HOPE– Type 2 Diabetes: Moving from Management to Remission

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The prevalence of type 2 diabetes is rising exponentially worldwide and becoming more and more common, even in younger people. Type 2 diabetes is a serious condition, which leads to micro vascular and macro vascular complications. The condition causes profound psychological and physical distress on patients and puts a huge burden on health-care systems. For hospital and community pharmacists alike, managing type 2 diabetes medications is important. It is my hope that in the future, we will be moving away from management via multiple medications, to remission using lifestyle or surgical approaches.

Commonly referred to as a 'chronic' and 'progressive' disease, we now know that remission of type 2 diabetes is possible.

Yes, type 2 diabetes is related to lifestyle, between 80-90% of people with type 2 diabetes are overweight or live with obesity. However, type 2 diabetes is complex. In managing type 2 diabetes, it is important to understand the underlying physiological insulin resistance and beta cell (insulin producing cells in the pancreas) dysfunction which occurs. If it were 'simply' a lifestyle disease, why are there some people with a normal BMI (body mass index) who develop type 2 diabetes?

Remission:

"There is ample evidence to support the statement that it is possible to achieve remission in type 2 diabetes."

Bariatric surgery remains the most effective and long-term method of weight loss and type 2 diabetes remission. It is known that meaningful, sustained reductions in weight over time are difficult to achieve with mainstream lifestyle modification alone, however, now scientific interest is growing in the use of intensive lifestyle interventions.

The pathological changes associated with type 2 diabetes can be reversed through intensive lifestyle and dietary changes, and in some cases bring about remission.

Low-calorie (also known as low energy diets) and low-carbohydrate diets are also effective at improving glycaemic control and placing type 2 diabetes into remission, but what does this actually mean?

The old notion that beta cell function inevitably declines over time in people who have developed type 2 diabetes has been definitively disproven. The renowned Professor Taylor's team in Newcastle University of DiRECT study fame, recently published, that with intensive weight loss lifestyle interventions, functional β-cell capacity increased over time in those who had achieved remission. This is why it is so important that these interventions are offered to patients as close to diagnosis as possible. Where beta cell failure has already occurred, weight loss is unlikely to be successful in reversing diabetes.

What does type 2 diabetes remission actually mean? Sometimes also known as 'reversal' of diabetes, it essentially means that the individual no longer has diabetes, at least for a point in time. Once achieved, remission appears durable provided weight regain does not occur. If weight re-gain does occur, diabetes will return so weight maintenance support and effective strategies are important. People who achieve remission should still continue yearly diabetes screening and monitoring.

There is currently no consensus on the exact definition of remission.

The Diabetes UK definition is defines remission as a person with a HbA1c of less than 48mmol/mol for 6 months off all diabetes medications. An updated consensus statement between Diabetes UK and the American Diabetes Association is expected later this year.

This is not only hugely important for healthcare systems across the world, it's incredibly important that patients know that some of them may be able to achieve remission. If not full remission, reducing some diabetes medication, including insulin, is possible for most patients, and life changing for some.

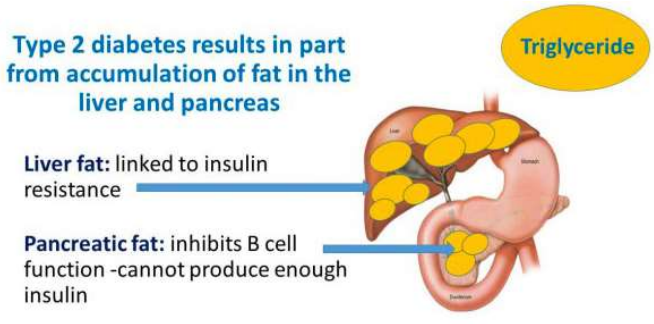
The current standard model of care after type 2 diabetes diagnosis may sometimes include a 3 month 'trial' of diet and lifestyle changes, often with little real support to the patient apart from 'you should try to lose weight'. Following this, the usual care process generally means starting metformin and progressing through second and third line drugs, eventually leading to insulin for many patients. This must no longer be accepted.

