Management & prevention of type 2 diabetes

Type 2 diabetes in young adults: Risks, research and reality

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Predictions of a worrying rise in the number of younger adults with type 2 diabetes are, sadly, now coming to fruition. The biggest driver for this pattern is, of course, rising levels of obesity. Young people have, on average, better pancreatic capacity to deal with insulin resistance than do older individuals. Most, therefore, need to be very overweight to develop diabetes, a finding in keeping with the inverse association of BMI and age at diagnosis of type 2 diabetes (Logue et al, 2011). That noted, a high proportion of younger adults with diabetes will be from ethnic minorities, given their greater diabetes risk for a given BMI, as was recently indicated in a study using UK Biobank data: South Asians with a BMI of 22 kg/m^2 had an equivalent diabetes prevalence to whites with a BMI of 30 kg/m^2, whereas the cut-offs for Chinese and black people were 24 kg/m^2 and 26 kg/m^2, respectively (Ntuk et al, 2014).

So, why should we worry about younger folk with type 2 diabetes? Several concerns are emerging. First, as obesity is usually, by necessity, a major feature of type 2 diabetes in this age group, these people have undergone, and continue to undergo, rapid weight gain that can be hard to slow, never mind reverse. This means glycaemic control may worsen more rapidly in young patients with type 2 diabetes than in those who develop the condition later in life. Secondly, evidence is emerging for greater rates of microvascular and macrovascular complications (particularly nephropathy) in younger adults with type 2 diabetes compared with age- and diabetes duration-matched patients with type 1 diabetes (Constantino et al, 2013). This is understandable if we recognise that the coexistent obesity in young people with type 2 diabetes means higher blood pressure and greater abnormality in lipid profiles – changes that synergise with hyperglycaemia to promote a greater risk of complications. Thirdly, such individuals are set to have a longer lifetime exposure to glycaemia, given their young diabetes onset, and so their area under the curve of glycaemia exposure could be much greater, leading to more risks. Finally, there are signs that cardiac function deteriorates more rapidly in such individuals, a finding that is now corroborated by a pilot study by Wilmot et al (summarised alongside).

There is a clear need for new research in young people with type 2 diabetes that addresses better ways to help tackle their obesity, optimise their risk factors, and improve their quality of life. More specifically, questions such as the scope for intervention with weight-losing therapies (or even bariatric surgery in a select group), ideal glycaemic treatment options, need for and timing of statin therapy (calculated absolute cardiovascular risk will be low in younger patients) and ideal blood pressure targets all remain unanswered and are important research topics. In short, type 2 diabetes care will need to embrace the needs of an increasing number of younger adults with the condition, and there is much work to be done. ■

Constantino MI, Molyneaux L, Limacher-Gisler F et al (2013) Long-term complications and mortality in young-onset diabetes: type 2 diabetes is more hazardous and lethal than type 1 diabetes. *Diabetes Care* **36**: 3863–9

Logue J, Walker JJ, Colhoun HM et al (2011) Do men develop type 2 diabetes at lower body mass indices than women? *Diabetologia* **54**: 3003–6

Ntuk UE, Gill JM, Mackay DF et al (2014) Ethnic-specific obesity cutoffs for diabetes risk: cross-sectional study of 490,288 UK Biobank participants. *Diabetes Care* **37**: 2500–7

Diabet Med

Cardiovascular dysfunction in young adults with T2D

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

1 Twenty people aged 18–40 years with T2D underwent detailed assessment of cardiovascular function and were compared with 10 lean and 10 obese control subjects without T2D.

2 All participants underwent cardiac magnetic resonance imaging, fasting plasma glucose, lipid and liver function tests, and an exercise test to determine maximal oxygen uptake (VO_{2max}).

3 Despite their young age (mean, 31.8 years) and short diabetes duration (mean, 4.7 years), these young adults with T2D had dyslipidaemia, hypertension, abnormal liver function, vitamin D deficiency and reduced VO_{2max}.

4 They also had a significantly higher left ventricular (LV) mass (P=0.002) and a trend towards a higher LV mass/volume ratio (P=0.052) compared with the lean controls.

5 There were no significant differences in these variables between the people with T2D and the obese controls, suggesting that these cardiovascular risk factors were a result of obesity.

6 However, peak early diastolic strain rate was significantly lower in the T2D group compared with both the obese and the lean controls, with a linear reduction through the three groups; this suggests that diastolic dysfunction in young people with T2D is further exacerbated by dysglycaemia.

7 The authors caution that this study had a small sample size and was cross-sectional in nature, so causation cannot be inferred.

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

J Diabetes Complications

Liraglutide reduces systolic blood pressure in T2D

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

1 Glucagon-like peptide-1 receptor agonists have been shown to lower blood pressure (BP) in addition to their effects on glycaemia.

2 The authors used pooled data from the six LEAD (Liraglutide Effect and Action in Diabetes) trials to compare the effects of liraglutide 1.2 mg, 1.8 mg and placebo on systolic BP (SBP).

3 A total of 2792 people were evaluated, of whom 898 received liraglutide 1.2 mg, 1366 received liraglutide 1.8 mg and 528 received placebo.

4 Compared with placebo, there were greater reductions in SBP with both the 1.2-mg (2.7 vs 0.5 mmHg; P=0.0029) and the 1.8-mg (2.9 vs 0.5 mmHg; P=0.0004) doses of liraglutide.

5 The effects on SBP were independent of, and appeared to be additive to, any coadministered antihypertensive medications.

6 Both liraglutide doses also resulted in reduced pulse pressure compared with placebo, although there was no significant effect on mean arterial BP.

7 The reductions in SBP were weakly but significantly correlated with weight loss, but not with HbA_{1c}, which suggests that the SBP-reducing mechanism is mediated partly by weight loss but not by long-term glycaemic control.

8 The authors observed that liraglutide resulted in an increase in heart rate of 3 bpm; this is grounds for caution as increases of ≥10 bpm are correlated with cardiovascular and all-cause mortality.

Fonseca VA, Devries JH, Henry RR et al (2014) Reductions in systolic blood pressure with liraglutide in patients with type 2 diabetes: insights from a patient-level pooled analysis of six randomized clinical trials. *J Diabetes Complications* **28**: 399–405

Diabetes Obes Metab

Factors linked to glycaemic control post-bariatric surgery

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

1 The authors report the 1-year outcomes of gastric band surgery in 187 people with T2D.

2 The proportion of participants who achieved good glycaemic control (HbA_{1c} <53 mmol/mol [<7%]) improved from 42.8% at baseline (time of surgery) to 72.2% at 1 year.

3 Multivariate analysis showed that shorter diabetes duration, not using insulin at baseline and greater percentage weight loss were associated with good glycaemic control at 1 year.

4 Device-related adverse events and reoperations were rare, occurring in 0.7% of participants at baseline and in 1.5% at 1 year.

Edelman S, Ng-Mak DS, Fusco M et al (2014) Control of type 2 diabetes after 1 year of laparoscopic adjustable gastric banding in the Helping Evaluate Reduction in Obesity (HERO) study. *Diabetes Obes Metab* **16**: 1009–15

Diabet Med

BMI independently associated with heart failure in T2D

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

1 The authors evaluated a large Swedish cohort of 83 021 people with T2D (mean age, 66 years) to determine the association between BMI and hospitalisation for heart failure (HF).

2 Over a median follow-up of 7.2 years, 13.2% of the cohort were hospitalised for HF.

3 When adjusted for other known risk factors, BMI was significantly associated with HF.

4 Compared with a BMI of 20 to <25 kg/m^2, the hazard ratios for the different BMI ranges were as follows: 25 to 27.5, 1.04 (P=non-significant); 27.5 to <30, 1.22; 30 to <35, 1.54; 35 to <40, 2.16; ≥40, 3.22.

5 There was a significant interaction between BMI and gender, so that high BMI was associated with a greater risk of HF in men than in women; indeed, men with a BMI of 27.5 to <30 kg/m^2 had significantly higher risk, whereas women with the same BMI did not.

Glogner S, Rosengren A, Olsson M et al (2014) The association between BMI and hospitalization for heart failure in 83 021 persons with type 2 diabetes: a population-based study from the Swedish National Diabetes Registry. *Diabet Med* **31**: 586–94

Diabetologia

Canagliflozin improves indices of beta-cell function

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

1 Using data from three phase III trials, the authors evaluated the effect of canagliflozin on model-based indices of beta-cell function.

2 A subset of participants in the trials (n=590) were given a mixed-meal tolerance test, and beta-cell function was estimated from plasma glucose and C-peptide levels using a previously described model.

3 Compared with placebo, canagliflozin 100 mg and 300 mg given over a period of 6–12 months increased the indices of beta-cell function. Compared with sitagliptin, canagliflozin improved these measures to a similar extent.

4 Further study will be required to demonstrate whether canagliflozin can help slow the decline in beta-cell function in T2D over the long term.

Polidori D, Mari A, Ferrannini E (2014) Canagliflozin, a sodium glucose co-transporter 2 inhibitor, improves model-based indices of beta cell function in patients with type 2 diabetes. *Diabetologia* **57**: 891–901

"Multivariate analysis showed that shorter diabetes duration, not using insulin at baseline and greater percentage weight loss were associated with good glycaemic control 1 year after gastric band surgery."