DANNY LENNON: Hello, and welcome to Sigma nutrition radio. I am your host Danny Lennon. This is episode 405 of the podcast. And today I'm delighted to be joined by Dr. Adrian Brown, who is a lecturer and research fellow in the center of obesity research at University College London. He's also a senior specialist, weight management and bariatric dietician with over 15 years of clinical experience, as well as a PhD in medicine from Imperial College, London and his research interest center around obesity type 2 diabetes, bariatric surgery, weight stigma, and then the use of formula based diets in different patient populations. And we're going to dive into a lot of that in the course of this conversation with a specific focus on type 2 diabetes, different dietary strategies that are used there, how we should think about remission, the low energy diet trials that have been used. And then what potential interventions we have for people with type 2 diabetes who are on insulin. And so a lot of really interesting concepts within here, and I really hope you enjoy this conversation. The show notes are going to be over at sigmanutrition.com/episode405. They're all link up to anything relevant to the podcast. You can get transcripts to the show there as well, and if you enjoy these podcasts, then please consider sharing them around. So that is it for me without further do, let me introduce Dr. Adrian Brown. Dr. Adrian Brown. Welcome to the podcast. How are you doing my friend?

ADRIAN BROWN: I'm very well, thank you very much for having me Danny, really looking to having a good chat today.

DANNY LENNON: Yeah, I, I'm, I'm very excited for this based on of our previous conversations off that we've had. And some of the really interesting work you've been doing and some of the really excellent publications, I must say that have been able to read that you've put out in recent times. So before I get to my questions can you maybe introduce yourself to people listening about your area of focus around research, how you kind of got there and other pieces of context that might be useful for them to know.

ADRIAN BROWN: Of course. Thank you. So, I'm a research fellow and lecturer and nutrition dietetics at the Center for Obesity research at University College London. So by background, I'm a senior specialist, weight management and bariatric dietician. So I worked in the NHS for around eight or nine years in the west Midlands. And from there, I set up a sort of helped set up the regional weight management service within our hospital. So at the start we literally had one clinic a week. That was a band five and a band seven dietician. By the time we left with the help of our consultant, we had 10 clinics, we had six groups working, we had three or four members of staff, so really developed how obesity was seen within the clinical service at the hospital. So I was very lucky then to get an opportunity to go and do a Ph.D.

So I moved down to London to Imperial College London, and I did my Ph.D. with Professor Gary Frost. And during that time, I looked at the impact of low energy diets in people with type 2 diabetes treated with insulin. And hopefully we'll talk a little bit about that later, after a wonderful time there, I then was very fortunate to on University College, London, where I am now. And I'm under Professor Rachel Batterham, who is a expert in, in, in obesity. So our group really looks at the sort of pathophysiology of obesity and type 2 diabetes in order to identify sort of new preventative and therapeutic strategies. And much of our work centers around appetite regulation and using bariatric surgery as a model alongside pharmacotherapy, we do both commercial and obviously independently research studies. In addition to that, I've got my research area re-center around obesity type 2 diabetes and the use of formula low energy diets in the variety of conditions, but sort of more recently.

And since coming to UCL, I've been focusing a little bit more on weight sigma and terminology and people living with obesity and during COVID I was involved in sort of three national surveys looking at the impact of COVID 19 on vulnerable people and identified at high risk of illness by the UK government and people living with the obesity and also weight management services. So very much that's my research. In addition to that I'm a, I'm vice chair of the specialist obesity group for the BDA and I'm honorary academic at public health England as well.

DANNY LENNON: Fantastic. So there's a lot of that that I want to try and plough through with, within the course of this conversation. And I think maybe a good place to start is if we look at type 2 diabetes and particularly if we're aiming to look at dietary strategies, one of the big conversation points is around remission of type 2 diabetes and how that should be viewed. Should that be a, a goal that we're setting out if someone is going to be working with patients with type 2 diabetes, can you maybe speak to a bit about that?

ADRIAN BROWN: Great question, Danny. Thank you. Of course obviously I would suggest that your listeners have, they've not already checked out podcast by Professor Roy Taylor and, and Nicola Guess who very, very eloquently talk about remission and type 2 diabetes. Hopefully I'll be able to give a bit more of a flavor today. So I think firstly, when we talk about remission, I think we need to really get a definition about what actually remission is. Cause I still think there's a lot of confusion on the definitions within different studies and different criteria that are used. And this can often lead to a little bit of confusion about if someone's in remission or if someone's not in remission and how do we compare different dietary approaches or different tree options to actually generate or, or elicit remission. So there's currently around four different definitions that look at remission.

So the first remission definition is the ADAs and that was from boost in 2009 and they had two separate definitions. So they had partial definitions. So that's no diabetes medications within HbA1c of less than 46 for over one year and complete, which was no diabetes medications and a fasting blood glucose of less than 5.6 millivolts per litre the greater than a year. So slightly different in terms of other

remission definitions that we've seen. And these were very much used when we started talking about bariatric surgery and remission. And its sort that historical bring in, how do we find remission of type 2 diabetes, because I can very much remember years of go working with, with surgeons and very much seeing patients having had bariatric surgery. And then the day after almost coming off their medications and hundreds of units of insulin and very much there was a sense of words being called quote unquote cure being bandied around.

