Management & prevention of type 2 diabetes

Very-low-energy diets: A useful tool in type 2 diabetes management?

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There is considerable interest in the idea of using very-low-energy diets (VLEDs) in well-motivated people with type 2 diabetes. Significant weight loss occurs and glycaemia can be normalised. So far, however, this has been demonstrated only in studies with fairly small numbers of participants.

In the high-quality systematic review and meta-analysis summarised alongside, the authors looked at all the current literature to describe the efficacy and acceptability of VLEDs in people with type 2 diabetes. Four randomised and five non-randomised studies were identified that met the inclusion criteria. These included a total of 346 participants, with ages ranging from 40 to 70 years and mean BMI ranging from 30 to 51 kg/m^2.

Meta-analysis showed that VLEDs (defined as diets comprising ≤800 kcal/day) induced greater weight loss than minimal interventions, standard care or energy-restricted diets (≤1500 kcal/day) at 3 and 6 months. Greater differences in energy prescription between intervention arms were associated with greater differences in weight loss and fasting glucose levels at 3 months. Attrition rates did not differ between the VLED and comparator arms at any measurement point. The attrition rates were low, suggesting either that very well-motivated individuals were recruited; that adhering to VLEDs is no greater challenge than adhering to other weight loss treatments, possibly owing to additional motivation in response to the early experience of considerable weight loss; or a combination of both these reasons.

The conclusion of this review is that VLEDs are effective in causing substantial weight loss among people with type 2 diabetes. Levels of adherence in the studies appear to be high, although behavioural support was often poorly defined. The authors note, however, that most of the trials reported in the analysis were conducted by a small number of research groups.

A large randomised controlled trial of VLEDs in people with type 2 diabetes (DiRECT [Diabetes Remission Clinical Trial]; available at: http://bit.ly/1PUGXUB) is currently underway in the UK. The results from this are eagerly awaited. ■

Diabet Med

VLEDs in people with long-duration T2D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 Previous studies of very-low-energy diets (VLEDs) in diabetes have only enrolled people with short-duration T2D.

2 Therefore, the current authors compared the effects of an 8-week VLED in 15 people with short-duration (<4 years) and 14 with long-duration (>8 years) T2D.

3 While the degree of weight loss was similar between the two groups, effects on glycaemic control varied, with 87% of the short-duration groups achieving non-diabetes fasting glucose levels versus only 50% in the long-duration group (mean final HbA_{1c}, 44 vs 64 mmol/mol [6.2% vs 8.0%]).

4 Clinically significant improvements in blood pressure and lipid profiles occurred regardless of T2D duration.

5 Thus, VLEDs may be effective in people with long-standing T2D, although the response rate is lower than in those with a more recent diagnosis.

Steven S, Taylor R (2015) Restoring normoglycaemia by use of a very low calorie diet in long- and short-duration type 2 diabetes. *Diabet Med* **32**: 1149–55

Diabet Med

Meta-analysis on very-low-energy diets for T2D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 The authors of this systematic review and meta-analysis compared very-low-energy diets (VLEDs; with or without behavioural intervention) with standard care, minimal intervention, less restrictive diet interventions or bariatric surgery in terms of their effects on weight loss and glycaemic parameters in people with T2D.

2 In total, four randomised and five non-randomised trials were evaluated, with a pooled sample of 346 participants.

3 Compared with other interventions, VLEDs typically resulted in significantly greater weight loss, with mean differences between groups of around 5–8 kg at 6 months.

4 In general, greater differences in caloric intake between study arms were associated with greater differences in weight loss, in a linear fashion.

5 There was some evidence of improved blood glucose levels and reduced need for medication early in the VLED intervention; however, these effects generally did not persist beyond 6 months.

6 There was no significant difference in outcomes between VLEDs and bariatric surgery.

7 The rates of adverse events and attrition were similar between VLEDs and comparators; however, reporting on these outcomes was not rigorous.

8 The authors conclude that VLEDs are effective for substantial weight loss in people with T2D, although high-quality evidence is severely lacking.

Rehackova L, Arnott B, Araujo-Soares V et al (2015) Efficacy and acceptability of very low energy diets in overweight and obese people with type 2 diabetes mellitus: a systematic review with meta-analyses. *Diabet Med* 22 Oct [Epub ahead of print]

Diabetes Metab Res Rev

Severe hypoglycemia risk in real-world sulfonylurea users

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 These authors used data from 1995 to 2013 taken from a large registry in Germany and Austria to determine the rate of severe hypoglycaemia among people who received sulfonylureas (SUs) in real-world clinical practice.

2 A total of 29 485 SU recipients (median age, 70.8 years; diabetes duration, 8.2 years) were reviewed.

3 One or more serious hypoglycaemic events were recorded during the most recent year in 826 participants (2.8%), including 531 (1.8%) cases of coma or convulsion and 501 (1.7%) requiring hospitalisation. This equated to 3.9 severe hypoglycaemic events per 100 patient-years.

4 The rate of non-severe hypoglycaemia was 32.7 per 100 patient-years.

5 People who received SUs in conjunction with insulin had the highest incidence, followed by those on SU monotherapy and then those on SUs with other oral agents (event rates, 6.7, 3.8 and 3.1 per 100 patient-years, respectively).

6 The risk was significantly higher in people with impaired renal function.

7 The rate of severe hypoglycaemia remained broadly the same over the 10-year study period.

8 In the multivariate analysis, severe hypoglycaemia was significantly associated with higher age, longer diabetes duration, lack of diabetes education, female gender, lower BMI, lower diastolic blood pressure, lower triglyceride levels and lower eGFR. Clinicians should consider SU treatment in such people with caution.

Schloot NC, Haupt A, Schütt M et al (2015) Risk of severe hypoglycemia in sulfonylurea-treated patients from diabetes centers in Germany/Austria: how big is the problem? Which patients are at risk? *Diabetes Metab Res Rev* **32**: 316–24

J Diabetes Complications

1–2-year efficacy and safety of SGLT2 inhibitors for T2D

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 This meta-analysis was performed to determine the mid long-term (follow-up, 1–2 years) efficacy and safety of sodium–glucose cotransporter 2 (SGLT2) inhibitors in adults with T2D.

2 Thirteen randomised controlled trials, all double-blind, with a mean participant age of 59 years, were evaluated. The general quality was good (modified Jadad score, 5–7 out of 7).

3 Compared with placebo, at 2 years' follow-up, SGLT2 inhibitors significantly reduced HbA_{1c} (weighted mean difference [WMD], 5.4 mmol/mol [0.50%]), fasting plasma glucose level (WMD, 0.76 mmol/L), body weight (WMD, 3.0 kg), systolic blood pressure (WMD, 7.5 mmHg) and diastolic blood pressure (WMD, 2.2 mmHg).

4 Compared with other oral antidiabetes drugs, SGLT2 inhibitors also reduced HbA_{1c}, fasting glucose, body weight and blood pressure significantly.

5 Regarding adverse events, compared with placebo or other oral agents, SGLT2 inhibitors increased the risk of urinary tract infections (odds ratios [ORs], 1.2–1.5) and genital infections (ORs, 4.2–5.7).

6 Surprisingly, unlike in previous meta-analyses, they also increased the risk of hypoglycaemia compared with placebo; however, this was likely because they were administered in conjunction with insulin or sulfonylureas in six studies.

7 SGLT2 inhibitors did not significantly reduce glomerular filtration rate compared with placebo or other oral agents.

Liu XY, Zhang N, Chen R et al (2015) Efficacy and safety of sodium–glucose cotransporter 2 inhibitors in type 2 diabetes: a meta-analysis of randomized controlled trials for 1 to 2 years. *J Diabetes Complications* **29**: 1295–303

Ann Intern Med

DPP-4 inhibitors or sulfonylureas: Which is safer to add to metformin?

Readability	✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓

1 In this large, population-based, observational cohort study from Taiwan, the authors compared the clinical outcomes of adding dipeptidyl peptidase-4 (DPP-4) inhibitors or sulfonylureas (SUs) to metformin therapy in patients with T2D.

2 Using national registry data, propensity scores were used to match and compare 10 089 pairs of people with T2D receiving metformin who initiated add-on treatment with either a DPP-4 inhibitor or an SU.

3 Over a mean follow-up of 2.8 years, compared with SUs, DPP-4 inhibitors were associated with a reduced risk of all-cause death (hazard ratio [HR], 0.63), major adverse cardiovascular events (HR, 0.68), ischaemic stroke (HR, 0.64) and hypoglycaemia (HR, 0.43).

4 There was no significant difference in risk of myocardial infarction or hospitalisation for heart failure.

5 The authors acknowledge limitations in their study, including the observational design and the absence of data on glycaemic control, and they note that DPP-4 inhibitors, as new drugs, still require longer-term studies of their safety and cardiovascular benefits.

6 Nonetheless, they conclude that their results support the benefits of adding DPP-4 inhibitors rather than SUs to metformin therapy, in terms of both hypoglycaemia risk and cardiovascular outcomes.

Ou SM, Shih CJ, Chao PW et al (2015) Effects on clinical outcomes of adding dipeptidyl peptidase-4 inhibitors versus sulfonylureas to metformin therapy in patients with type 2 diabetes mellitus. *Ann Intern Med* **163**: 663–72

> *"The authors conclude that very-low-energy diets are effective for substantial weight loss in people with type 2 diabetes, although high-quality evidence is severely lacking."*