Management & prevention of type 2 diabetes

DIABETOLOGIA

T2D reversed by restricted diet

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓✓

1 T2D is a chronic, progressive condition; as beta-cell function declines, insulin therapy is required to maintain good glycaemic control.

2 Studies have shown that T2D can be reversed following bariatric surgery, with normalisation of glycaemia possibly predicted by altered secretion of incretin hormones.

3 The authors hypothesised that the effect of an acute, negative energy balance caused by dietary restriction can normalise beta-cell function and insulin sensitivity, thus reversing T2D.

4 Study participants comprised 11 people with T2D aged 35–65 years with a BMI of 25–45 kg/m^2, an HbA_{1c} level of 48–75 mmol/mol (6.5–9.0%) and a diabetes duration of <4 years.

5 Assessments of beta-cell function, insulin sensitivity, liver and pancreatic triacylglycerol content and total body fat were made at baseline immediately before diet intervention, and after 1, 4 and 8 weeks on a low-energy diet restricted to 2.5 MJ (600 kcal) per day.

6 After 1 week of dietary restriction, fasting plasma glucose normalised in the diabetes group; HbA_{1c} decreased and by 8 weeks reached normal values.

7 Hepatic triacylglycerol content fell from 12.8±2.4% to 2.9±0.2% by week 8 (P=0.003); pancreatic triacylglycerol decreased from 8.0±1.6% to 6.2±1.1% (P=0.03).

8 The authors concluded that dietary energy restriction resulted in normalisation of both beta-cell function and hepatic insulin sensitivity.

Lim EL, Hollingsworth KG, Aribisala BS et al (2011) Reversal of type 2 diabetes: normalisation of beta-cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia* **54**: 2506–14

Taking the (ectopic) fat out of diabetes

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The link between obesity and type 2 diabetes has been know for as long as one can remember. However, the concept of ectopic fat and the metabolic perturbances it engenders has become better understood only in recent years.

In particular, there is now clear and strong evidence that excess hepatic fat is a strong correlate to hepatic insulin resistance, and thus also to impaired insulin-mediated suppression of gluconeogenesis (Taylor, 2008). Moreover, the majority of people with type 2 diabetes appear to have non-alcoholic fatty liver disease (NAFLD), further emphasising the importance of liver fat in the pathogenesis of diabetes (Preiss and Sattar, 2008). What is less clear is the extent to which fat accumulation in other organs, in particular the pancreas, might further contribute to hyperglycaemia and to what extent such fat accumulation might be altered by dietary restrictions.

The Newcastle group, led by Roy Talyor, has examined such issues in a small but elegant study of 11 people diagnosed with diabetes in the last 4 years (Lim et al, 2011; summarised alongside). Their findings of a rapid decline in blood glucose level within 1 week and in HbA_{1c} level by 8 weeks with a 600 kcal diet demonstrates that significant calorie intake reductions can rapidly "normalise" blood glucose levels. More interesting, that HbA_{1c} changes were accompanied by a striking reduction in liver fat and a more modest but nevertheless significant reduction in pancreatic fat is of major interest. Such changes were accompanied by measurable and sizeable improvements in first-phase insulin secretion, almost towards levels seen in non-diabetes controls.

These observations challenge the dogma that beta-cell function is gradually lost (i.e. inevitable beta-cell death) over time and cannot necessarily be recovered. Furthermore, evidence that some people with diabetes previously on insulin can also normalise their blood glucose levels after bariatric surgery (Dixon et al, 2008) further supports an emerging concept of beta-cell "hibernation" in the face of excess ectopic pancreatic fat, although the precise mechanisms for this fat-mediated loss of function remain to be established.

> ***"These observations challenge the dogma that beta-cell function is gradually lost (i.e. inevitable beta-cell death) over time and cannot necessarily be recovered"***

Clearly, there is a need to take these observations forwards to the clinic. People cannot be expected to maintain 600 kcal diets in the long term – such diets are simply not sustainable. However, if we could manage to reverse diabetes in some and then sustain their gains by more modest but sustainable changes in dietary intake, then this would a step forward.

In short, we need to invest more time in understanding how best to help people at risk of diabetes, or in its early stages, to achieve modest dietary changes. Only then can we begin to take the (ectopic) fat out of diabetes.

Dixon JB, O'Brien PE, Playfair J et al (2008) Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. *JAMA* **299**: 316–23

Preiss D, Sattar N (2008) Non-alcoholic fatty liver disease: an overview of prevalence, diagnosis, pathogenesis and treatment considerations. *Clin Sci (Lond)* **115**: 141–50

Taylor R (2008) Pathogenesis of type 2 diabetes: tracing the reverse route from cure to cause. *Diabetologia* **51**: 1781–9

"C-peptide–creatinine ratio may provide a practical measure of insulin deficiency for routine use."