And I remember a lovely cartoon that was brought out of two children playing in the sun saying my, my daddy's a doctor. He treats diabetes. And then the other child saying my daddy's a surgeon and he cures it and this is very much the sense that there was an idea that we could cure diabetes. When you started looking at the data for remission data with diabetes, you did see that initially we saw large amounts of people achieving remission, but gradually over time, significant numbers of those would actually then come back into possibly having diabetes. So there was very much a sense of how to be able to define what remission was and, and this original ADA guideline very much helped with that. Obviously more recently there's been the direct definitions. So they define remission as having an HbA1c obviously less than 48 millimoles per mole and I should have said earlier, that is the cut off for someone being diagnosed with having diabetes.

So having a blood glucose of less than of those thresholds and then being on no diabetes medications for two to three months in the previous 12 months, so slightly different than the ADA criteria, then virtual health and also have some different definitions. Again, they use a similar definition to ADA. So remission is no diabetes medications HbA1c than 48 and over one year. But then they brought out a new term, which was quote unquote reversal, which was again an HbA1c under threshold for greater than year, but they were allowing people to be on Metformin. The concept was, it was a remission, it was reversal. And we can talk about sort of terms and how patients might find that quite confusing.

I'm reversing my diabetes. So you mean I don't have it anymore. And I think terminology is really important when

we start talking about it and you'll see it in the literature, the difference between people saying pure reversal remission. And I think we've got to be very clear with patients when we are talking to them about what we mean. The final one is by the ABCD, and this is a, a UK based diabetes group. So this talked about again, an HbA1c of less than 48 or a fasting glucose, less than seven for over six months and session of all diabetes medications. But they said that that had to occur along eye weight loss. And so that was quite an interesting introduction. And, and what we'll talk about later on is, is a review that we did really looking at those definitions and starting to understand, okay, weight loss doesn't happen that might actually be needed for some of the mechanisms or the drivers of type 2 diabetes to be addressed.

Is that truly remission? So I really think right at the start, we need to be thinking about defining remission in a way, in a better way. Hopefully there is going to be an agreed guideline coming out from the ADA and diabetes UK, but that hasn't been published yet, but hopefully it'll be on the way. And hopefully that will then bring together all those definitions. So we can really get to the crux and talk about remission on, on an even keel. I do agree that remission in terms of being used a regular term has only really come out regularly. And I really do think, as you were saying at the start, that it should be thought as a treatment option, how it's over only, just recently being thought of originally very much diabetes treatment focused predominantly on controlling blood glucose, but then didn't necessarily look at the underlying causes of type 2 diabetes.

So one of those would possibly be excess obesity in the body impacting glucose regulation and would be a key factor. So it was very much around medication escalation to control like glucose. So it's very much like having a leaking roof and instead of fixing the leak, you simply put buckets out as a solution. And when they fill up, you simply replace it with another one. That's very much how we would see that where people would just have these dose escalations and some people might not have needed those escalations if we'd look to a addressing their diabetes in a different way, but it was very much that's how I was seeing people in, in, in, in clinical practice. So more recently, as I was saying, we published some data, a review looking at dietary approaches. So we

published that in the general human nutrition dietetics very recently.

So we had a group of diabetes experts academic dieticians myself involved in Dr. Dwayne Miller, who was the corresponding author on that. But also we had experts within low energy diets, but also proponents of low carb. So we had people like David Unwin, we had Trudi Deakin. We did have Dr. Maholtra, because we really felt it was important to engage with the low carb doctors and physicians and to really get a good balance of, of saying, well actually potentially low carb could be an option. So, I mean, from our findings, we, we very much found that as we were saying before type 2 diabetes remission should be a primary treatment. And what we found is that there's multiple dietary approaches that can bring around remission though at present mere replacements. So low and very low energy diets offer the best quality evidence.

Low carbohydrate diets have been shown to be effective in UK clinical audit data. And we are seeing that within clinical practice, some great results coming out from clinical practice from Dr. David and when some really great results there. And it should be considered as a dietary approach. Weight loss does tend to be from our looking at the data, the primary driver and looking at the data that's come out from direct. When we look at bariatric surgery, weight loss is that primary driver. However, if weight loss isn't achieved, but people do achieve non-diabetic blood glucoses. So for example, in low carbohydrate, if I remove carbohydrate, there is an opportunity that I get my blood glucose less than 48. If I don't lose weight, have I actually impacted the mechanisms that have driven my blood glucose to be impacted? So for example, things like, I know you've talked about atopic fat, deposition that impacts on the liver and the pancreas, have those actually been impacted by the lack of weight loss or are we seeing normal blood glucose?

So instead of us calling that remission, we've suggested that instead it should be called mitigation. So it's mitigating the fact. So as opposed to remission, cause we haven't actually changed the underlying biology. So if I reintroduced carbohydrate someone's blood glucose would go back up, haven't dealt with the underlying causes, very much there's,

there's a variety of different options available. I think what you need to do is you need to speak to your patient initially if you, they, if they wish to get remission, but understand that there's in terms of the evidence, there are, there are some options that have higher quality evidence behind them at the present time, but there are some highly effective treatments out there including low carbohydrate that should also potentially be considered.

DANNY LENNON: Yeah. Fantastic. And, and there's, there's a lot within that to, to kind of unpack. And I think one really useful point is that movement from, like you said, previous times of thinking about how do we manage this condition and through medication, and then some maybe dietary advice to now through a number of, of different ways, different people are thinking about it, but still with that same idea of, we can put this into remission and again, we can get some clarity over what thresholds we're going to use for that going forward, but it's still the same idea that we can aim for remission as opposed to really manage it. And we can have people maybe reduce their levels of medication as opposed to this dose escalation, which is really interesting, before we get into maybe some of the, the specifics around some of those as particular interventions. One thing that I wanted to ask about was when we consider the ability for a patient to potentially achieve remission, is that something that we know is plausible for all patients? Is it going to be a certain subset of them? Are there certain factors that would increase the likelihood or the, the ability for someone to be able to have remission as an option or not what we know about that type of issue?