Patients with type 2 diabetes are often on a cocktail of anti- diabetes drugs, anti- hypertensive drugs. It is estimated that the cost of diabetes medications alone, on average is €6500 per year. Patients should be given appropriate and relevant information on how improving their lifestyle, diet, and reducing their weight is likely to lead to an improvement in their glycaemic control. With weight loss and intensive lifestyle modifications, not only do we see an improvement in glycaemia, we see other markers of metabolic syndrome improve, an increase in HDL cholesterol, reduced waist circumference, reduced blood pressure, and triglycerides, the list goes on.

For people living with Type 2 diabetes, the possibility of achieving remission can be highly motivating and more importantly gives the patient hope. We've all seen patients on multiple medications, sometimes with side effects, who remain to have poorly controlled diabetes despite all the medication. It's like putting a plaster on the problem without fixing the root cause. These people with type 2 diabetes need to know there are other options. People tend to engage with diabetes management more when there is real hope of improving the condition, rather than the usual burden they carry.

Low energy diets (LEDs) also known as Low Calorie diets

Earlier in 2020, NHS England in the UK commissioned a pilot of 5,000 patients to undertake a low calorie diet program based off the work of Professor Taylor in Newcastle University. Perhaps one of the most important diabetes research studies of the last decade, the Diabetes in Remission Clinical Trial (DiRECT) showed that type 2 diabetes remission is achievable (when delivered in primary care) for about 46% of people at 1 year with 39% remaining in remission at 2 years.



Reversal of type 2 diabetes: Normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. Lim EL1, Hollingsworth KG, Taylor R. Diabetologia. 2011 Oct;54(10):2506-14. doi: 10.1007/s00125-011-2204-7.

Fig 1: the 'twin cycle hypothesis' (Professor Roy Taylor). Type 2 diabetes results in part from accumulation of fat in the liver and pancreas. Significant weight loss can reduce fat in the liver within day, and within week to months from the pancreas.

A low energy diet typically contains between 800-1200 calories per day. The evidence currently strongly favours the use of Total Diet Replacement products (usually nutritionally complete shakes and soups) for 12 weeks followed by a stepped re-introduction of food, although some food based plans are now being studied.

I was lucky enough to work on the DiRECT trial. One thing which really surprised me while working on this study was that after the first week or two, patients rarely reported hunger, or any side effects for that matter. Many participants reported improved energy and mood. Most surprising is that participants reported they were actually happy to get a break from food, not having to think about the next meal but knowing it would be a shake or soup, helped break negative food habits along the way.

Although this may sound like other commercial programmes that we have all heard of in the past, when these programmes are delivered as part of a multidisciplinary team with appropriate expertise, support and weight maintenance strategies, patients can see sustained results. It is not advisable that a patient with type 2 diabetes undertakes this type of approach at home without support.

Low Carbohydrate Diets

A low carbohydrate diet (usually defined as a diet containing <130g of digestible carbohydrates per day) is recognised as an effective option that is clinically inexpensive with few side effect for treating type 2 diabetes. Many patients are achieving significant improvements in glycaemic control, with associated reduction in drug costs from cessation of hypoglycaemic agents.

When compared with low-fat diets, low carbohydrate diets consistently show an improvement in HbA1c and body weight in the short term (up to 12 months) with no difference between the groups after 12 months. This may be due to randomisation of patients to these diets. No one diet fits all and it's important a patient who follows a low carbohydrate (or any diet) finds it acceptable and affordable. Being able to offer patients something other than the usual 'low-fat' and calorie counting approach is exciting for patients. Digital health programmes for diabetes remission are being delivered at scale internationally. One digital program in the UK (The Low Carb program) found that 60% of patients following a low carbohydrate digital program significantly reduced or eliminated insulin altogether, and 1 in 4 patients were in remission one year after the programme.

