

Diabetes Digest

Diabetes Digest summarises recent key papers published in the area of coexistent diabetes and obesity – diabetes. To compile the digest a PubMed search was performed for the 3 months ending September 2013 using a range of search terms relating to type 2 diabetes, obesity and diabetes. Articles have been chosen on the basis of their potential interest to healthcare professionals involved in the care of people with diabetes. The articles were rated according to readability, applicability to practice, and originality.



Combination treatment for diabetes

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With the dearth of long-term successful treatments for obesity, practitioners need to be inventive in order to induce significant weight loss. More drugs are being banned than licensed, and calorie counting, low-fat approaches and fad diets are being shown to be ineffectual in sustaining weight loss. Very low energy diets (VLEDs; or very low calorie diets) have consistently been shown to induce safe weight loss of a degree only paralleled by bariatric surgery, but there is a suspicion that weight regain is a common long-term outcome. Weight loss programmes tend to consist of one single intervention (e.g. *Weight Watchers* or *Slimming World* or *LighterLife* or orlistat, and so on). Even Tier 3 services will try a VLED, then try cognitive behavioural therapy if the diet is unsuccessful.

The concept of combining two different modalities simultaneously is often anathema. Whereas, in the management of blood pressure, for instance, the use of different modalities is almost invariable: prescribing two or more drugs, and advising to reduce salt-containing foods and to optimise physical activity. Trials by researchers such as Tom Wadden have shown that, for instance, behavioural therapy had a limited effect and

sibutramine had a small, but useful, effect, but together they induced an impressive weight loss.

The paper summarised alongside is not well written, is incomplete (it discusses taranabant – which never made it to launch – but not rimonabant), flawed (VLEDs are perfectly safe, and widely recommended for individuals with BMI <32 kg/m²), disorganised and chaotic. It only discusses six papers from over 40 years, each using different pharmacological agents: four of which induced weight loss and two which didn't. The pharmacological agent in question is only revealed

in the two unsuccessful trials, so we are shown a 10 kg loss without knowing the drug involved. Apart from a few confusing tables of completer analyses, there are no graphs of weight loss over time. Nevertheless, it serves to remind clinicians that, in diabetes, it is worth considering combinations of interventions.

VLEDs can be initiated in clinic and are good interventions for rapid weight loss, and drugs are moderately successful, although few survive. Putting the two together = very effective. Until the day the anti-obesity magic bullet arrives, more adventurous combinations of interventions for diabetes might work. ■

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Diabetes Metabolism Research and Reviews

Systematic review and meta-analysis: VLEDs followed by pharmacotherapy

Readability	✓✓
Applicability to practice	✓✓✓
Originality	✓✓✓

1. A systematic review and meta-analysis were performed to investigate the effectiveness of the combination of prescribing very low energy diets (VLEDs) followed by pharmacotherapy in regard to weight loss.
2. In current VLEDs, food intake is usually completely replaced with liquids or specific foods so that calorie intake is ≤800 kcal/day.
3. A MEDLINE search was undertaken, and articles from 1970–2009 were considered. In total, 183 articles were found.
4. Only randomised controlled trials that compared a placebo to the pharmacotherapy were selected for the meta-analysis; therefore, six studies were appropriate to include, comprising 1401 individuals.
5. Four studies showed a positive effect for the combination of a VLED followed by pharmacotherapy for weight loss, and two studies showed a negative effect.
6. There was a net effect of 6.1 kg placebo subtracted weight loss after 1 year.
7. A limitation of the systematic review was that only one database was used in the search. Limitations of the meta-analysis were that heterogeneity among the studies was very high ($I^2=93.72\%$) and no risk bias assessment was performed for the six studies.
8. This study contributes to the general understanding that combination therapy can achieve greater weight loss than monotherapies.

Eleni K, Olga P (2013) Combination of very low energy diets & pharmacotherapy in the treatment of obesity: a meta-analysis of published data. *Diabetes Metab Res Rev* 20 Sep [Epub ahead of print]