ADRIAN BROWN: Yeah. So another great question. I think there are multiple factors that can impact on a patient achieving remission and there's multiple interventions that you might wish to look at. First of all we'll, we'll, we'll talk a little bit about bariatric surgery, because you spoke about it right at the start and, and that was one of the treatment options that really sort of brought forward to say, okay, actually we might be able to achieve remission in large numbers of people. And, and if you look at the nice guidelines that came out in 2014 and they were the updated, they, it talk about the use of bariatric surgery to help people with type 2 diabetes. And they actually lowered the, the threshold for the BMI lower than it was. So it should be used as an option. Bariatric surgery has been

shown to be the most effective treatment for both treatment of obesity, but also type 2 diabetes.

However, is completely underutilized in the UK. Less than 1% of people who are eligible actually get bariatric surgery and those numbers have decreased even further due to COVID. And obviously it being a, an elective surgery and, and aerosol forming meant that the surgery lists were canceled so large numbers of people. And will, we can possibly talk about this later on, actually ended up having like operations paused and canceled. So really impacted on people, but sort of coming back to sort of those, those mechanisms per se. So when we start looking at what potentially impacts glycaemia after bariatric surgery, there's a variety of different aspects. There's changes in gut hormones. So very much around this idea of incretin. So GLP-1, PYY, GIP those sort of hormones that might end up impacting on, on blood glucose. There's the around bile acid metabolism, reprogramming of intestinal glucose metabolism have also been linked and vagal tone.

But more recently when they've been looking at the data, they very much found that actually the initial improvements, those first seven days are very much related to energy restriction. So the significant reduction of energy going into the body, and they've done some studies and Roy Taylor and Rachel Batterham my boss did a study a few years ago that looked at that and very much found, saw that that, that energy restriction was key in those, that initial period. In terms of long term remission, very much it's around weight loss. So when people lose weight and see them weight, we gain often we see diabetes come back. Obviously there, there there's been a lot of work looking at sort of the mechanisms related to type 2 diabetes. And you obviously, I mentioned Professor Roy Taylor earlier on who very eloquently talked about the work that he did talking around the twin cycle theory and did a huge amount of work there.

But when we start looking at some of his work that went into responders non-responders, so this was the Stevens work in sort of 2016. And what they did is they compared the people that achieved a blood glucose of less than seven. So that's how they were defining remission quote unquote at that time, not so a normalization of blood glucose. So what they

found is they tended to have a lower body weight. At baseline, they tend to have a higher plasma glucose, a lower HbA1c or fasting glucose. They were younger. They tend to be on lower medication duration. So they tend to not have be on medication for as long. They tend to have fewer medications as well. And most importantly, and probably linking in with the twin cycle theory, they had lower pancreatic fat. So that was very much from the, from the initial work that was done by Roy Taylor.

More recently, George Thom from Glasgow has looked at the, at the direct data and has started to come out with some potential other predictors that might predict people achieving remission, again, strongest predictor. And I'm going to say it again, weight loss, both at 12 and 24 months. And when we start looking at the at, at the data for every additional kilo of weight loss in the first year, you are 32 times more likely to achieve remission. And at 24 months, 25 times more likely. So the odds ratio are really high to achieving it for additional kilos that you can lose. It doesn't mean that people will not achieve remission at lower body weights because some did in the control group for direct, but they did lose larger amounts of weight. So we do see around 10 to 15 kilos being needed to lose, to actually achieve remission in terms of baseline predictors, fewer diabetes medications.

So very much marrying what was seen potentially in, in bariatric surgery, better quality of life was quite interesting, but also at 12 months it was a lower HbA1c at 24 months, older age and male. So actually there's heterogeneity and there's not a confirmed area apart from weight loss. So I think it can be quite challenging to say exactly how are we going to say, someone comes into my clinic, are you going to achieve remission, in each time? So I think we've got to be honest, not everybody is going to achieve remission. If you attempt to do that as a treatment option. However, it's important that we do offer it as a key aspect. Other mechanistic actions, very much from Roy Taylor's work. And this is low looking at the direct data. I was very much the ability to restore first phase insulin response.

And when they look further, they noticed that there was a reduction in the production of very low density, lipoprotein

triglycerides released from the liver, and they appeared to be key mechanisms, but how do we translate that? That's great to know, but do I translate that into Bob who's come and seen me? I think it's very difficult, cause I'm not going to be able to look at his first phase insulin response. No, I'm not going to be able to do see that diet. I'm not going to be able to look at these, these aspects. So these are great to know and, and it's understanding, but how we translate those into clinical practice, it's understanding that there's going to be a variability in people achieving remission, but there does appear to be some guys to potentially those people that might achieve it more than others.

DANNY LENNON: Fantastic and I definitely want to talk a bit more about that translation of some of these interventions into practice in a bit, but first at, at this point, given that we've brought up some of these interventions, you've referenced a low energy diet trials as well. Maybe we can discuss the specific trial and that that you've published in relation to low energy diets. And I think this is an area where thankfully more people are becoming aware of this and the success of these types of trials. But certainly at first there was a lot of confusion and particularly when it started getting rolled out within the NHS. And so maybe you can clarify first what we're talking about with these low energy diet trials, and then maybe introduce specifically how you set up your published study.