DIABETIC MEDICINE

Urinary C-peptide creatinine ratio may be a practical test

Readability	✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 Measuring C-peptide can be used to assess insulin secretion, enabling diabetes diagnosis and prediction of treatment response; however, the practicalities of measuring serum C-peptide limit widespread use.

2 The objective of this was to determine how urinary C-peptide–creatinine ratio (UCPCR) compared with serum C-peptide measurement during a mixed meal tolerance test in 51 people with insulin-treated, late-onset diabetes.

3 Results showed that 90-minute serum C-peptide and 2-hour urinary UCPCR were highly correlated.

4 The authors concluded that urinary (UCPCR) may provide a practical measure of insulin deficiency for routine use.

Jones AG, Besser REJ, McDonald TJ et al (2011) Urine C-peptide creatinine ratio is an alternative to stimulated serum C-peptide measurement in late-onset, insulin-treated diabetes. *Diabet Med* **28**: 1034–8

ANNALS OF THE RHEUMATIC DISEASES

Glucose intolerance is underestimated in people with RA

Readability	✓✓✓✓
Applicability to practice	✓
WOW! factor	✓✓✓

1 Although impaired glucose metabolism may contribute to accelerated atherogenesis in people with rheumatoid arthritis (RA), the role of glucocorticoids (GCs) in glucose intolerance in this group is uncertain.

2 The authors compared glucose tolerance and parameters of insulin sensitivity and beta-cell function in people with RA who were chronic GC users (n=58) or who were GC-naïve (n=82) with 50 controls with normal glucose tolerance.

3 Participants in the GC-using and GC-naïve groups had comparable metabolic parameters and showed decreased insulin sensitivity and beta-cell function when compared with those in the control group without RA.

4 Although the prevalence of previously undiagnosed T2D was comparable between both RA groups, cumulative GC dose was associated with incident T2D.

5 It was concluded that glucose intolerance is a significant problem in people with RA.

Hoes JN, van der Goes MC, van Raalte DH et al (2011) Glucose tolerance, insulin sensitivity and β-cell function in patients with rheumatoid arthritis treated with or without low-to-medium dose glucocorticoids. *Ann Rheum Dis* **70**: 1887–94

DIABETES

Family history and genes determine glycaemic trajectory

Readability	✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓

1 Previous studies have shown that a genetic susceptibility for T2D could induce early beta-cell dysfunction.

2 This study aimed to determine the impact of a genetic predisposition to T2D on fasting glucose, HbA_{1c} level, insulin sensitivity and beta-cell secretion over time in a large cohort of people without diabetes.

3 In total, 4774 people participated in DESIR (Data from an Epidemiological Study on the Insulin Resistance Syndrome); data were collected every 3 years during the 9-year study.

4 In the 3 years before incident diabetes, beta-cell secretion markedly decreased in line with a steep increase in HbA_{1c}.

5 The authors concluded there was a joint effect of family history of T2D and the *TCF7L2* risk variant on the evolution of glycaemia.

Gautier A, Roussel R, Lange C et al (2011) Effects of genetic susceptibility for type 2 diabetes on the evolution of glucose homeostasis traits before and after diabetes diagnosis. *Diabetes* **60**: 2654–63

NEW ENGLAND JOURNAL OF MEDICINE

Moving away from poor neighbourhood reduces obesity and diabetes

Readability	✓✓✓
Applicability to practice	✓
WOW! factor	✓✓✓✓

1 Studies have suggested that neighbourhood environment might influence health; however, it is uncertain whether neighbourhood environment directly contributes to the development of obesity and diabetes.

2 Data were obtained from Moving to Opportunity, a social demonstration project set up by the Department of Housing and Urban Development, to determine the effects of neighbourhood environment on obesity and diabetes.

3 Participating families included 4498 women with children living in public housing in high-poverty neighbourhoods (≥40% of residents had incomes below the poverty threshold).

4 Families were randomly assigned to one of three groups: those to receive housing vouchers if the families moved to a less impoverished neighbourhood (n=1788); those to receive traditional vouchers with no moving restrictions (n=1312); and those assigned to a control group with no new assistance (n=1398).

5 Measures included BMI (84.2% of participants) and HbA_{1c} (71.3%).

6 After 10–15 years of follow-up, women in the housing voucher group had lower prevalences of a BMI ≥35 kg/m^2 and HbA_{1c} level of ≥48 mmol/mol (≥6.5%) than those in the control group; differences in BMI and HbA_{1c} between the housing voucher and the traditional voucher groups were not significant.

7 It was concluded that moving to an area with lower poverty had a modest effect on reducing obesity and diabetes.

Ludwig J, Sanbonmatsu L, Gennetian L et al (2011) Neighbourhoods, obesity and diabetes – a randomised social experiment. *N Engl J Med* **365**: 1509–19

"Lifestyle modifications causing weight loss had beneficial effects on non-alcoholic fatty liver disease, and should be the therapy of choice."

