



Diabetes Remission: Maintenance after weight loss with total diet replacement

Webinar

Tuesday 12th April 2022 14:00-15:30 BST; 15:00-16:30 CEST; 16:00-17:30 EEST

European countries face levels of obesity and diabetes that will overwhelm capacity for healthcare provision. All European countries require effective programmes for diabetes prevention, diabetes remission and obesity prevention and reduction.

Weight loss has been recognised as the key component for diabetes prevention and key to effective diabetes prevention. A recent review [1] concluded that the best way to achieve the initial weight loss was with total diet replacement, but much needs to be learned about effective weight loss. Dietary glycaemic index has been an important part of dietary management of diabetes for some time and recent evidence from the EU funded PREVIEW trial [2] indicates that low GI/low GL diet facilitated maintenance of weight loss and lower blood glucose. Clinical and public health guidelines are in the process of being reviewed.

During this webinar, we heard from experts in the field on the latest evidence on Total Diet Replacements' (TDR) effectiveness in supporting diabetes remission and the facilitation of weight maintenance. The abstracts for the different presentations can be found below.

[1] Churuangsk C et al. Diets for weight management in adults with type 2 diabetes: an umbrella review of published meta-analyses and systematic review of trials of diets for diabetes remission. *Diabetologia* doi: 10.1007/s00125-021-05577-2. Online ahead of print 17 Nov 2021

[2] Zhu, R.et al. Dose-dependent associations of dietary glycaemic index, glycaemic load, and fiber with 3-year weight loss maintenance and glycaemic status in a high-risk population: A secondary analysis of the diabetes prevention study preview. *Diabetes Care* 2021, 44, 1672.

Abstracts

An update on development of guidelines for diabetes remission - remission possible!

Professor Mike Lean, University of Glasgow, Scotland

Until very recently, 'remission' of type 2 diabetes (T2D) was an unknown concept. Results from the UK Diabetes Remission Clinical Trial (DiRECT), supported by near-identical findings from DIADEM-1 in Qatar, have challenged and changed the old paradigm of T2D being a permanent condition, treatable by life-long glucose-lowering drugs, an inconvenience of ageing. The new evidence reveals T2D as a very serious life-shortening and disabling disease, part of the disease-process of 'obesity' in genetically predisposed people, but preventable and reversible at an early stage.

DiRECT included people with T2D up to 6 years from diagnosis. A structured dietary programme (Counterweight-Plus: Total Diet Replacement for 12 weeks, transferring to a food-based maintenance diet with about 50% energy from carbohydrate) achieved remission (HbA1c <48mmol/mol (<6.5%)) for 46% of all participants randomized to the intervention, with mean 12m weight loss 10kg. Those who maintained >15kg loss had over 80% remissions at both 12 and 24 months, and >10kg loss brought remissions for over 70%.

With slightly younger participants and shorter diabetes duration, using similar total Diet Replacement and food-based maintenance, DIADEM-1 achieved 61% remissions at 12m.

These are the only randomized controlled trials of diet interventions reporting remissions of diabetes. Several observational studies have employed low-carbohydrate diets, but while some have led to good weight losses, the remission rates are rather lower. The large VIRTAs-Health study in US achieved 13kg weight loss, but only 19% remissions. A failure to withdraw glucose lowering drugs may have obscured some more remissions, but these results are in, one with evidence that lower carbohydrate diets are associated with higher, not lower HbA1c.

Criteria for remission of T2D entail (1) a cut-off of HbA1c to denote freedom from diabetes, and (2) a duration of non-diabetic HbA1c without glucose-lowering medication. There are now internationally agreed criteria, by ADA, EASD, Diabetes UK, the Endocrine Society, and the Diabetes Surgery Summit (2021): HbA1c <48mmol/mol (6.5%), >3 months without glucose-lowering medication.

Following publication of DiRECT, the wishes of people with T2D seeking freedom from the disease have been important in stimulating adoption of remission programmes, for local services, in national Clinical Guidelines (e.g., Australia, New Zealand) and from international organisations such as forthcoming 2022 evidence-based Guidelines from the Diabetes Nutrition Study Group of EASD.