Another American research team delivering digital very low carbohydrate (ketogenic) interventions founds significant improvements in HbA1c, triglycerides, weight, blood glucose at 2 years and are working with insurance companies in the states. For health care systems, the potential cost savings on medications and long-term complications for people who improve their diabetes should be a no-brainer.

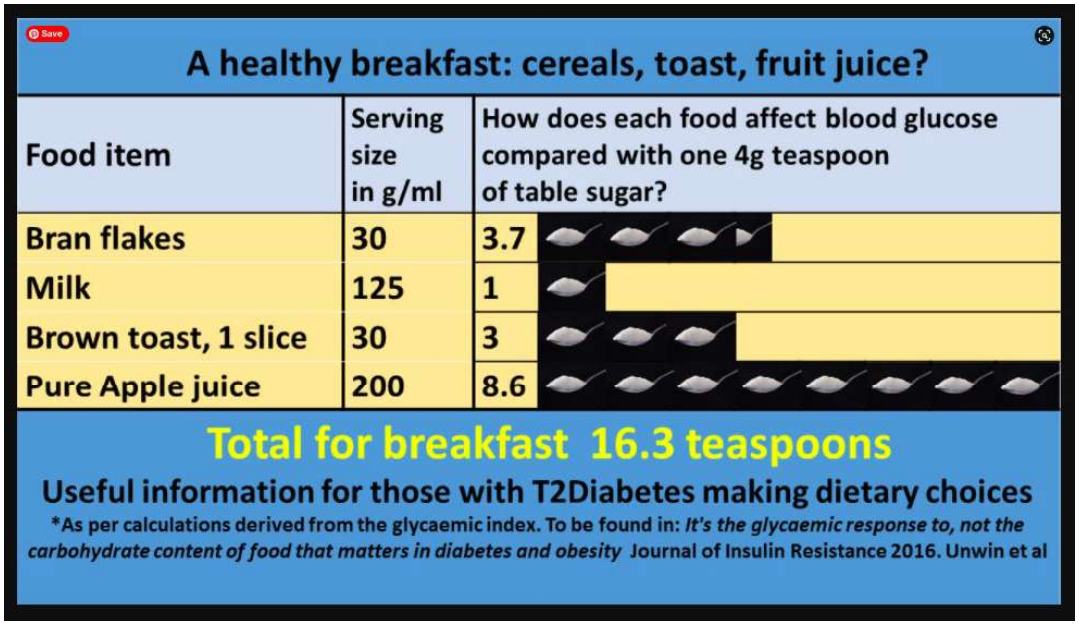
International consensus statements agree that a low carbohydrate diet in people with type 2 diabetes is a safe and effective option for the management of type 2 diabetes.

A study published only this month showed a single primary care GP in North East of England recommending a low carbohydrate diet has 85 patients in his practice in drug free remission, in some of the patients up to 6 years. Dr Unwin et al describe the methods used to treat patients in their paper. The same GP practice save £50,000 in de-prescribed diabetes medications saving on average every year.

Teaching patients the impact of their food choices on their blood glucose levels, to me, is a far more important bit of education than teaching patients to follow healthy eating guidelines which were developed for the general population, and not specific to people with type 2 diabetes. Within hours of reducing added sugar and starchy carbohydrates, literally, a patient can see the positive impact on their blood glucose.

For example, a patient with type 2 diabetes might think that a breakfast of bran flakes, with one slice of brown toast, skimmed milk and freshly squeezed orange juice might be a healthy breakfast. What about the impact of that glycaemic load of that meal on that patients blood glucose levels? What if they were to eat a vegetable and cheese

