

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 March 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.



DCCT/EDIC update: What are the real causes of diabetes complications?

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DCCT/EDIC (Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications) – studies of type 1 diabetes – do not naturally represent what we understand as “diabetes”, but this paper describes insulin-induced metabolic syndrome with weight gain and the fascinatingly controversial topic of the risks versus benefits of insulin. Insulin has saved countless lives, but has considerable faults; almost 100 years after its introduction, there is a veiled suggestion that alternatives might be preferable.

The DCCT/EDIC research team churns out high quality papers at a spectacular rate, recently on the genetics of erectile dysfunction (Hotaling et al, 2012), and on cardiac autonomic neuropathy (Pop-Busui et al, 2013), but this one is more engaging and clinically useful. David Nathan, Harvard Professor, described the importance of DCCT: “More than 99% of the patients stayed with it for an average of 6.5 years. I’d suggest that’s a world record. We were looking to reduce complications by about 30% and we ended up with a reduction that was more than double that (Watts, 2012).” At the time of the setting up of DCCT, there was controversy about benefits of tight glucose control; some thought that complications had more to do with genetic susceptibility or other factors.

What DCCT originally revealed seems obvious in hindsight precisely because of the wisdom of DCCT and its like which illustrated the evolution of diabetes. DCCT studied insulin use in type 1 diabetes, but its message is relevant to type 2 diabetes: optimising glycaemic

control by responsibly intensifying treatment reduces the risk of complications (DCCT Study Group, 1993). On the negative side, however, risks of hypoglycaemia and severe hypoglycaemia alongside weight gain increased. In 1993, when DCCT ended, the same cohort of patients were recruited for the EDIC study, which showed that intensive diabetes therapy had long-term beneficial effects on the risk of cardiovascular disease (Nathan et al, 2005).

However, as shown in the present study, the quartile from the intensive treatment group with the highest weight gain moved on average from a normal BMI 24 kg/m² to an obese 31 kg/m², displaying metabolic syndrome including worsening waist circumference. The study sheds light on the effects of insulin-induced weight gain on cardiometabolic health: those who gained most weight suffered the worst deterioration in HbA_{1c}. Total cholesterol was higher in weight gainers, as was LDL, with a reduced quality of the LDL particle, alongside raised blood pressure, significantly increasing percentage of patients achieving metabolic syndrome eligibility. Furthermore, intima-media thickness was greater in high-gainers, with coronary artery calcium also trending higher.

Finally, in a fascinating dénouement, comes a suggestion that complications are actually caused by genetic susceptibility, not HbA_{1c} at all! We live and learn. ■

DCCT Study Group (1993) *N Engl J Med* **329**: 977–86
Hotaling JM et al (2012) *J Urol* **188**: 514–20
Nathan DM et al (2005) *N Engl J Med* **353**: 2643–53
Pop-Busui R et al (2013) *J Am Coll Cardiol* **61**: 447–54
Watts G (2012) *Lancet* **379**: 2233

Circulation

The effects of excess weight gain with intensive therapy on cardiovascular risk factors and atherosclerosis

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

1. The study examined the effects of excess weight gain on atherosclerotic disease in the DCCT/EDIC (Diabetes Control and Complications Trial/ Epidemiology of Diabetes Interventions and Complications) cohort.
2. DCCT participants underwent intima-media thickness (IMT; *n*=1015) and coronary artery calcium (CAC; *n*=925) measurements during the follow-up EDIC study.
3. Excess weight gainers maintained greater BMI and waist circumference, needed more insulin, had greater IMT (+5%, *P*<0.001 EDIC year 1, *P*=0.003 EDIC year 6), and trended toward greater CAC scores (OR 1.55; *P*=0.07) than minimal gainers.
4. Participants meeting metabolic syndrome criteria for waist circumference and blood pressure had greater IMT in both EDIC years (*P*=0.02 to <0.001); those meeting HDL criteria had greater CAC scores (OR 1.6; *P*=0.01) during follow-up.
5. Increasing frequency of a family history of diabetes, hypertension and hyperlipidemia was associated with greater IMT with intensive but not conventional treatment.
6. The authors concluded that excess weight gain in DCCT is associated with sustained increases in central obesity, insulin resistance, dyslipidaemia and blood pressure, as well as more extensive atherosclerosis during EDIC.

