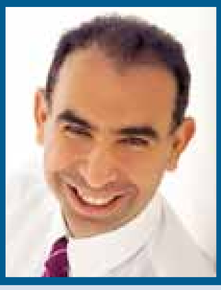
Obesity



Lifestyle interventions for type 2 diabetes: Time for translation

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The pandemics of obesity and T2D are serious challenges to healthcare services and have major societal implications. Increasingly, obesity and diabetes are seen at younger ages than previously observed (Haines et al, 2007; Shield et al, 2009) with the potential to track into adulthood with serious health consequences (Guo et al, 2002). T2D at a younger age also increases the risk of both macro- and microvascular diabetes complications. For example, a population-based Swedish study reported that T2D conferred a three-fold higher risk for severe retinopathy compared to T1D (Henricsson et al, 2003); thus, T2D is not a benign disease.

The prevention of diabetes is key and should be targeted at high-risk individuals. Impaired glucose tolerance (IGT) is a major risk factor for T2D and confers its own vascular disease risks. About a third of obese adolescents with IGT will progress to T2D at what appears to be a more rapid pace (within 24 months) than older individuals (Weiss et al, 2005). This observation, however, is not universal since others have reported reversion to normoglycaemia in about a half of young individuals with IGT (Libman et al, 2003).

Adult diabetes prevention studies have shown that intensive lifestyle interventions are effective in reducing the progression of IGT to T2D (Thomas et al, 2010); in the American Diabetes Prevention Study, intensive lifestyle intervention reduced incidence of T2D by 58% compared to placebo (Knowler et al, 2002). Metformin without lifestyle intervention also reduced progression to diabetes by about one third. The use of metformin in adolescents with diabetes and obesity has been examined in several studies (a recent systematic review in 2013 by Brufani and colleagues included 11 trials), and the majority of the studies reported only a modest reduction in BMI compared to controls. Fasting insulin levels were also reduced in many of the studies.

In a Cochrane review, it was concluded that lifestyle interventions are effective at reducing obesity in children (Oude Luttikhuis et al, 2009). The lifestyle interventions have, however, been heterogeneous using diet, physical activity, and behavioural change either alone or in various combinations. Some have also involved family participation.

In the article summarised alongside, Savoye and colleagues examined the impact of their multidisciplinary lifestyle intervention programme (biweekly sessions over 6 months) on glucose homeostasis and other parameters (e.g. blood pressure) in obese adolescents with IGT. The intervention arm had improvements in fasting glucose and insulin, and Homeostatic Model Assessment as an index of insulin resistance (HOMA-IR). Interestingly, despite these changes, there was no difference in HbA_{1c}, which appears a poor marker for IGT and its response to treatment. The intervention group benefitted from significant reductions in body weight, BMI and body fat percentage. Given that diabetes has important macrovascular complications, the intervention group had significantly lower blood pressure, and changes in insulin sensitivity and diet are further reflected by lower triglyceride levels. It would be of importance to know whether the positive improvements observed are sustainable in the long term.

Intensive lifestyle interventions are effective for reducing the development of diabetes in both adults and adolescents. These interventions, however, need to be translated into clinical services. Currently, the provision of clinical services to address obesity and its major complications, such as diabetes, in younger individuals are insufficient in the UK. Existing services are inadequately supported and lack the capacity to deliver intensive lifestyle interventions with close medical monitoring. Services should be supported to screen for IGT and provide evidence-based interventions such as the intervention employed by Savoye and colleagues. Obesity, IGT and diabetes in young people can be devastating and need to be addressed as a priority. ■

Diabetes Care

Obese youth: Reversing irregular glucose metabolism

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

1 A randomised controlled trial was carried out to measure the impact of the Bright Bodies (BB) Health Lifestyle programme (Yale University, CT, USA) on 2-hour oral glucose tolerance test (OGTT) results in obese youth compared to standard care (CC).

2 The programme was tailored for inner-city minority children, and 75 adolescents were randomised to either group (inclusion criteria: 10–16 years of age and Tanner stage >2, BMI >95th percentile and 2-hour OGTT plasma glucose between 130 mg/dL [7.2 mmol/L] and 199 mg/dL [11.0 mmol/L]).

3 The BB programme comprised attending two meetings a week for 6 months with a weekly weigh-in and a 40-minute nutrition and behaviour modification class, plus two 50-minute exercise sessions per week.

4 The CC group were given instructions on diet and exercise every 2–3 months.

5 The primary outcome was the change in 2-hour OGTT and percentage conversion from elevated 2-hour blood glucose to non-elevated 2-hour blood glucose over 6 months.

6 Significant reductions from baseline in 2-hour OGTT glucose were observed in both BB and CC groups.

7 There was a greater improvement in 2-hour OGTT blood glucose in the BB group compared with the CC group from baseline to 6 months (P=0.005).

8 The BB programme significantly decreased 2-hour glucose in children at high risk of diabetes after 6 months compared to CC.

Savoye M, Caprio S, Dziura J et al (2014) Reversal of early abnormalities in glucose metabolism in obese youth: results of an intensive lifestyle randomized controlled trial. *Diabetes Care* **37**: 317–24

Diabetes Metabolism

Very-low calorie diet improves GFR in people with morbid obesity and T2D

Readability ✓✓✓

Applicability to practice ✓✓✓

WOW! Factor ✓✓

1 In a preliminary proof-of-concept study, the effect of acute calorie restriction on renal function, as measured by glomerular filtration rate (GFR), was investigated as some evidence has shown that calorie restriction can reduce proteinuria.