Body	Guideline	Year	Recommendation
Diabetes UK (UK)	Diabetes UK evidence-based nutrition guidelines for the prevention and management of diabetes	2011	The Diabetes UK 2011 guidelines support the view that low-carbohydrate diets may be considered an option for weight loss in people with Type 2 diabetes when supported by a registered healthcare professional.
SIGN Guidelines (UK)	Management of Diabetes—A National Clinical Guideline	2015	People with Type 2 Diabetes can be given dietary choices for achieving weight loss that may also improve glycaemic control. Options include simple calorie restriction, reducing fat intake, consumptions of carbohydrates with low rather than high glycaemic index and restricting the total amount of dietary carbohydrate (a minimum of 50g per day appears to be safe for up to 6 months)
National Institute of Clinical Excellence (UK)	Type 2 diabetes in adults: management	2015	Individualise recommendations for carbohydrate and alcohol intake, and meal patterns.
American Diabetes Association and European Association for the Study of Diabetes (USA & Europe)	Management of Hyperglycaemia in Type 2 Diabetes. A consensus Report.	2018	**Nutritional therapies:** Low-carbohydrate, low-glycaemic index and high-protein diets, and the Dietary Approaches to Stop Hypertension (DASH) diet all improve glycaemic control, but the effect of the Mediterranean eating pattern appears to be the greatest.
Diabetes Australia (Australia)	Low carbohydrate eating for people with diabetes—position statement	2018	For people with type 2 diabetes, there is reliable evidence that lower carb eating can be safe and useful in lowering average blood glucose levels in the short term (up to 6 months). It can also help reduce body weight and help manage heart disease risk factors such as raised cholesterol and raised blood pressure. All people with any type of diabetes who wish to follow a low carb diet should do so in consultation with their diabetes healthcare team.
American Diabetes Association (USA)	Nutrition Therapy for Adults with Diabetes or Prediabetes: A Consensus Report	2019	Reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence for improving glycaemia and may be applied in a variety of eating patterns that meet individual needs and preferences. For select adults with type 2 diabetes not meeting glycaemic targets or where reducing anti-glycaemic medications is a priority, reducing overall carbohydrate intake with low or very low carbohydrate eating plans is a viable approach.
Diabetes Canada (Canada)	Diabetes Canada Position Statement on Low-Carbohydrate Diets for Adults With Diabetes: A Rapid Review	2020	Healthy low- or very-low-CHO diets can be considered as one healthy eating pattern for individuals living with type 1 and type 2 diabetes for weight loss, improved glycemic control and/or to reduce the need for antihyperglycemic therapies. Individuals should consult with their health-care provider to define goals and reduce the likelihood of adverse effects.



filled omelette instead? There would be much lesser impact on blood glucose levels. Patients who follow a low carb diet tend to eat plenty of unprocessed meat, fish, salad, vegetables, low sugar fruit, unsweetened dairy and healthy fats.

Teaching the basic Physiology of diabetes and eating, in a simple way, to my patients has been the biggest game changer in my career to date. Patients have been told for years by their GP, Dietitian, nurse, and pharmacists to 'simply lose weight, just eat less and do more exercise'. This doesn't work. It's not sustainable in the long term and any diet where a patient is hungry and relying on willpower is destined to fail eventually. This is, in my opinion, an unfair thing to ask patients to do, especially those with obesity where underlying physiological drivers can make weight loss more difficult.

