Reflecting on the DiRECT trial

The DiRECT trial has revealed how weight loss can lead to remission of Type 2 diabetes and shows that lifestyle intervention can work in tackling the challenge posed by the condition. Professor Matti Uusitupa, University of Eastern Finland, explains why these new findings are so encouraging.

Type 2 diabetes has long been considered as a lifelong condition, caused by various degrees of insulin resistance and progressive deterioration of insulin secretion. It is associated with microvascular complications and increased occurrence of atherosclerotic vascular diseases. Genetically, Type 2 diabetes is quite a heterogeneous disease. Most of the genetic risk variations of Type 2 diabetes identified so far are linked with insulin secretion defects, whereas insulin resistance seems to be associated with lifestyle related factors – in particular with obesity, low physical activity and unhealthy dietary habits.

In the early 1970s, when I was a young GP working for a primary healthcare centre in a small rural district in Finland, most of the people with diabetes that I saw had Type 1. However, when I started to specialise in internal medicine and during my doctoral studies – on cardiovascular disorders at the time of diagnosis of Type 2 diabetes – in the late 1970s, the incidence of Type 2 diabetes was already increasing in Finland and globally. Today, Type 2 diabetes is a global health burden. In the UK the disease affects one of 10 adults, as it does in Finland, and globally over 420 million people have Type 2 diabetes.

The promise of prevention

Luckily, we also have good news. Well-controlled prevention trials, carried out in China, Finland and the USA some 20 years ago, have shown that Type 2 diabetes is either preventable or can be postponed by lifestyle change (losing weight, increasing physical activity and making healthy dietary choices).

In the December 2017 issue of The Lancet, Mike Lean and colleagues reported on the one-year results of their lifestyle intervention trial DiRECT in people with recently diagnosed Type 2 diabetes. The trial was a cluster-randomised study carried out in either control or intervention primary care practices in England and Scotland. Both groups included 149 patients, with diabetes duration of between 0 and six years. Antidiabetic and antihypertensive medicines were discontinued in the intervention group at the onset of the study, while the control group was treated according to best practice guidelines.

The one-year remission rate in the DiRECT intervention group was 46 per cent. The two co-primary study outcomes were weight reduction of 15kg or more and remission of Type 2 diabetes based on glycaemia (glycated HbA1c <48 mmol/mol). The one-year remission rate in the intervention group was 46 per cent, while it was only 4 per cent in the control group. Body weight decreased by 10kg in the intervention and 1kg in the control group, the mean difference being 8.8kg between the groups. Not surprisingly, remission rate increased with the amount of weight lost, reaching 86 per cent in those patients with weight reduction of at least 15kg. Weight management intervention also resulted in better quality of life, lower need of antihypertensive drugs and clinically meaningful reduction of serum triglycerides, which are typically high in people with Type 2 diabetes.

DiRECT implications

Altogether, these results are impressive and they have important implications for future research and clinical practice. First, these results show that weight reduction is the primary goal in the treatment of overweight patients with Type 2 diabetes. Weight loss results in better insulin sensitivity, which means a lower requirement for insulin to control glucose metabolism. This may help to save insulin-secreting beta cells in the pancreas in the long term. Furthermore, weight reduction decreases liver fat content, which normalises liver glucose and lipid metabolism. Additionally, there are some studies to suggest that weight reduction may reduce pancreatic fat content and, consequently, preserve beta cell mass. We also know that, besides weight reduction, increased physical activity and healthy dietary choices (increasing dietary fibre by using wholegrain products, vegetables and fruit and replacing saturated fats by unsaturated fats) can play a role in the non-pharmacological treatment options of Type 2 diabetes.

What, then, are the practical implications of the DiRECT trial for primary healthcare? The details of the trial are described in Faye Riley’s article, which follows on page 27. It is important to recognise that motivation to make any lifestyle change is typically high in people with Type 2 diabetes. The study authors promise long-term follow-up results that should strengthen the scientific and practical implications of this important study.