Diabesity Digest

Diabesity Digest summarises recent key papers published in the area of coexistent diabetes and obesity – diabesity. To compile the digest a PubMed search was performed for the 3 months ending August 2014 using a range of search terms relating to type 2 diabetes, obesity and diabesity. Articles have been chosen on the basis of their potential interest to healthcare professionals involved in the care of people with diabesity. The articles were rated according to readability, applicability to practice, and originality.

Now it's official; yo-yo dieting is dangerous

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The Diabetes Prevention Program (DPP) published in 2002 remains a landmark paper. It showed that diet and lifestyle interventions alone can induce sufficient weight loss to prevent diabetes in people with impaired fasting glucose or impaired glucose tolerance – a 58% reduction in cumulative diabetes incidence at 4 years – after an initial weight loss of around 7 kg after the 6-month core treatment, dwindling to less than 4 kg at 4 years. The remarkable conclusion was that lifestyle intervention knocks metformin into a cocked hat in diabetes prevention, showing its importance in any glucose-lowering strategy.

The DPP team have produced numerous papers, but the prospect of a new publication has the feel of one's favourite old rock band reuniting one more time for another comeback album. One such comeback was a paper last year that looked at the predictors of modest weight loss – which individual should we best dedicate our time and resources to for the best bang for our buck? The answer: someone of White origin, older age, older age when first overweight and fewer past self-implemented weight loss attempts. These were the independent, non-modifiable pre-treatment predictors for achieving 7% weight loss (Delhanty et al, 2013).

So, to complete the circle, the next question was, which weight loss characteristics are the best predictors for the prevention of diabetes? The resulting paper, summarised alongside, was limited to analysing data from those individuals receiving lifestyle intervention for at least 2 years, in order that subsequent weight fluctuations after the 6-month "core curriculum" could be monitored. Greater weight loss in the first 6 months and from 6 months to 2 years were both predictive of reduced diabetes incidence; although overall weight loss from baseline to 2 years was the strongest single predictor of lower diabetes incidence. Absolutely no surprise there – weight loss reduces risk of diabetes and prolonged weight maintenance is more effective than brief weight loss.

However, the crunch is that weight cycling was predictive of an increased incidence of diabetes. Conventional wisdom has always decreed that "yo-yo" dieting is probably a mistake, but the proof has been difficult to provide – studies have been unconvincing and methodologically flawed (Atkinson et al, 1994). But now it's official; yo-yo dieting is dangerous. A random search of the internet revealed that 54% of us are currently dieting, and on average we try four different diet plans per year. This paper confirms what bad news this is; cumulative weight gain, regardless of the weight loss episodes in-between, is harmful and increases diabetes risk. Diabetes prevention programmes, however, seem to be best targeted on white, more elderly, weight loss novices who should be persuaded to lose weight gradually and maintain it. Woe betide the rest! ∎

Atkinson RL, Dietz WH, Foreyt JP et al (1994) Weight cycling. National task force on the prevention and treatment of obesity. *JAMA* **272**: 1196–202

Delahanty LM, Peyrot M, Shrader PJ et al (2013) Pretreatment, psychological, and behavioral predictors of weight outcomes among lifestyle intervention participants in the Diabetes Prevention Program (DPP). *Diabetes Care* **36**: 34–40

Diabetes Prevention Program Research Group (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New Engl J Med* **346**: 393–403

Diabetes Care

What is the effect of weight management on diabetes incidence and changes in cardiometabolic traits?

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

1. Within the lifestyle intervention arm of the Diabetes Prevention Program, nine weight measures were analysed in relation to incident diabetes and improvement in cardiometabolic risk factors over a 2-year period (e.g. characteristic baseline weight, short- versus long-term weight loss, short- versus long-term weight regain and weight cycling).

2. In total, there were 1000 participants in the lifestyle intervention arm. Average age was 51 years (standard deviation [SD] 11 years), 68% were women and mean BMI was 33.77 kg/m^2 (SD 6.56). In total, 54% were white, 18% African American, 16% Hispanic American and 6% Asian American by self-reported ethnicity.

3. Weight loss was found to be protective of diabetes and cardiometabolic risk factors at 6 months ($P<0.01$).

4. Long-term weight loss at 2 years was the strongest predictor of reduced diabetes risk and improvements in cardiometabolic traits.

5. The number of weight cycling events ranged between 0–6 per participant and was positively associated with incident diabetes ($P<0.01$), fasting glucose ($P=0.02$), HOMA-IR ($P=0.04$) and systolic blood pressure ($P=0.03$).

6. After adjustment for baseline weight, increased weight cycling was a statistically significant risk factor for diabetes incidence ($P=0.03$) but not for cardiometabolic traits.

Delahanty LM, Pan Q, Jablonski KA et al (2014) Effects of weight loss, weight cycling, and weight loss maintenance on diabetes incidence and change in cardiometabolic traits in the Diabetes Prevention Program. *Diabetes Care* **37**: 2738–45

Diabetologia

1-year effect of intensive glycaemic control

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

1. The ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial investigated the effectiveness of maintaining glycaemic control after a 4-year period of tight, intensive glycaemic control followed by a year of "relaxed" glycaemic control. Tight glycaemic control was defined as an HbA_{1c} of <6.0% (42 mmol/mol) and relaxed was defined as 7.0–7.9% (53–63 mmol/mol).

