MAKING REMISSION A REALITY: THE LATEST
Earlier results

In Update this time last year, we reported on the first-year results of the landmark Diabetes Remission Clinical Trial. DIRECT is looking at whether Type 2 diabetes can be put into long-term remission using a structured low-calorie diet weight management programme, delivered through NHS primary care. Professors Mike Lean, from the University of Glasgow, and Roy Taylor, from the University of Newcastle, showed that almost half (45.6%) of those taking part in the programme were in remission after 12 months. Remission was defined as having an HbA1c of less than 48mmol/mol at 12 months, with at least two months without any Type 2 diabetes medication. The world had the first robust evidence that significantly restricting calories, to lose around 15kg, followed by long-term support from a healthcare professional to help keep the weight off, could result in the remission of Type 2 diabetes.

The biology of remission

The chances of remission were closely linked to weight loss: nearly nine in 10 people were in remission if they lost 15kg or more. This significant weight loss resulted in a drop in fat in both the liver and pancreas. One participant went from 36% liver fat to 2%, as shown in the figure.

Despite this fat loss, only 45.6% of the participants were able to achieve remission. Prof Taylor decided to study a subgroup of people taking part in DIRECT to see if there were any differences in metabolism or pancreas function of the people who achieved remission after 12 months, or ‘responders’ (n=29) compared to those who didn’t achieve remission, or ‘non-responders’ (n=16).

Prof Taylor and his team found that the biggest difference between the two groups of people lay within their beta cells. After losing significant weight, the beta cells of people in remission ‘rebooted’, and started to release the right amount of insulin the body needs. They even gradually improved over time. There was no change in the amount of insulin being made by the non-responders – their beta cells had not survived the stress of being surrounded by internal fat.

We’re still trying to work out why this is the case. One difference between the two groups is that responders had lived with Type 2 diabetes for slightly less time compared to non-responders (average of 2.7 years vs 3.8 years). But both groups lost a similar amount of weight, which in turn was linked to a similar reduction in levels of fat in the liver and pancreas.

Overall, these findings add evidence to the theory that shedding liver and pancreas fat is a vital part of how to put Type 2 diabetes into remission. But this research suggests it’s only effective if the beta cells can be ‘rebooted’ as a result of that weight loss.

Unanswered questions

Aside from understanding how remission works, there are still lots of unanswered questions. Firstly, we want to find an approach that works for as many people as possible. That includes people of different ethnicities and people who aren’t overweight.

Diabetes UK is funding Prof Taylor’s ReTUNE study, safely testing a low-calorie diet in people with Type 2 diabetes who already have a healthy weight. Participants will be asked to consume 800 calories a day (from soups, shakes and non-starchy vegetables) for up to two weeks, while being supervised by a medical team. After this, they’ll be supported to gradually return to eating normal food and to keep off the weight they lost.

They’ll be asked to repeat this cycle of a low-calorie diet and weight loss maintenance up to three times. After each cycle, the research team will measure the amount of fat in the pancreas and liver, and establish at which point people may achieve Type 2 remission. This can give a greater insight into the biology behind Type 2 diabetes, and why it may develop in people who aren’t overweight.

Counting the costs

Alongside understanding whether a programme like DIRECT could help people achieve remission of their Type 2 diabetes, we need to know whether it’s economically feasible to deliver. We committed a further £300,000 towards DIRECT so that participants could be followed for a further three years, and to evaluate the cost-effectiveness of the programme.

Led by Prof Lean and a team of health economists at the University of Glasgow, the analysis published in the Lancet Diabetes and Endocrinology found that a Type 2 diabetes remission programme in the NHS could cost around £1,067 per participant in its first year – or, factoring in the likelihood of success, £2,564 for each case of remission.

The team compared the treatment costs of the two groups in DIRECT: those on the weight loss programme (the intervention group), and those receiving current standard NHS care (the control group). They took into account the cost of healthcare professional training, providing the low-calorie formula diet, review appointments with healthcare professionals and supporting literature. The team also factored in the costs of any routine healthcare during the 12 months
Lesley Slaughter is a community dietitian in Stirling, and is one of the healthcare professionals involved in DiRECT. She has helped many participants through the study, from introducing the low-calorie soups and shakes, through to providing support to re-introduce normal food and, importantly, maintain weight loss.

“I approached DiRECT with the same apprehension and caution as any other dietitian would. This is something which, until then, I would never have recommended to my patients, never mind deliver it. But part of what I really enjoy about dietetics is that our practice is constantly changing as new research is published. So to be involved in a piece of research like this was exciting. It was all brand new – for me and for the people coming along. There was a mixture of emotions – nerves, excitement, caution, determination. They might be thinking, “How will this be different to things I’ve tried in the past? Will I be able to do this?”

The person that stands out to me is my very first DiRECT patient, who achieved a HbA1c of less than 48mmol/mol after 12 weeks, and was in remission at one year. He is still in remission nearly four years later. The impact this has had on his life is incredible. Anyone who achieves remission after years of taking prescribed medications is amazing.