Diabetes, Obesity and Metabolism

DPP-4i and pancreatitis risk: Meta-analysis

Readability	✓✓✓
Applicability to practice	✓✓✓
Originality	✓✓✓

- Concerns have been raised about the increased risk of pancreatitis associated with dipeptidyl peptidase-4 inhibitors (DPP-4i). The authors, therefore, carried out a systematic review and meta-analysis to investigate the association.
- A search of the Cochrane, EMBASE and MEDLINE databases was carried out up to 1 March 2013, and the European Medicines Agency (EMA), Food and Drug Administration (FDA) and www.clinicaltrials.gov were also searched for unpublished data.
- Inclusion criteria for studies were a randomised controlled trial of ≥ 12 weeks duration that was comparing the treatment of T2D with a DPP-4i or a comparator (placebo or another drug).
- From 134 article results, 109 were eligible for inclusion in the meta-analysis. In total, 20 cases of pancreatitis were reported as serious adverse events in the DPP-4i group. Fifteen were reported in the comparator groups.
- The overall risk of pancreatitis was not different between those being treated with DPP-4i or a comparator (Mantel-Haenszel Odds Ratio [MH-OR]: 0.93 [0.51–1.69]; $P=0.82$). Neither did DPP-4i increase the risk of pancreatic cancer (MH-OR: 0.72 [0.32–1.61]; $P=0.42$). The risks of pancreatitis for the individual DPP-4i drugs were also all not significant.
- Potential limitations of the study given by the authors include the small number of trials (with few observed cases of incident pancreatitis) and the wide confident intervals of risk estimates.
- These data contribute to the hypothesis that there is no increased risks of pancreatitis with DPP-4i.

Monami M, Dicembrini I, Mannucci E (2013) Dipeptidyl peptidase-4 inhibitors and pancreatitis risk: a meta-analysis of randomized clinical trials. *Diabetes Obes Metab* 9 Jul [Epub ahead of print]

J Clin Endocrinol Metab

Activity in pregnancy and insulin sensitivity

Readability	✓✓✓
Applicability to practice	✓✓✓✓
Originality	✓✓✓✓

- The authors investigated whether moderate-to-vigorous physical activity (MVPA) increased insulin sensitivity in overweight and obese pregnant women at risk of gestational diabetes ($n=24$).
- Accelerometers were used to measure the time spent in MVPA at gestation week 15, and its effect on fasting glucose, HbA_{1c}, fasting insulin and insulin sensitivity were assessed at week 24 or 32 gestation.
- MVPA in early pregnancy was significantly associated with increased insulin sensitivity, and was associated with an improved insulin response and decreased triglyceride levels, but MVPA was not associated with improved glucose parameters.

van Poppel MN, Oostdam N, Eekhoff ME et al (2013) Longitudinal relationship of physical activity with insulin sensitivity in overweight and obese pregnant women. *J Clin Endocrinol Metab* 98: 2929–35

Critical Public Health

“Diabetes”: when obesity and T2D converged

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓
Originality	✓✓✓

- The author looked at government reports, journal articles and media coverage published in, or about, Australia since 1988 to trace when discourses on overweight, obesity and diabetes began to converge. In total, 81 items were evaluated.
- Over time, obesity has become perceived as a “contributing factor” of diabetes, rather than a symptom (i.e. weight reduction or management is often a central aim of glucose control).
- The author expresses caution to not overstate the association between obesity and T2D, as the aetiology of T2D is still not well-understood.

McNaughton D (2013) ‘Diabetes’ down under: overweight and obesity as cultural signifiers for type 2 diabetes mellitus. *Crit Public Health* 23: 274–88

BMC Public Health

Systematic review: long-term health benefits of physical activity

Readability	✓✓✓
Applicability to practice	✓✓✓✓
Originality	✓✓✓✓

- A systematic review was undertaken by the authors to determine the long-term health benefits of physical activity on the development of a range of noncommunicable diseases (NCDs): weight gain and obesity; coronary heart disease (CHD); T2D; and Alzheimer’s disease (AD) and dementia.
- Pubmed, BASE and Ovid were scanned for articles published between January 1980 and May 2012. Study inclusion criteria were a longitudinal study design with ≥ 5 years follow-up; involvement of more than 500 healthy, adult participants; and the occurrence of intentional physical activity. Also, only articles published in English were considered.
- Eighteen papers from 15 longitudinal studies were included, with some papers investigating more than one NCD: weight gain and obesity ($n=4$); CHD ($n=6$); T2D ($n=5$); and AD and dementia ($n=6$). A total of 288 724 participants were studied.
- Overall, the studies suggested physical activity has a positive long-term effect for protecting against the development of the selected NCDs.
- Two of the three studies looking at the effect of physical activity on weight gain and obesity found a positive effect for physical activity.
- Physical activity protected against the development of CHD, T2D, and AD and dementia.
- The authors cite limitations such as the limited number of studies in this area (suggesting more long-term research must be done) and the fact that most of the studies only used self-reported or estimated physical activity for measuring physical activity.

Reiner M, Niermann C, Jekauc D, Woll A (2013) Long-term health benefits of physical activity – a systematic review of longitudinal studies. *BMC Public Health* 13: 813

“In overweight and obese pregnant women, moderate-to-vigorous physical activity in early pregnancy was significantly associated with increased insulin sensitivity, and was associated with an improved insulin response and decreased triglyceride levels.”