ADRIAN BROWN: The first one. I, I'm going to go into definitions again. Cause again, there is some confusion and, and there's different terms that are banded around. And I think it's important when I'm talking today, I'm going to be talking about low energy diets, so low calorie diets or as better described low energy diets. So a calorie is a unit of energy. Therefore, strictly speaking, it should be low energy and not low calorie, however, in popular culture and everywhere else, people throw out low calorie. So I'm very much a person. If I get a document and I see low energy, I will cross it out or low calorie I'll rule, cross it out for energy. But unfortunately it's in popular culture and people use it between each other. So, so it can be used interchangeably. However, I'm going to be talking about low energy diets. So the first one is very low energy diets.

So very low energy diets are, are diets that are less than 800 calories. So this was defined by NICE again in 2014, their original definition of very low energy was less than a thousand calories. These diets also codex in, I believe in 1995, defined it as darts containing 450 to 800 calories. Now these diets are designed to replace your entire diet. So they're what we call total diet replacements. So the diets that I'm going to be talking about today and the diets within direct are not food diets. They are specially formulated products. So the specially formulated products tend to consist of soups, shakes, bars, and porridges and meals. And they tend to consist of any calories around 200 calories. They tend to be higher amounts of protein to minimize lean tissue loss. But also in addition to that, they tend to be recommended in the UK to population recommended intakes of vitamins and minerals.

So each product has around a third of your population recommended intakes. And so on three, you would in theory, be nutritionally complete for those, for those limits. And more recently the European food safety agency came out with a report that looked at the use of very low energy diets. It still is an in, in circulation and there's still discussion whether it's going to be. So they did a big review of all the data, but they were suggesting that very low energy diet should be a minimum of 600 calories per day. And that was on their review of the data that particularly looked at composition and the need for things like glycolysis and, and the requirement for carbohydrate and fat. And they came up with 600, but those are in circulation yet. So very low energy diets, less than 800 low energy diets are 800 to 1,200.

Again, they can be TDR. So Total Diet Replacement, usually around four products, or they can be within additional meals. So they would be partial meal replacement. So they would have maybe three or four products and then you'd have an additional meal taking up. We'll talk later on about food reintroductions. So this is often how very low energy and low energy diets go. You have a, what we call a TDR phase or a Total Diet Replacement usually lasts between 12 and 16 weeks. And then you gradually introduce food back. So isn't we just stop. And then people go back to their normal diet. There's actually a gradual food reintroduction that helps people to start to feel more confident about introducing before we literally just take it away. And what

you see when you speak to people is people are quite nervous. They actually quite like these, these periods of time where we take away food.

And part of the reason is, is that there's a control element. They don't need to think, oh, I, goodness me, what am I going to have for breakfast? What am I going to have for lunch, oh I'm really busy, actually, I don't have time for lunch to actually I'm going straight into a meeting. Oh, you know what, there are there some biscuits there or there's the, the takeaway shot there. So people feel far more in control during their periods of time. And so bringing food back in that can often have a sense where people have a lot loss of control, re introducing something that gives that feelings can be quite, can be quite stressful. So we gradually reintroduced food and then we go back to more traditional diets. There is data out there suggest that the continuation of using one product today can actually help with weight maintenance and there's data sort of up to four years in patients with osteoarthritis.

So the continued use or behavior change have been shown to help with the, the maintenance. They're very much the definitions that we have at the present time. And so when I'm going to be talking about very low energy diets, I'll talk about it. But within my study that I'm going to be talking about, we used a low energy diet, so that was four products around 800 to 820 calories. And we actually use the same products as the direct study. So very sort of comparable in terms of the, the results. And we, we can talk about that in a minute.

DANNY LENNON: Fantastic. Yeah. So let, let's, let's get into some of how that, that trial was designed. And, and particularly from the outset, what you were looking to answer with your particular trial and maybe some the outcomes that you are planning to evaluate.

ADRIAN BROWN: I think first off, I I'd like to just talk a little bit about type 2 diabetes and people treated with insulin. If you look currently at the goals and the focuses of NHS England, they are focus on prevention. So that is the diabetes prevention program, huge and absolutely fantastic, amazing program and remission. So they've just introduced a low calorie diet

pilot, so very much two ideas, and I can see why they've done it. There's huge potential for greater healthcare savings, preventing someone getting diabetes, complications, medications, but also putting people into remission and reducing down that medical burden and complications. However, we've forgotten a big group here, and there's still no effective treatments currently available for people with type 2 diabetes on insulin. And when you speak to people that are on insulin, a lot of it is dose escalation trying to prevent hypos that can end up in impacting on your body weight.

So it's a very complex group of people, but if I look at externally at what's available is a very under-resourced group. So in terms of people, when we look at type 2 diabetes, what from the UK PDS data. So this was a large trial done in the nineties that looked at long term impact of diabetes. What they found is that around 50% of people with type 2 diabetes will actually require insulin within 10 years, when we start looking at other data, in terms of how numbers have increased, there was a 6.5 fold increase in insulin use between 91 and 2010. And what we see in clinic unfortunately is there appears to be some clinical inertia to actually initiating insulin. And you can understand why. I mean, there's a lot of potential issues with insulin. There's issues of weight gain. And we see that after people start insulin that they gain on average between three and nine kilos, there's a variety of different mechanisms related to that.