ARCHIVES OF DISEASE IN CHILDHOOD

Weight loss improves NAFLD in obese children

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓

1 Non-alcoholic fatty liver disease (NAFLD) is increasingly being diagnosed in children, and is associated with the increasing prevalence of obesity.

2 The authors used transaminase as a surrogate marker of NAFLD to determine the prevalence of abnormal liver function in obese children and the response to weight loss with lifestyle modifications; the association between transaminitis, glucose metabolism and the metabolic syndrome was also explored.

3 Participants comprised 216 children with a median age (range) of 12.4 years (2.9–17.6) and a median BMI standard deviation (range) of 3.36 kg/m^2 (1.92–6.22); 90 children participated in a lifestyle modification intervention to lose weight.

4 Data collected included an oral glucose tolerance test (OGTT) with fasting lipid and liver profile, weight, height, waist circumference, percentage body fat and parental history of T2D; data were collected at baseline and re-assessed at 1 year.

5 Results showed that 34 children (16%) had raised alanine aminotransferase, with greater prevalence in boys and those with a parental history of T2D; they were more likely to fulfil the criteria for the metabolic syndrome (P<0.001) and have subtle abnormalities in glucose metabolism during an OGTT.

6 A mean BMI/BMI SDS reduction of 1.51 and 0.3 kg/m^2, respectively, achieved normalisation of transaminitis.

7 The authors concluded that lifestyle modifications causing weight loss had beneficial effects on NAFLD, and should be the therapy of choice.

Wei C, Ford A, Hunt L et al (2011) Abnormal liver function in children with metabolic syndrome from a UK-based obesity clinic. *Arch Dis Child* **96**: 1003–7

DIABETIC MEDICINE

Very low CVD rates in current Japanese people with T2D

Readability	✓✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓✓

1 The authors sought to determine whether cardiovascular disease (CVD) incidence can be reduced in 2984 Japanese people with T2D undergoing multifactorial treatment and followed in primary care settings, compared with earlier cohorts.

2 In this prospective study, participants were followed until first non-fatal or fatal coronary heart disease (CHD), ischaemic stroke, peripheral artery disease (PAD), death or study end.

3 Forty-eight CHD events occurred over 10 827 person-years of follow-up, representing a remarkably low CHD event rate of 4.4 per 1000 person–years, much lower than prior studies.

4 The authors suggested that the low incidence of CVD in this cohort could be attributed to the primary care provision of multifactorial therapy.

Yokoyama H, Matsushima M, Kawai K et al (2011) Low incidence of cardiovascular events in Japanese patients with type 2 diabetes in primary care settings. *Diabet Med* **28**: 1221–8

J CLIN ENDOCRINOL METAB

Lifestyle intervention reduces weight and CV risk in PCOS

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓

1 Polycystic ovarian syndrome (PCOS) is a complex functional disorder that typically presents during adolescence.

2 In this study the authors analysed the impact of a 1-year lifestyle intervention, based on nutrition, exercise and behaviour therapy, on the features of PCOS and the metabolic syndrome.

3 In total, 59 obese girls with PCOS aged 12–18 years underwent the lifestyle intervention; weight, menstrual cycle, hyperandrogenaemia, CV risk factors and intima-media thickness (IMT) were evaluated at baseline and at 1 year.

4 During the intervention, the 26 girls who reduced their BMI (by a mean –3.9 kg/m^2) also decreased their CV risk and their IMT (by a mean –0.01 cm).

5 Weight loss as a result of the lifestyle intervention also decreased menstral irregularities and normalised androgens in girls with PCOS.

Lass N, Kleber M, Winkel K et al (2011) Effect of lifestyle intervention on features of polycystic ovarian syndrome, metabolic syndrome and intima-media thickness in obese adolescent girls. *J Clin Endocrinol Metab* **96**: 3533–40

DIABETIC MEDICINE

Evidence in support of new gestational diabetes criteria

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 Gestational diabetes (GD), defined as glucose intolerance developed during pregnancy, requires early diagnosis and management to prevent complications.

2 Criteria exist for diagnosing GD in an attempt to minimise maternal, perinatal and neonatal adverse outcomes.

3 The International Association of the Diabetes and Pregnancy Study Group (IADPSG) Consensus Panel has reconsidered the current diagnostic thresholds and formulated new criteria for diagnosing GD.

4 Of the 2138 classified with GD using the new criteria, 112 (2.8%) would have been classified as normal according to previous criteria. However, these 112 had similar outcomes to women with GD by prior criteria.

Lapolla A, Dalfrà MG, Ragazzi E et al (2011) New IADPSG recommendations for diagnosing gestational diabetes compared with former criteria. *Diabet Med* **28**: 1074–7