Purnell JQ et al (2013) *Circulation* **127**: 180–7

Pediatrics

Management of type 2 diabetes in children and adolescents

Readability ✓✓

Applicability to practice ✓✓

Originality ✓✓

1. This technical report describes, in detail, the procedures undertaken to develop the recommendations given in the accompanying clinical practice guideline, and provides in-depth information about the rationale for the recommendations and the studies used to make the clinical practice guideline's recommendations.
2. After retrieving thousands of articles, 58 relating to the treatment of type 2 diabetes and 26 relating to the screening and treatment of type 2 diabetes comorbidities, both in those aged 10–18 years, were retained for systematic review.
3. Therapeutic recommendations for hypertension, dyslipidaemia, retinopathy, microalbuminuria, and depression, summarised from expert guideline documents, are presented in detail.
4. The guideline emphasises the use of management modalities that have been shown to affect clinical outcomes in this population.
5. It addresses situations in which either insulin or metformin is the preferred first-line treatment of children and adolescents with type 2 diabetes.
6. It suggests integrating lifestyle modifications in concert with medication rather than as an isolated initial treatment approach.
7. Guidance for frequency of monitoring HbA_{1c} and finger-stick blood glucose concentrations is also presented.
8. This clinical practice guideline is intended to assist clinician decision-making rather than replace clinical judgment and/or establish a protocol for the care of all children with this condition.
9. This document does not pertain to those with impaired glucose tolerance, isolated insulin resistance, or prediabetes, nor does it pertain to young people who are obese but who do not have diabetes.

Springer C et al (2013) *Pediatrics* 131: e648–64

PLOS Biology

Relationship between white adipose tissue lipolysis and glucose metabolism

Readability ✓

Applicability to practice ✓✓

Originality ✓✓✓

1. In this study, clinical observation in 367 individuals revealed that a high lipolytic rate was associated with low insulin sensitivity.
2. Partial inhibition of white adipose tissue lipolysis resulted in improvement of insulin sensitivity in mice without gain in body weight and fat mass.
3. Mechanistic studies in mice and human fat cells showed that blunted lipolytic capacity increased the synthesis of new fatty acids from glucose, a pathway linked to insulin sensitivity.
4. The researchers concluded that partial inhibition of white adipose tissue lipolysis can be a plausible strategy in the treatment of obesity-related insulin resistance.

Girousse A et al (2013) *PLoS Biol* 11: e1001485

Acta Obstetrica et Gynecologica Scandinavica

Pregnancy after bariatric surgery

Readability ✓✓✓

Applicability to practice ✓

Originality ✓✓

1. This systematic review included 17 studies.
2. Eight studies described lower birthweight and lower risk of macrosomia after bariatric surgery.
3. Five studies indicated a higher risk of small-for-gestational-age infants.
4. One study suggested a higher risk of birth defects after surgery.
5. Pregnancy after bariatric surgery seems safe but larger studies are needed to improve the surveillance of these pregnancies.

Kjaer MM, Nilas L (2013) *Acta Obstet Gynecol Scand* 92: 264–71

European Journal of Nutrition

Does high-fat dairy consumption increase the risk of obesity, cardiovascular disease or type 2 diabetes?

Readability ✓✓✓

Applicability to practice ✓✓

Originality ✓✓

1. This systematic review of observational studies that had attempted to shed light on the specific health effects of dairy fat aimed to investigate the relationship between high-fat dairy foods and obesity and cardiometabolic disease.
2. These findings were integrated with data from controlled studies showing effects of several minor dairy fatty acids on adiposity and cardiometabolic risk factors, and data on how bovine feeding practices influence the composition of dairy fat.
3. In 11 of 16 studies, high-fat dairy intake was inversely associated with measures of adiposity.
4. Studies examining the relationship between high-fat dairy consumption and metabolic health reported either an inverse or no association.
5. Studies investigating the connection between high-fat dairy intake and diabetes or cardiovascular disease incidence were inconsistent.
6. The authors concluded that in contrast to the prevailing scientific and public sentiment, dairy fat consumption is not typically associated with an increased risk of weight gain, cardiovascular disease or type 2 diabetes; this may be particularly true when dairy cows were raised on pasture.
7. This is also in contrast to most current dietary guidelines recommending the consumption of fat-reduced milk and dairy products.
8. Well-controlled intervention studies on the health effects of milk produced by traditional pasture-based versus grain-based husbandry practices should be an important research priority in this area.

Kratz M et al (2013) *Eur J Nutr* 52: 1–24

“In contrast to the prevailing scientific and public sentiment, dairy fat consumption is not typically associated with an increased risk of weight gain, cardiovascular disease or type 2 diabetes.”