But that's what we see. So patients know that GPs know that. If someone's living with overweight and obesity, adding on additional weight, is that where we want to go? There's fear of hypos. No one really wants to have a hypo. They're, they're, they're awful things. I've got a friend who has type 1 diabetes and I've I've seen him have a hypo. I've seen multiple people have a hypo. It's not an enjoyable experience. People don't want to have those. And obviously that increases with insulin. There's a fear of failure. That is the top of the tree. Insulin is up here. So as we gradually progress through these treatment options from diet to medications, there's a sense that at actually I am failing, I am unable to control this. You are having to give me insulin and it almost feels and similar to how people feel when they have bariatric surgery.

And maybe it hasn't worked. I feel like that's the top of the tree. That that's the last option they have for their diabetes management, but also there's the injections and the social stigma. Injecting yourself on repeated occasions, doing blood glucose tests. If you've ever done a fingerprint test doing that five, six times a day, start getting bruises. It's not enjoyable. So you can see why people don't necessarily want to do it. But when we look at GP data in the UK, the main HbA1c from data out there looking within primary care is around 9.5 to 9.85%. So we are waiting until people have actually got really poor control before we're initiating insulin, obviously there's those factors, but we should be, there's almost a clinical inertia related to that. So I think often in insulin might not be initiated quickly enough or are there other ways that we can actually help this group to prevent them actually having to go on insulin or those that are on insulin can we actually help them to come off insulin?

And at the present time we didn't have any data sort of say, well, actually we could actually help people in this patient group. So this was very much where our study was born from what we were looking for is looking at this advance people with type 2 diabetes, a very under resourced group. And we are really trying to answer the question, could a low energy diet be safe and effective in people with type 2 diabetes treated with insulin and could we get them to lose significant amounts of weight and hopefully reduce down their insulin burden?

DANNY LENNON: So let's talk about that of initially the setup, but also maybe if you can give people an idea of some of the participants within this study of, maybe is there a, a typical dose that they were on? Do we know how long these participants had been on insulin therapy and some of the other factors that may be relevant to thinking about how we're actually going to, is this a viable treatment for this certain subset of people if that makes sense?

ADRIAN BROWN: What we did is we got 90 patients with advanced type 2 diabetes. And what we did is we randomized them either into an intervention, which was a low energy diet for a period of 12 weeks, following that we did 12 weeks of food

introduction, so slightly different diet direct. They did up to eight weeks. We had a slightly extended period, with our patient group we actually found that they quite enjoyed that more extended period. They got to have a bit more control. So we did six weeks on a thousand calories. So what we did is we had four product initially, and then we took one product off. So they had three product. And then we introduced a small meal that tended to be lowering carbohydrate and protein to start to get them have those start to reintroduce food.

And so they wouldn't see these sunrises in blood glucose, getting them confident and then would gradually reintroduce carbohydrates, small amounts as, as we went through. And then after initial six weeks, we had another sort of two weeks and two products and then two meals. And that was 1,200. And then after that, they returned onto sort of healthy eating advice, very much focusing on the on the diabetes UK guidelines that were produced in 2018 reproduced in terms of the dietary guidelines there, they also got behavior change as well. So we gave them things like our goal setting. We gave them emotional eating advice. We gave them slip up setback information, but also we discussed around self-monitoring. So it wasn't just as, as direct people think, oh, we just give you the diet and that's why they're not achievable. And that might have been true in, in studies in the past.

But very much now our total dart replacement programs, based around looking at physical activity, which we advise people to try to aim for 150 minutes through the week of moderate activity to try and help them during that time and the behavior change and the diet element. So very much these lifestyle interventions. We compared that to a control group. So that was a traditional 600 calorie deficit diet. So that was calculating someone's estimated calorie intake using an estimated equation. So we use a Mifflin St. Jeor and the reason that we use that is that has the best sort of comparison to indirect telemetry out of all the estimated equations, particularly for people living with obesity. And there was a nice review done by Hilda Mulrooney in the general of human nutrition dietetics that looked at that if anyone's interested and again, within that group, we both gave them dietary advice, behavior change advice, and advice around physical activity.

And the reason was, is we just wanted to see if that it was the low energy diet. So we gave them everything the same. And that's why when you look at our data, the intervention group at 12 months lost 9.8 kilos. So around the same as the direct study, even though that they were on insulin, so incredible losses and very similar to the droplet study, they again, lost around 10 kilos. So it does appear that at 12 weeks, this 10 kilo weight loss tends to be a sort of a number that we're seeing throughout these large clinical trials and the control group. We threw this kitchen sink at them. They lost 5.6 kilos. So it really impressive amount of weight loss, they were in control. So although the, the, the effect sizes in our study were smaller, it really shows that actually with the right balance, whether it be using a low energy diet or more traditional ways of calorie restriction with behavior change and physical activity can still engender large significant amounts of weight loss. In terms of the amounts of medication we were seeing.

So on average, people were on around four years of insulin. They were around 13 years of being diagnosed with diabetes. So if we think about the direct study that had less than six years, and if you looked at the average year, there were about three years as a mean, if you look at the DIADEM study, which is to showed hear we study in Qatar, they had even less. And what you noticed there is that, that they were sort under two years and that actually significantly impacted the chances of getting remission. So they actually had 61% compared to 46% in direct. So we really noticing that if you get them early, you're more likely to be able to achieve remission in this patient group, in terms of the insulin doses, we're seeing people and sort of in the intervention group around 73, but the control group we had about 79.