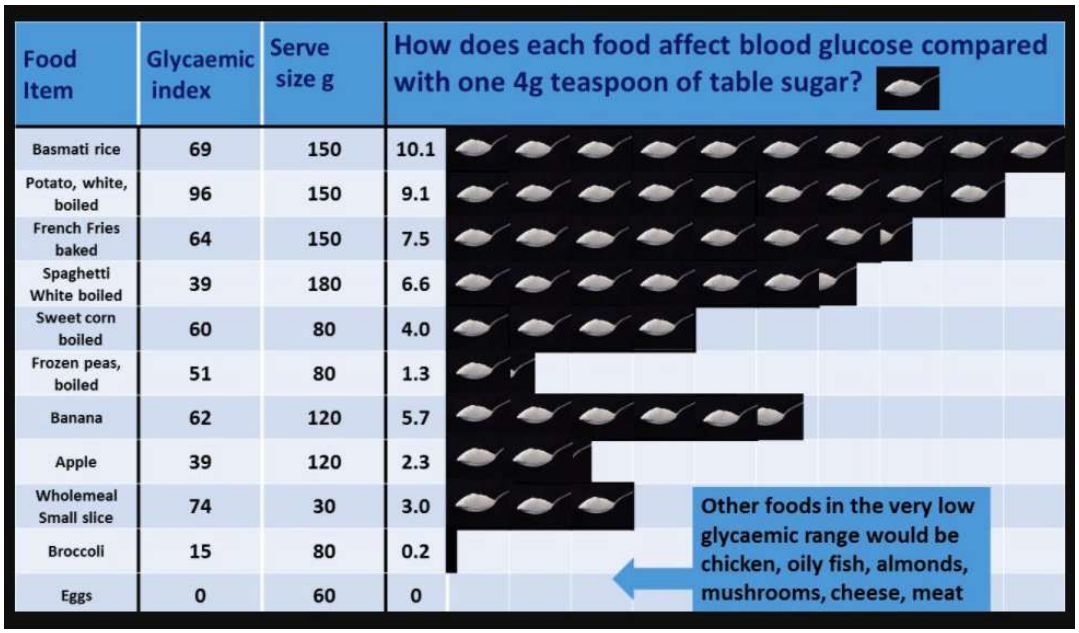
If a patient understands why they need to reduce added sugar and refined and starchy carbohydrate in their diet it can be easier for them to make those changes.

These info graphics describe the *equivalent of teaspoons of sugar* of certain foods on blood glucose.

The role of the pharmacist

Although further research is needed to understand the long-term impact of remission on complications and the impact on local health economies, community and hospital pharmacists may, in the future, have an additional role in de-prescribing, where patients in the community are undertaking such interventions. A guide for medication de prescription has been created and published by a group of pharmacists and clinicians.

Patients should not undertake a low carbohydrate or low calorie diet without first consulting with their Dietitian or GP. It is important nutritional adequacy is considered in both diets, along with other factors like fibre intake. While dietitians remain the best healthcare professional for a patient to see for individual dietetic advice, there is a significant lack of whole time equivalent for specialist diabetes dietitians (74%) and also for endocrinologists (72%) in Ireland. It's difficult to imagine how novel interventions will be taken up in Ireland currently despite the potential for millions of euros in de-prescribed medications costs.



In the meantime, what is the best advice that pharmacists can give to patients who want to improve their diet and lifestyle?

- Reduce highly processed foods (ultra-processed foods)
- Reduce added sugar
- Reduce refined carbohydrates in the diet
- Focus on other lifestyle factors such as activity and sleep
- Focus on healthy protein, vegetables, fruit, healthy fats, unsweetened dairy and some wholegrains (eg; pulses, lentils, quinoa) depending on their goals
- A focus on nutrient density of foods, rather than solely calorie content. I have found that calorie counting leads to an increase in consumption of 'light' and 'fat free' foods which generally means more added sugar. It also means hunger is never far away.

Further information for healthcare professionals

- The DiRECT study team at Newcastle University have a website containing more information https://www.ncl.ac.uk/magres/research/diabetes/reversal/#publicinformation
- NHS (England) information on low calorie diet pilot of 5,000 patients https://www.england.nhs.uk/diabetes/treatment-care/low-calorie-diets/
- Sugar equivalent info graphics available freely to use
- British Journal of General Practice meds management for low carbohydrate diets
- Dr Unwin (GP using low carbohydrate diets) has published his protocol for initiating low carbohydrate diets in 10 minute primary care appointments. Unwin D, Khalid AA, Unwin J, et al Insights from a general practice service evaluation supporting a lower carbohydrate diet in patients with type 2 diabetes mellitus and prediabetes: a secondary analysis of routine clinic data including HbA1c, weight and prescribing over 6 years. BMJ Nutrition, Prevention & Health 2020;bmjnph-2020-000072. doi: 10.1136/bmjnph-2020-000072
- Low-Carbohydrate Diets in the Management of Obesity and Type 2 Diabetes: A Review from Clinicians Using the Approach in Practice
- Digital apps such as the Low Carb Program and Diet Doctor can provide further information on a low carbohydrate diet

References on Request