which includes some genetics, whether it's family history or actual genetic-, the idea you combine things into an algorithm which looks very simple in the end on your phone, helping you make choices, I think is really the future of where we're going. You can't stop it now, I think everyone has realised this is the future and you go shopping with your phone, people are doing it in many countries now, in France it's huge, you put your phone in front of something and it gives you this recommendation about what you're going to eat. I think this is going to be a future, and it's going to mean that these guidelines are going to be meaningless, and the manufacturers will have to keep up with the consumer, the citizen scientist, every day, in the same way we're dealing with COVID, making the same choices they are with their food. I think it's going to be a very exciting time as we use big data for the individual and try and get it right. It's going to take a while to refine it so that it's really good, but it's definitely good enough now to be useful, and it's just going to keep getting better as more people use it. So it's a very exciting time.

JW: It is very exciting, thank you both so much for being here and sharing both that excitement, the fascination, and that cutting-edge scientific side of things. So, Giles, your book is out now and is available in the link on the Cheltenham Science Festival website. Tim, there is also going to be a link from Waterstones there to yours, and yours is out towards the end of August.

TS: Yes, because of COVID, my book launch, which was supposed to be last week, is not happening until the end of August, but do pre-order it and you'll just have to wait and savour the moment.

JW: Thank you both so much for being here, and thank you to everybody for watching, for being part of this, for supporting the festival in this way. If you would like to donate that would be lovely, there is a link, again, on the Cheltenham Festival website. We look forward to seeing you back on the stage in Cheltenham one day soon, and in the meantime take care, keep safe.