So around 76 units of insulin. So these were patients that had advanced type 2 their HbA1c varied between sort of around 8.7 to sort of 9.3, as mean between the, between two groups. So poor diabetes control, large amounts of insulin. And they've had diabetes for a significant period of time. So really challenging people. These are the paid that you walk into diabetes clinic and go, what am I going to do with you? Cause you are a challenging group and your HbA1c has gone up and what am I meant to do while the doctor's going to increase

insulin and it's not going to help precipitate weight loss, which we see it possibly doesn't cause it encourages weight gain. So that sort of the baseline where we were starting on some really complex people.

DANNY LENNON: Yeah. And, and that, that's the fantastic thing about that, where when you look at that patient population, and I think there's also a really important point that you brought up that I wanted to just reemphasize for people about actually how you went about doing that study, comparing the intervention to the control group, because like you said, by giving the control group, all the other interventions, just apart from the dietary change, that was really useful then, and being able to, when you, we see the differences in the weight loss and therefore some of the other results at the end, you can therefore point to this low energy diet being that kind of factor. Whereas like you said, if just wanted to go for big effect sizes, you could just give the control group nothing, see even a, a bigger weight change. But again, then that just leads to so much confusion as to what actually led to that difference. So I think that's just a really interesting point for people who are interested in learning a bit about how to do studies in a, in a correct way. That's a, a really good point to emphasize.

ADRIAN BROWN: Yeah and in indeed. And that's why we really, we, we wanted to have this very clear distinction. If you, if you think about drug trials that placebo not placebo, all the trial is the same and we really tried to make sure that there was a, it's actually the low energy diet that, that generated this. Some of the most impressive things actually came in with insulin reductions. So we got 39% of people completely off insulin. We got certain, we within some people were off insulin within a week. And so it really started me thinking are we are some people out in the, the community on insulin that don't need to be on it. And the simple thing that we can do is we can use low energy diets or get them to significantly reduce down their energy intake and actually get them off insulin.

And so that was what I was saying, huge amounts. We had a reduction of insulin of around 75% in the intervention group and around 40, 49, I do believe percent in the control group. So still significant reductions. What we did notice is that we had a really nice reduction in blood glucose up to around six

months. And that was when we reintroduced food. And a lot of people had stopped insulin in that point. And we actually had about a reduction in blood glucose around 1.4% at that point, what we notice is, and this sort of goes out to how people then use low energy diets in practice is we wanted to see actually you are likely within a NHS service to get a really intensive block of care in the first six months. And then they'll go, we're going to release you now. And now we're going to have three and six months. And what you notice is that there was a gradual weight regain people that had stopped insulin did not want to restart insulin.

Despite potentially HbA1c getting back up. People didn't want to start it. And I think this really comes down to how we might then think about translating that into clinical practice, is we need to have continued impact during that next six months. So it's not just that initial period of time. It's about that continued contact. It's also then about potentially using meal replacements to help people to maintain that. So thinking about that data that did come out, can we continue to use that to then help people? And in the future, when we're going to be looking at these types of design and these types of trials, that's very much where we're going to be going, where we're going to have this initial block of time. And then we will be introducing, continuing to use one product a day to help with weight maintenance up to 12 months, but still at 12 months, 10 kilos, weight loss, 75% reduction in insulin and also 39% off insulin completely.

So if we start thinking about the insulin burden and the cost on the NHS, there's a huge cost at the present time relates to medications. Type 2 diabetes, estimated cost around 10 billion with large amounts of that being related to medications and complications. So where are the complications going to come? They're not going to be coming up in newly diagnosed. They're going to be in the advanced people. So the people that on insulin. So if we can help them to reduce down that insulin burden, help to reduce down costs, improve that blood glucose. We see an improvement also in other markets in particularly around quality of life. We saw a significant impact on that. So despite the control group, losing 5.6 kilos there, their quality of life improvement using EQ-5D so visual analog scale. So it's the same one that direct use. So what you do is you ask someone

today, how do you feel about your health so, in general how is your health today?

Zero is the worst imaginable health a hundred is the best. Yeah. And people score themselves. And what we noticed is there was an 11 point increase as a mean in the people that use the intervention. There was less than a one point increase despite people losing 5.6 kilos in the control. So very much a sense that actually this reduction in insulin burden, this reduction in stopping insulin has really helped people. And we were seeing that people were literally, some were skipping in at the end, I'm looking at me I'm often slim and I can't believe it. And so, yeah, we really feel felt that we were changing people's lives. The thing now is that at the present time we've got some evidence, some high quality evidence, how can we get it into NHS? How can we now translate that and get that in? Who do we need to be knocking on the doors with and say, hey guys, we can actually people on insulin and how can we basically be using this similar to direct similar to the diabetes prevention program in this patient group and can NHS England and Dr. Jonathan Valabhji pick it up hopefully.

DANNY LENNON: Yeah. I mean, that's where I was going to ask where we have these really interesting and important questions now are coming off the back of what we have clear interventions that are evidence-based that have dramatic effects on reducing medications that people are using that are putting diabetes into remission that are improving quality of life. So we have the evidence on that front, I suppose, the questions now that pop up, come around logistically how to roll that out. So research can still answer some of those questions over what is the best way to maybe plan out that aftercare, for example, and is there differences there, but a lot of it will come down to, like you say, on the frontline, how does this get rolled out with registered dieticians and in clinical settings? And there's a number of different areas that we can discuss barriers from other, getting that, those recommendations out there to even then having that service provision available and right, right. At the top of the podcast, you mentioned, for example, COVID alone has been a huge barrier to putting certain service provision in place. And so it seems like they're the next steps and the challenges, and I'm sure those types of questions are at the forefront of your mind, given the, I

suppose, different worlds that you've had a foot in, both on the clinical side, as well as the research side.