The success of DiRECT has to be, in part, due to the level of support people received. The total diet replacement is only one piece of the jigsaw – the change in behaviour and habits takes a long time. The learning for me has been absolutely huge and I feel fortunate to have had the research team on hand. They’ve been an incredible support. I think that learning with practitioners could be shared, so when thinking about delivering something like this in the future, there’s a pool of us willing to share.”

In my experience, the participants who are most successful at staying in remission are those who are monitoring. So weighing themselves frequently, continuing to monitor their dietary intake using a diary or an app. Reinroducing healthy food is difficult – that idea of handing back control on food choices was a bit overwhelming for some participants. One programme isn’t going to fit everyone, despite how desperately you want it to work for them.

For the people taking part, there’s also that fear of the unknown about the programme. You would sometimes hear they’d been told it was just a fad and were being put off taking part. But when more DiRECT results are published, I hope that feedback will disappear.

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months, including primary care, community care, hospitalisations, and anti-diabetes and anti-hypertensive medications.

The cost of the 12-month programme, allowing for savings for reduced drug and medical needs, was £1,067. By the end of the first 12 months of the DiRECT study, 46% of participants were in remission. Taking this likelihood of achieving remission into account, the team estimated that each case of remission would cost £2,564.

The most recent, comprehensive analysis in 2010, cited the cost of a case of remission would cost £2,564 (£2,810 if allowing for inflation). However, it is important to note that this figure includes the treatment of serious complications and covers all stages of Type 2 diabetes throughout a person’s lifetime, which this new analysis does not.

The DiRECT remission programme, delivered within NHS primary care, is therefore relatively inexpensive when compared with the serious and expensive complications of Type 2 diabetes, which remission might avoid. As we continue the study we will learn more about the balance of financial costs and benefits for this approach. These findings support the case for considering weight reduction interventions as compelling option for some people to put their Type 2 diabetes into remission.

Professor Andrew Briggs, Health Economist at the University of Glasgow, explains: “This intervention is relatively inexpensive when compared to managing Type 2 diabetes, and we anticipate that there will be cost savings further down the line. If people can stay in remission and therefore reduce their chances of developing diabetes complications, the cost savings to the NHS could be substantial.

“We can’t know this for certain yet. Which is why the long-term follow-up of these participants – alongside those accessing any NHS remission pilots in the near future – is very important. However, these findings are encouraging, and – in our view – begin to make the case for shifting resources to offer remission-based models of care in the future.”

Dr Elizabeth Robertson, Director of Research at Diabetes UK, said: “It is critical that we understand the real world costs of new, promising, remission interventions like DIRECT. The second-year results of the DIRECT study are eagerly anticipated, as the case for remission-centred Type 2 diabetes care as an option for some individuals depends upon a thorough understanding of the longer-term benefits.

“If people can remain in remission, and therefore reduce their risk of developing serious diabetes-related complications in the future, the cost savings to the NHS could be significant. Costs aside, remission from Type 2 – and the possibility of living free of the condition – has to be the preferred option for people and clinicians alike.”

Bridget Turner, Director of Policy and Campaigns at Diabetes UK, said: “The first-year results of DIRECT were very encouraging and, while we don’t yet have all the answers, this economic study, and its findings, are particularly timely.

“We’re delighted that, thanks to a growing body of evidence – including that from DIRECT – NHS England and Scotland have committed to exploring the potential of intensive lifestyle interventions as an option which may lead to remission for more people with Type 2 diabetes near to diagnosis.

“We hope this economic analysis will help to inform the set-up and delivery of more pilots – with appropriate monitoring, follow-up and support – in the future.”

Advice for you in the clinic
Do you see patients who have put their Type 2 diabetes into remission? Or perhaps people who would like to?

Last year’s news from NHS England and Scotland, who have both committed to piloting remission programmes, is exciting. But what happens in the meantime? Diabetes UK has developed an Information Prescription, together with healthcare professionals and people with Type 2 diabetes, to support you to have conversations with your patients about what remission really means. Alongside this, here are Diabetes UK’s top messages:

- Remission is when a person with Type 2 diabetes has healthy blood glucose levels for the long term, without any diabetes medications.
- Remission can be life-changing. No more diabetes medications, and healthy blood glucose levels lead to a lower risk of diabetes complications.

- We know that remission isn’t possible for everyone. But if you’re overweight, there are real benefits to losing weight. Fewer medications, and lower blood pressure, blood glucose levels and cholesterol: all risk factors for diabetes complications.

- We recommend that people with Type 2 diabetes maintain a healthy weight through regular physical activity and a balanced diet. This means choosing less red or processed meat, and more fruit and vegetables, wholegrains, fish, pulses and nuts.

- We recommend that people who are in remission still attend their annual health checks, to check that their Type 2 diabetes hasn’t returned and they haven’t developed any complications.

REFERENCES: