

People of normal weight with type 2 diabetes can achieve remission by losing weight

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New research presented at the Annual Meeting of the European Association for the Study of Diabetes (EASD), held online this year, found that contrary to the perceived wisdom, people of normal weight

with type 2 diabetes (T2D) can reverse the condition through substantial weight loss.

Eight of the 12 participants achieved remission after losing 10-15% of their [body weight](#), despite having a BMI that fell in the [normal weight](#) range. Levels of fat in the liver and pancreas fell substantially and the activity of the insulin-producing cells in the pancreas was restored.

The finding clearly demonstrates weight loss can be beneficial in type 2 [diabetes](#), even in those who are of normal weight, says Professor Roy Taylor, of Newcastle University, Newcastle, UK, the principal investigator on the trial.

It also supports the idea that we each have a "personal fat threshold"—a level of body fat we can cope with—and if we go above it, we will develop T2D, even if we are still of normal weight.

Professor Taylor explains: "Our previous research has shown that weight loss of 10-15% can achieve remission in people with type 2 diabetes who are overweight or obese.

"Doctors tend to assume, however, that type 2 diabetes has a different cause in those who aren't overweight. This means that, unlike those who are overweight, those who are of normal weight aren't usually advised to lose weight before being given diabetes drugs and insulin.

"Instead, there's a tendency to start them on insulin and other medication at a much earlier stage.

"What we've shown is that if those of normal weight lose 10-15% of their weight, they have a very good chance of getting rid of their diabetes.

"This should be a wake-up call to doctors and, with one in ten of the 4.5 million people with type 2 diabetes in the UK of normal weight at diagnosis, there is no time to be lost in getting the message across."

Affecting one in 11 of the world's adult population (415 million people), and on the rise, T2D occurs when the pancreas can't make enough insulin (a hormone which helps turn the sugar in food into energy) or the insulin it makes doesn't work properly.

Previously, the landmark Diabetes Remission Clinical Trial (DiRECT), from Glasgow and Newcastle universities, showed that an intensive weight loss programme delivered by GPs can put T2D into remission in people who are overweight.

The latest results are from the Reversal of Type 2 Diabetes upon Normalisation of Energy Intake in the Non-obese (ReTUNE) trial, which is looking at whether weight loss can also reverse the condition in people of normal weight.

Twelve men and women who had T2D and were of normal weight (average BMI of 24.5) followed a weight loss programme in which they consumed 800 calories a day (from low calorie soups and shakes) for two weeks, followed by four to six weeks in which they received support to maintain their new weight. They completed up to three rounds of this diet/weight maintenance cycle until they had lost 10-15% of their body weight.

The participants underwent a range of tests at the start of the study and after each round of dieting and weight maintenance. Their results at the end of the study were compared to those of a group of controls—people without diabetes who were matched for age, sex and BMI.

Average [weight](#) fell by 8.2kg, from 69kg to 61.8kg—a reduction of

11.9%. Total body fat fell from 33.1% to 27.4%. This compares to a figure of 25.4% for the controls.

Scans showed that the average amount of fat in the liver fell from 4.4% - more than twice as high as in the controls—to 1.4%.

Fat in the pancreas fell from an average of 5.1% to 4.5%. Average levels of triglycerides (plasma TG, a measure of fat metabolism efficiency) fell dramatically from 1.6mmol/L to 1.0mmol/L—on a par with the controls.

In eight of the 12 participants (67%), diabetes went into remission, a similar proportion to previous studies involving overweight and obese participants. Remission was defined as HbA1c (average blood sugar level) of less than 48mmol/mol and off all medication.

Professor Taylor says: "These results, while preliminary, demonstrate very clearly that diabetes is not caused by obesity but by being too heavy for your own body. It's due to having too much fat in your liver and pancreas, whatever your BMI.

"In the liver, this excess fat prevents insulin from working normally. In the pancreas, it causes the beta cells to stop producing insulin.

Dr. Ahmad Al-Mrabeh, the study's first author and co-investigator, who has recently moved from Newcastle University to the University of Edinburgh, adds: "We've already shown a process called hepatic lipoprotein export to be key.

"Lipoproteins are substances made of protein and fat which export fat through the bloodstream. Excess fat is normally stored in the subcutaneous fat areas under our skin. However, when the stores are filled up, or became dysfunctional, excess fat will spill over into the bloodstream before being stored in the liver and exported by lipoproteins

to other tissues.

"We've demonstrated that this process is the driver of the fat build-up in the pancreas believed to damage the insulin-producing cells and cause type 2 diabetes.

"Weight loss by calorie restriction is powerful in achieving remission of type 2 diabetes and it is remarkable to have 67% remission in this non-obese group.

"However, this approach is challenging for many people including those with normal BMI. Our team here in Edinburgh is exploring the exact mechanisms that lead to remission during [weight loss](#), which we believe will inform prevention, as well as the design of more targeted novel therapies both in addition to and as alternatives to calorie restriction."

Professor Taylor adds: "As a rule of thumb, your waist size should be the same now as when you were 21. If you can't get into the same size trousers now, you are carrying too much fat and therefore at risk of developing type 2 diabetes, even if you aren't overweight."

Provided by Diabetologia

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