ADRIAN BROWN: Yeah, very much so Danny and I, and we actually did a survey of dieticians last year looking at their experiences and their views of using low energy diets. And currently the papers are under review. So I can't share too much. But what we did see was that there were multiple barriers, including things like costs and also the thought of adherence being an issue. But also there did, there was a feeling that there doesn't appear to be the infrastructure to allow these types of diets to be used within clinical practice and particularly around making sure we've got sufficient numbers of people, but also around funding. And there's a lack of funding. And the question is who should be given the cost? And this goes down to low energy diet with the low cut, low calorie diet program, is that the currently it's going to be the provider that takes on that cost, is that a sustainable model in the long term only time will tell, but once that data comes out, we'll be able to hopefully answer some more of those questions that you were talking about. And maybe we could come back on and we can talk a little bit more about sort of the, the, those, those experiences that dieticians had and what they felt might be some really great things actually helped translate that more into clinical practice.

DANNY LENNON: Yeah. And that's it because, I mean, even thinking about the comprehensive nature of some of these interventions, that obviously requires a skilled professionals who, who can interact with patients. So we need to get patients access to them first of all. And then that's that there's a whole lot of logistical issues, which are interesting to consider, but that might be a conversation for another day. So both before we start wrapping up here, Adrian, is there any open loops or open tabs that we haven't closed off yet that we've brought up that you might want to address? Or where do you think the kind of next steps in our thinking on this issue are that you would like to maybe mention before we close this out?

ADRIAN BROWN: I think related to remission, I think if we're going to be honest, I think we, we need to be considering this more widely within clinical practice. I know that it's been discussed, but there are lots of different treatment options and our review and the journal of human nutrition dietetics.

If you go and have a look at it, outlined some of those options. And I really think dieticians should be thinking about that as a primary treatment options so many of the people, who really focusing not on escalation of medications, but really starting to think, how can we start to actually address the underlying causes or, or issues that might be precipitating someone's alter blood glucose. From a patient group in terms of type 2 diabetes on insulin. I think we've got very complex group. I, again, I think there are treatment options for them. I would really love to see low energy diets come in as a treatment option for this patient group as standard rather than within clinical trials, it's still not being picked up.

So hopefully this podcast will help to propel it into people's minds. And hopefully that can help, but very much in terms of what we do have within our, within our publication, which has published last year. What I would say is we have titration algorithms in there to help people in terms of helping them to titrate insulin down. So what we did initially is we reduce everyone on the low energy, low energy diet group by 50%. And then we monitored hyperglycaemic episodes and adjust accordingly. And we have an algorithm for that. And reduced it around down by about 30% within the control group, but one of the issues, and I'm sure as on the tip of your tongue, and we haven't mentioned that is around hyperglycemia and what is the risk of hyperglycemia? And we're like, oh my goodness, me, they're all going to have hypos on 800 calories.

Actually, when we looked at the number of hypos compared to the control group, the control group had more, why do we, that is, and I'm not in shock, entire sure, we know, but a potential mechanism might be the fact that actually controlling insulin is quite challenging, whether you're on a biphasic. So that is a mixed insulin. And that will be a mixture of a long acting insulin and a short acting insulin. And that can either be given once a day or twice a day, or they are on a basal bolus. So they're on a long acting insulin that's given once or twice a day. And then they're on basal, which is at meal times. And that basal insulin relates to the amounts of generally your, your endogenous glucose production. So that's produced from insulin and these boluses are related to the carbohydrate in your meal.

Now carbohydrate and meals tends to vary quite significantly from day to day. And even myself as a dietician, looking at amounts of carbohydrate, you're like, oh, is that 20? Is that 50 is that a 60 grams. And so it's trial and error in terms of that. And you need to understand how your body's going to react to it in terms of the amounts of insulin and the units that you're giving yourself. And so with the low energy diet, they knew what to give. It was 30 grams of carbohydrate, four times a day, around 120 grams. They were like, okay, I know how much insulin to give herself. And so really more even keel. And when we are, we've got some CGM data as well. And you notice that the blood glucose significantly improves and compared to control. So in terms of that, I really think that people might be worried about hypoglycemia, but using an effective titration regime, keeping contact with your, with your patients as well, can really help to reduce down those risks. And we actually found that the low energy diet, actually had lower risk in that, in that patient group. But if people are really wanting to chat to me, feel free to reach out and we can leave some details later on hopefully at the end about where they might be able to catch up with me.

DANNY LENNON: Yeah. And we will get to that in a moment. And, and really there's a whole host of things I could have talked to you about today. We, we didn't even get to some of your other publications that maybe for another podcast we can definitely get into that, people might check out in relation to some of the weight-related terminology by healthcare professionals. Some of those papers you referenced in COVID-19 and that's impact on some of service provision in obesity treatment and so on. So some fascinating areas that we'll definitely do a round two about, but in relation to today's topic for everyone listening, I will link up to any of the publications and trials that we have referenced throughout this discussion that you can check out Adrian, for people who want to find out more about what you've been specifically doing. Maybe find you on social media or any other specific places you want to send their attention. Where are some places you'd like them to check out?

ADRIAN BROWN: Of course, yeah. I'm going to go with my main place. I can only cope with one social media accounts at a time. So I am currently on Twitter. I am at thehandleatbrownad, so please check me out. I tend to chat about diets and other aspects

and, and around sigma. So we we've got some interesting studies, hopefully coming out soon. So keep you abreast of that. If you're interested in contacting me you can go onto the UCL website and find my email there, if you wish to email me. And that's absolutely great. If you want to talk more about using low energy diets in people with type 2 diabetes on insulin, or if you want to talk anything around our weight stigma or the information around terminology or the COVID work that we've been doing, as you said, Danny, I could probably be here for another hour or so. So we'll keep it succeed today. Yeah.

DANNY LENNON: Excellent. So I look forward to your inbox, getting flooded now with some fascinating questions, cause we have quite the smart bunch that listened to this podcast. So that brings us to the final question that we always round out the podcast on. And of course this can be completely separate from what we've discussed
here today. And it's simply, if you could advise people to do one thing each day, that would have a positive impact on any area of their life. What might that one thing be?

ADRIAN BROWN: Great question Danny. And I love this question by the way, I've listened to it multiple times and people are shocked about it. I'm like, I know this is coming, but whenever I hear about it, I always think the same and that's meditation. So for me it's been absolutely life-changing. It makes me mindful of the things around me. I'm more in the moment. It's helped me to control my emotions. I started it. And I've been on a constant run for 944 days now. So that is either morning or evening and it senses me, it gets me going, starting in the day for the rest of the day, as I'm not sure if you can imagine, I'm sure you are Danny busy. As soon as that day starts, it's, it's like a treadmill. It just goes and goes and goes and goes and goes and getting those minutes to really get yourself ready for the day.

Often aren't, aren't available later on in the day. So that first bit of the morning where you're waking up and you're getting that time and in the evening or those my time that, that, that, that really helps to sense me back. If people haven't tried it, I'll go with meditation. I use guided apps in order to help me. And there's a huge number of them available or for people to try a lot of people that I speak to go, but I can't meditate. It's

too difficult. I'm always thinking the biggest thing for me was realizing that the whole point of meditation is being mindful that your mind is wandering and then bringing it back to the breath, bring it back to that focus. And it's not the fact that some days I'm all over the shop, my mind is just racing and, and I might not feel it's the best practice, but I keep on doing it. And, and so being mindful of where you are, has really changed my life. So meditation's mind.

DANNY LENNON: Fantastic. And did you notice it was a specific amount of time that passed before you start to notice that it was having a benefit? Was there a cumulative effect? Because I think oftentimes it's, people will try it for a while and then say, oh, nothing really happened. But then others that I've talked to have said, there was almost like a tipping point that once they got beyond that, it's the cumulative effect if it done consistently. So seen as you've done it for 900 plus days I think you've got the consistency part down.

ADRIAN BROWN: Yeah. I originally started it and then I had a gap of a few days, and then I got back in this my 944 stretch. And I guess I'm quite all in kind of guy, I'm all in, I'm all in. And so I was meditating a lot. I was meditating Sundays like 50 minutes and I was doing more meditations. I was doing guided stuff. And I started to notice that I was being more grateful and more mindful about the people that were in my life around stuff. So I noticed it sort of more near the start. Now, what was quite interesting is speaking to my friends because I was just like, oh, I'm meditate regularly. And then when I can tell, I was like, how can you tell me? I said, well, you're more balanced and you're more calm and you're more considered. I was just like, oh, wow.

So they were actually noticed that my, that I changed in terms of how I was just holding myself and how I was being more mindful. And so that's really driven me to continue it. The others have noticed a positive change in me, not just myself and I think particularly in, in life. And I live in London, it's a go-go city. So sometimes just having those moments, being able to reflect is, has been a real game changer, but I would say stick with it. Don't try and be perfect. I think people go in there and they think if I'm, if I think about something I failed, I'll give up. And that's often the conversations I have with people who are like, I want to

start, but I'm rubbish at it. Well, don't have to be perfect at it. And that's what I think people try to with meditation, from my experience, I'm not a meditation expert. I just enjoy doing it. So there's far more, there's far better people to discuss this than me, but yeah, I would say, just keep on doing, keep on going back to it and, and you'll hopefully notice the difference.

DANNY LENNON: Fantastic. Well there you go. If that was ever an endorsement for it, then now is the time if people are on the fence about it with that Adrian, let me say thank you so much for taking the time to come and talk to me today for the work that you've put out and for our conversations about it, it's been very, very useful and I know people will find useful too. So yeah. Thank you so much.

ADRIAN BROWN: Thank you very much for inviting me and yeah. Have a great day. Thanks Danny.

DANNY LENNON: So that was our conversation today with Dr. Adrian Brown. Remember, you can get the show notes, this conversation over at sigmanutrition.com/episode405. They're all link up to any of the studies we referenced today, as well as a transcript. And then you can also look at the other content available on the Sigma nutrition website, including our written series of Sigma statements and our back catalog of podcast episodes. If you want to get my email newsletter at the Sigma synopsis, that's free to do so. Just look for the Sigma synopsis tab on the website. And if you'd like to support the podcast, you can do so over on Patreon, by going to patreon.com/sigmanutrition. So that is it or this week. Thank you for listening. I hope you enjoyed. And I will be back next week with another episode until then hope you stay safe and take care.

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