According to Diabetes UK, there are around 3.1 million people with type 2 diabetes in the UK, and a further 1.1 million estimated to be living with the disease, but not yet diagnosed. People over 40 years old (or over 25 years old if of South Asian, African-Caribbean or Black African descent) are more at risk and the condition can also run in families.

However, for the most part, type 2 diabetes – in which the pancreas gradually loses the capacity to produce enough insulin and the body becomes resistant to its effects – is widely regarded as a lifestyle disease. Inactivity and obesity, in particular a large waist circumference, are the biggest modifiable risk factors, and even quite modest weight loss can reduce a person’s chance of developing the disease. For example, the US-based Diabetes Prevention Program (DPP) found that losing just 5–7% of body weight, i.e. 10 to 14 pounds (4.5–6.4kg) for someone weighing 200 pounds (14st 4lb, or 91kg), could prevent or delay diabetes.

Losing weight through a healthy diet and lifestyle is also recognised to be beneficial for those with pre-existing type 2 diabetes. To help manage blood glucose levels and insulin sensitivity in those who are overweight and have the disease, NICE recommends setting an initial body weight loss target of 5–10%.

But can these benefits be magnified – to the point of remission of type 2 diabetes – if the calorie restriction and weight loss is far more drastic? The DiRECT trial set out to discover this in a group of overweight and obese type 2 diabetes patients in a general practice setting.

Teams at Newcastle and Glasgow universities, led respectively by Professor Roy Taylor and Professor Mike Lean, were awarded Diabetes UK’s biggest ever research grant (£2.5 million) for DiRECT after two previous small studies produced the
first evidence that a low-calorie diet could put type 2 diabetes into remission. These studies tested 11 and 30 people with type 2 diabetes and found that, after eight weeks on an 800 calorie a day diet, participants started to produce normal levels of insulin in response to meals and achieved remission from diabetes that persisted for up to six months.

**Aim and design of DiRECT**

DiRECT was designed to build on these results in a bigger cluster randomised trial involving a total of almost 300 participants with type 2 diabetes (approximately half intervention, half control) from 49 GP practices in Scotland and Tyneside. The patients needed to have been diagnosed in the last six years and not be on insulin. Each of the GP practices were randomised either to deliver best-practice diabetes and obesity management in accordance with current NICE guidance (the usual care group), or to deliver a low-calorie liquid diet programme (the Counterweight Plus programme, detailed in Box 1) using nutritionally complete soups and shakes (the intervention group).

The aim of the trial was to establish whether a very low-calorie diet programme delivered in primary care could lead to substantial weight loss and reversal of type 2 diabetes symptoms. The diet intervention aimed to stimulate a distinct period of rapid weight loss with the aim of losing about 15% of body weight. In practice, the researchers aimed for 15kg weight loss, as most of the patients were around the 100kg mark at the beginning of the study.

Those on the low-calorie diet (which comprised 61% energy from carbohydrate, 13% from fat and 26% from protein) consumed a maximum of 825 to 853 calories per day from the liquid meal replacements for a period of between three and five months, followed by structured food reintroduction and long-term weight loss maintenance. Those in the intervention group also stopped their diabetes and antihypertensive medications. When food was reintroduced, this was done so over several weeks, with structured support for long-term weight loss maintenance being provided by a nurse or dietitian. Use of a pedometer with the aim of achieving 15,000 steps a day was also encouraged.

**What did the trial find?**

December 2017 saw release of the 12-month primary outcome results, showing impressive results. Weight loss of 15kg or more was achieved by 24% in the intervention group compared with none in the usual care group. Average weight loss was 10kg in the intervention group versus 1kg in the usual care group. Only 32 of the 150 participants randomised to the 800-calorie diet plan dropped out.

More remarkably, nearly half (46%) of patients in the intervention group were in remission from diabetes a year later, whereas only 4% went into remission in the usual care group, who were being given the best treatments currently used. The chance of a patient in the DiRECT intervention arm achieving remission from diabetes symptoms was dependent upon how much weight was lost, with 86% who lost 15kg (2st 5lb) or more putting their type 2 diabetes into remission (see Figure 1). Remission was defined as an HbA1c of less than 6.5% (48mmol/mol) after at least two months without any diabetes medications.

So what is actually happening in those who lose weight to produce such impressive results? Professor Roy Taylor, co-senior author of DIRECT and Professor of Medicine and Metabolism at Newcastle University says the work confirms the ‘twin cycle’ hypothesis – that type 2 diabetes is caused by accumulation of fat within the liver and secondarily within the pancreas leading to impaired insulin secretion and hyperglycaemia. He comments: "With the approach used in DiRECT, we track the return to normal function of liver and pancreas as the fat levels drop.”

**Remission or cure?**

Diabetes UK says ‘remission’ is the best term for what the diet can achieve. Dr Emily Burns, Head of Research Communications at Diabetes UK, explains: “We use the term remission because there is a chance the type 2 diabetes could return, and it’s important that people still have regular health check-ups.”

**Cost effectiveness**

An initial cost analysis that compared weight loss using bariatric surgery with the use of the Counterweight Plus programme as employed in the DiRECT trial demonstrated that for £1 million of health service resources, 15kg or more of weight loss
How this strict intervention affects patient quality of life is also critical. “The research team are interviewing trial participants and the healthcare professionals delivering the treatment, to really understand their experiences,” says Dr Burns. “They’ll help us understand the potential barriers to people taking part or staying involved in a treatment like this.”

Currently, the DiRECT/Counterweight Plus programme is only available on the NHS free of charge in a small number of test sites, but can be accessed privately, via www.counter-weight.org. Says Dr Burns: “While some CCGs could commission low-calorie diet services for weight loss (as part of a tier 3 weight management service), the programme involved in DiRECT is very unlikely to be embedded across the NHS until we have sufficient evidence about its effectiveness.”

There are other unknowns – the programme is unlikely to be suitable for people already taking insulin and probably wouldn’t be appropriate for people who are not obese (the average BMI of people entering the study was 35). Because the participants were predominantly of white ethnicity, it’s also unclear whether the approach would be suitable for other groups – for example, for people from an Asian background, who have a higher risk of diabetes.

For now though, the intervention shows promise. If further

**Case study**

Tony Mason, aged 52 from Hexham, Northumberland took part in the DiRECT trial.

He says: “I went to the doctors with a knee injury originally, but while I was there they did a blood test, as I was feeling quite unwell generally, and tired. “I got a call the next day and was asked to go back as my blood sugar levels were very high. They put me on metformin straight away and did some more tests. I was shocked to be told I had type 2 diabetes, as my father also had type 2 diabetes and had died a few years previously with complications.

“When I was contacted to participate in the trial, I was happy to give it a go. It seemed a bit daunting as I was going to be on 800 calories a day with no solid food – it was all just liquid. But by the second day, I was starting to get a bit of energy, starting to pick up a bit and by the third or fourth day I was starting to feel better and thought “well maybe I can do this after all.”

“By the end of the programme, I was down to 68kg from 94.5kg and I had stopped taking all my medication. I’ve noticed my tastes have changed – previously, I’d never have eaten vegetables like pepper or celery but I’ve started to quite enjoy them.

“My blood pressure had been sky high, but that went back to normal too. My long-distance eyesight also came back – I used to wear glasses for driving but no longer need to.

“I am in remission from my diabetes and feel 10 years younger. I feel like I have a new lease of life.”

study backs DiRECT as being effective and practical longer term, it could completely transform the way type 2 diabetes is treated, saving both money and much human misery.

References

Declaration of interests
None to declare.

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