2. Maintaining tight glycaemic control for 4 years was associated with long-lasting glycaemic control. Those who achieved an HbA_{1c} <6.5% (<48 mmol/mol) during intensive control were four times more likely to have a final HbA_{1c} <6.5% compared with those who were not able to achieve such tight control on intensive therapy.

Punthakee Z, Miller ME, Simmons DL et al (2014) Durable change in glycaemic control following intensive management of type 2 diabetes in the ACCORD clinical trial. *Diabetologia* **57**: 2030–7

Diabet Med

Diabesity in young adults: Early cardiovascular dysfunction

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

1. The aim of the study was to phenotype young people with T2D (range 18–40 years; mean 31.8 years) to investigate, in particular, their cardiovascular risk profile in comparison to age- and sex-matched lean and obese controls.

2. Twenty people with T2D and 10 lean and 10 obese controls underwent detailed assessment of cardiac structure and function, inflammatory proteins, lipids, vitamin D levels and maximal oxygen uptake.

3. Those with T2D had more harmful profiles for hyperlipidaemia,

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Addition of empagliflozin to multiple daily injections of insulin

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

1. Empagliflozin is a sodium–glucose cotransporter 2 inhibitor, and its efficacy and safety were tested in combination with multiple daily injections of insulin in obese people with inadequately controlled T2D.

2. Participants with a mean HbA_{1c} 67 mmol/mol (8.3%), BMI of 34.8 kg/m^2 and insulin dose 92 IU/day were randomised and treated with once-daily empagliflozin 10 mg (n=186), empagliflozin 25mg (n=189), or placebo (n=188) for 52 weeks.

3. The addition of empagliflozin significantly reduced HbA_{1c}, weight and insulin requirement in people with inadequately controlled T2D on insulin or metformin or both.

Rosenstock J, Jelaska A, Frappin G et al (2014) Improved glucose control with weight loss, lower insulin doses, and no increased hypoglycemia with empagliflozin added to titrated multiple daily injections of insulin in obese inadequately controlled type 2 diabetes. *Diabetes Care* **37**: 1815–23

vitamin D deficiency, inflammation and maximal oxygen uptake relative to body mass compared to the lean controls. The T2D cohort had a significantly larger left ventricle mass than the lean controls. They also tended to have a larger left ventricle mass:volume ratio, but this was not significant.

4. There were no significant differences in these variables between the people with T2D and the obese controls, suggesting that obesity is associated with an adverse cardiovascular risk profile.

5. Diastolic dysfunction in people with T2D may be caused by the additive effect of dysglycaemia in diabetes. Diastolic dysfunction is a precursor to diabetic cardiomyopathy, so the authors encourage the weight loss and medicines therapy to reverse diastolic dysfunction.

Wilmot EG, Leggate M, Khan JN et al (2014) Type 2 diabetes mellitus and obesity in young adults: The extreme phenotype with early cardiovascular dysfunction. *Diabet Med* **31**: 794–8

Diabetes Care

Effectiveness of low-carbohydrate, low-saturated fat diet in weight loss

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

1. The authors compared the effects of a very low-carbohydrate, high-unsaturated/low-saturated fat diet (LC) to a high-unrefined carbohydrate, low-fat diet (HC) on glycaemic control and cardiovascular disease risk factors among people with T2D.

2. A total of 115 obese adults (BMI 34.4±4.2 kg/m^2) with T2D were randomised to either diet, which were individualised and matched for energy levels with moderate restriction (500–1000 kcal/day). In addition, all received 24 weeks of structured exercise.

3. Ninety-three participants completed the intervention and both groups achieved similar completion rates and weight loss (LC −12.0±6.3 kg; HC −11.5±5.5 kg; P ≥0.50).

4. Blood pressure (−9.8/−7.3 ± 11.6/6.8 mmHg), fasting blood glucose (21.4±2.3 mmol/L), and LDL-cholesterol (20.3±0.6 mmol/L) all decreased, with no difference between either diet (P ≥0.10).

5. The LC diet did achieve greater reductions in triglycerides, antiglycaemic medication effects score and glycaemic variability, and induced greater HbA_{1c} reductions and HDL-cholesterol increases in participants with HbA_{1c} and HDL-cholesterol baseline values of >62 mmol/mol (7.8%) and <1.29 mmol/L respectively.

6. LC and HC diets can both improve glycaemic control and several cardiometabolic risk markers in obese adults with T2D. However, the LC diet induced greater improvements in glycaemic control, blood glucose profiles and induced reductions in diabetes medication requirements compared with the HC diet.

Tay J, Luscombe-Marsh ND, Thompson CH et al (2014) A very low carbohydrate, low saturated fat diet for type 2 diabetes management: A randomized trial. *Diabetes Care* **37**: 2909–18

"Maintaining tight glycaemic control for 4 years was associated with long-lasting glycaemic control once glycaemic control was 'relaxed'."