1. Churuangasuk C., et al Diets for weight management in adults with type 2 diabetes: an umbrella review of published meta-analyses and systematic review of trials of diets for diabetes remission. *Diabetologia* (2022) 65, 14–36 <https://doi.org/10.1007/s00125-021-05577-2>
2. Lean MEJ, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. *Lancet* (2018) 391(10120) 541-551
3. Thom, G. et al. (2021) Predictors of type 2 diabetes in the Diabetes Remission Clinical Trial (DiRECT). *Diabetic Medicine*, 38(8), e14395. (doi: 10.1111/dme.14395) (PMID:32870520)
4. Riddle M, et al; Consensus Report: Definition and Interpretation of Remission in Type 2 Diabetes. *Diabetes Care* 1 October 2021; 44 (10): 2438–2444. <https://doi.org/10.2337/dci21-0034>

Biographical note:

MA, MB, BChir, MD, FRCP (Edinburgh), FRCPS (Glasgow), FRSE

Professor of Human Nutrition, Glasgow University, and consultant physician at Glasgow Royal Infirmary.

Visiting professor, Universities of Otago and Sydney (to 30/06/2021).

Professor Lean leads 'broad-focus' translational, integrative, research and teaching within medical and nutrition training, integrating biomedical research at basic science, clinical and public health levels. Awards include Diabetes UK-Rank Prize Lecturer (2014), Banting Memorial Lecturer (2020/21), Tenovus Medal for Research (2017), elected Fellow of Scotland's National Academy (FRSE, 2018).

Currently PI on the largest research grant ever awarded by Diabetes UK, the Diabetes Remission Clinical Trial (DiRECT, £2.6m), an NIHR-funded weight loss for long COVID (ReDIRECT, £1.0m), collaborative dietary diabetes remission projects in Nepal and Australia, and pharmaceutical trials.

Published over 600 scientific articles and books, G-Scholar H-Index=116

Outside research he makes and plays fiddles, and escapes to climb mountains.

Maintenance of weight loss and diabetes remission: barriers and solutions

Professor Gary Frost, Imperial College London, England

Long term weight loss and maintenance of weight loss over the life course remains a major unachieved goal (1). Only 20% of people meet the criteria of long-term weight loss (10% of their initial body weight for one year) (2). This disappointing statistic is common across all dietary profiles. There are a number of common traits that are associated with maintenance of weight loss include positive emotional regulation such as low levels of dietary disinhibition and low levels of depression, dietary consistency, weight gain management and high contact with a counsellor. Unfortunately, evidence suggest that physiology starts to work against the maintenance of weight loss maintenance. Energy balance starts to favour weight regain (1); appetite regulation favours a low appetite suppression tone (3). In recent year my team have used some of these observations to design a method to nudge anorectic systems to prevent weight gain. We had achieved this using a short chain fatty acid propionate. Short chain fatty acids are produced by the microbiome in the human colon. We have developed a method to deliver propionate to the colon and demonstrated positive effects on appetite regulation, hedonic wanting and liking of food and energy expenditure (4). It is possible such systems could impact on weight loss maintenance.

At the present time there is no high-quality evidenced based guidelines to enhance weight loss maintenance. There is a number of good practice points that may enhance weight loss maintenance.

1. Maintaining contact with professional support
2. The use of corrective intervention
3. Realistic but clinically important targets
4. Physiological support
5. Methods to support appetite regulation

References

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Biographical note:

Professor Frost qualified as a dietitian in 1982 and has maintained a clinical input throughout this career, coupled with a deep interest in the use of research to inform clinical practice. In 1988 he joined Hammersmith Hospital as a research dietitian, completing his PhD in 1997, while working full time. Where he developed a highly successful innovative research group within the clinical department of Nutrition and Dietetics developing a unique research avenue in the impact of dietary carbohydrate in

the management of diabetes. He then joined the University of Surrey as Professor of Nutrition and Dietetics in 2005 and created a flagship doctoral training program (SlowCarb) bringing together a consortium of industrial partners. In 2008 he returned to Imperial College as Professor of Nutrition and Dietetics to set up the Nutrition and Dietetic Research Group and was awarded a NIHR senior investigator fellowship (2008 to current).