2 The participants comprised fourteen morbidly obese people (BMI >40 kg/m^2) with T2D, good metabolic control and stage 2 chronic kidney disease. They all completed a 7-day "wash-out" period to remove all hypoglycaemic and anti-hypertensive medications from their system, and baseline measurements were taken.

3 After the "wash-out" period, the participants followed a very-low calorie diet ([VLCD] 400 kcal/day and standardised water and salt intake of 1.5 L/day and <6 g/day, respectively) for 7 days.

4 The 7-day VLCD resulted in significant decreases in weight (3.58±0.6 kg), BMI (from 44.8±1.6 kg/m^2 to 43.5±1.6 kg/m^2 [P=0.001]) and waist circumference and in significant improvements in glucose disposal related to increased beta-cell function, particularly, first-phase insulin secretion.

5 Renal function, as measured by GFR, significantly increased and improved following the VLCD from 72.6±3.8 mL/min/1.73 m^2 (adjusted to body surface area [BSA]) to 86.9±6.1 mL/min/1.73m^2 BSA (P=0.026).

6 Short-term calorie restriction is associated with acute improvement in renal function.

Giordani I, Malandrucco I, Donno S et al (2014) Acute caloric restriction improves glomerular filtration rate in patients with morbid obesity and type 2 diabetes. *Diabetes Metab* **40**: 158–60

Diabetes

Limited recovery of beta-cell function after gastric bypass

Readability ✓✓✓

Applicability to practice ✓✓✓

WOW! Factor ✓✓✓

1 How Roux-en-Y gastric bypass (RYGBP) results in T2D remission is unclear. To elucidate the role of the gut in this mechanism, the authors compared beta-cell function assessed during an oral glucose tolerance test (OGTT) and an isoglycaemic intravenous glucose clamp (iso-IVGC) before and after RYGBP.

2 Three participant cohorts were included in the analysis: 16 severely obese people with T2D up to 3 years post-RYGBP; 11 severely obese normal glucose-tolerant controls; and 7 lean controls.

3 T2D remission was observed after RYGBP.

4 When measured during the OGTT, beta-cell function (which was significantly lower prior to RYGBP) normalised to levels observed in both of the control groups.

5 In contrast, during the iso-IVGC, beta-cell function improved minimally and remained significantly impaired compared to lean control participants up to 3 years post-RYGBP.

6 Weight loss appeared to be the strongest predictor of beta-cell function after RYGBP.

7 The results show that beta-cell dysfunction persists after RYGBP in people with clinical diabetes remission when glucose is administered intravenously. This highlights the important role of the gut during digestion in stimulating insulin secretion, and suggests RYGBP leads to an important gastrointestinal effect that is vital for improved beta-cell function.

Dutia R, Brakoniecki K, Bunker P et al (2014) Limited recovery of beta-cell function after gastric bypass despite clinical diabetes remission. *Diabetes* **63**: 1214–23

Diabetologia

Physical activity levels and metabolic risk factors

Readability ✓✓✓✓

Applicability to practice ✓✓✓

WOW! Factor ✓✓✓

1 The study aim was to examine the associations between sedentary time (SED-time), time spent in moderate-to-vigorous-intensity physical activity (MVPA), total physical activity energy expenditure (PAEE) and cardiorespiratory fitness with metabolic risk among individuals with recently diagnosed T2D.

2 Using data from the ADDITION-Plus (Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen Detected Diabetes in Primary Care) trial of individuals with T2D, activity was measured using a combined activity and movement sensor, and clustered metabolic risk was calculated (by summing standardised values for waist circumference, triacylglycerol, HbA_{1c}, systolic blood pressure and the inverse of HDL-cholesterol).

3 Each additional 1 hour of SED-time was positively associated with clustered metabolic risk, independently of sleep duration and MVPA. Associations between SED-time and metabolic risk were generally stronger in the low- compared with the high-fitness group.

4 PAEE was inversely associated with metabolic risk, whereas SED-time was positively associated with metabolic risk.

5 Encouraging people with recently diagnosed T2D to increase the amount of overall physical activity may have beneficial effects on disease progression and cardiovascular risk.

Cooper AJ, Brage S, Ekelund U et al (2014) Association between objectively assessed sedentary time and physical activity with metabolic risk factors among people with recently diagnosed type 2 diabetes. *Diabetologia* **57**: 73–82

> "*Obesity, impaired glucose tolerance and diabetes in young people can be devastating and need to be addressed as a priority.*"

References from commentary

Brufani C et al (2013) *Horm Res Paediatr* **80**: 78–85

Guo SS et al (2002) *Am J Clin Nutr* **76**: 653–8

Haines L et al (2007) *Diabetes Care* **30**: 1097–101

Henricsson M et al (2003) *Diabetes Care* **26**: 349–54

Knowler WC et al (2002) *N Engl J Med* **346**: 393–403

Libman IM et al (2003) *Diabetes Care* **26**: 2871–5

Oude Luttikhuis et al (2009) *Cochrane Database Syst Rev* CD001872

Shield JP et al (2009) *Arch Dis Child* **94**: 206–9

Thomas GN et al (2010) *Curr Diabetes Rev* **6**: 378–87

Weiss R et al (2005) *Diabetes Care* **28**: 902–9