Over his career Professor Frost has made a number of land-mark findings in the field of physiological effects of dietary carbohydrate and dietary monitoring:

1. First to describe that increase intake of fermentable carbohydrate increases insulin stimulated uptake in adipocytes and decrease free fatty acid output (Frost GS et al Metabolism (1998), 47(10): 1245-1251)
2. First to demonstrate the direct relationship between increase carbohydrate quality HDL-cholesterol (Frost et al. Lancet 1999)
3. Discovered that the short chain fatty acid acetate has a direct effect on central appetite regulation (Frost G et al. Nat Commun. 2014)
4. Conducted the first in human studies using inulin propionate ester to increase colonic propionate and demonstrate reduce appetite, body weight gain and hepatic lipid (Chambers et al. Gut 2015)
5. Development of independent dietary assessment using metabolite profiling (Garcia et. al Lancet Endocrinology and Diabetes), achieving a major step forward in understanding food intake in large numbers of people in their home environments.

Glycaemic index: feasibility of using low GI/low GL diets in Mediterranean countries to facilitate weight maintenance

Elena Philippou, University of Nicosia, Cyprus

Long-term weight loss maintenance is a challenge with most overweight individuals regaining weight in the long-term (Dombrowski et al, 2014). A number of factors such as increased hunger, reduced satiety, preference for palatable foods, reduced total energy expenditure and poor adherence to behavioural changes are implicated (MacLean et al, 2015).

The glycemic index (GI) is a ranking of carbohydrate-containing foods based on the extent to which they raise blood glucose concentration after consumption, while glycaemic load (GL) is calculated by multiplying the food's GI by the amount of carbohydrate contained, all divided by 100. Post-hoc analyses of the PREVIEW study, in which overweight individuals with prediabetes who lost $\geq 8\%$ of body weight were randomized to a 146-weeks weight loss maintenance phase, showed that each 10-unit increment in GI was associated with a greater regain of weight (0.45 kg/year, 95% CI: 0.23, 0.68; $p < 0.0001$), fat mass (0.39 kg/year, 0.15, 0.63; $p = 0.002$) and HbA1c (0.02%, 0.01, 0.03; $p < 0.001$) (Zhu et al, 2021). In the same study, each 20 unit increment in GL was longitudinally associated with increases in hunger (0.92 mm/year; 0.33, 1.51, $P = 0.002$), desire to eat (1.12 mm/year, 0.62, 1.62, $P < 0.001$), desire to eat something sweet (1.13 mm/year, 0.44, 1.81, $p < 0.001$) and greater weight regain (0.35%/year, 0.18, 0.52, $P < 0.001$) (Zhu et al, 2022). The above findings support the carbohydrate-insulin model of obesity proposing that increasing body fat deposition resulting from hormonal responses to a high GL diet drives positive energy balance (Ludwig et al, 2021).

The Mediterranean diet (MD), rich in unprocessed cereals, legumes, fruit, vegetables, nuts and extra-virgin olive oil and low in meat, could serve as a model of a low GI/GL diet. In the PREDIMED study, an inverse association was seen in multivariate adjusted models between GL and MD enriched with extra virgin olive oil ($\beta = -8.52, -10.83, -6.20$) and MD enriched with nuts ($\beta = -10.34 (-12.69, -8.00)$) when compared with the control group (Rodríguez-Rejón et al, 2014). Nevertheless, evidence from several Southern European countries shows that adherence to the MD is only moderate-to-weak suggesting that MD recommendations are overlooked (Quatra et al, 2021). The feasibility of using low GI/GL diets in MD countries will be illustrated by providing practical examples on how high GI carbohydrates can be replaced with low GI alternatives within the MD.

References:

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Biographical note:

Dr Elena Philippou PhD, RD, FHEA is an Associate Professor in Nutrition-Dietetics at the University of Nicosia and a Visiting Lecturer in Nutritional Sciences at King's College London, UK. Dr Philippou's research focuses on diet for prevention of degenerative disease, and more specifically, the effects of the Mediterranean diet and carbohydrate manipulation on cognitive function, cardiometabolic factors and rheumatic disease, aiming to identify dietary factors that can prevent disease and/or improve outcomes.

In addition to publishing a number of peer-reviewed papers, Dr Philippou is also the Editor of the book: *The Glycemic Index: Applications in Practice* (CRC Press, 2017) with contributions from all the leading names in the field of glycaemic index. She has a number of National and International collaborations, including being a member of the MEDIWEB group studying associations between the Mediterranean diet and wellbeing, and an active member of the American Congress of Rehabilitation Medicine Neurodegenerative Diseases Networking Group. Dr Philippou also has extensive experience as a registered dietitian and practices advising adults and children on diet-related issues.

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