Obesity

The changing face of type 2 diabetes

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A major long-term trend in diabetes has been the emergence of type 2 diabetes in young adults and children. Previously, increasing age was a dominant risk factor for type 2 diabetes. While type 2 diabetes in children is still relatively uncommon in the UK, it accounts for a substantial and increasing proportion of childhood diabetes in some populations (Ehtisham et al, 2000).

This entity, or more accurately group of entities, poses a unique clinical challenge to diabetes teams, as the traditional mantra of healthy diet, a physically active lifestyle, weight control and adherence to life-long pharmacological treatment is a decidedly unappealing prospect for these youngsters.

In view of its comparative rarity until recent years, there have been few large prospective studies on type 2 diabetes in the young and there are few long-term data to guide treatment decisions. The TODAY (Treatment Options for Type 2 Diabetes in Adolescents and Youth; Copeland et al, 2011; summarised alongside) study is set to change this: the authors have established a large randomised controlled trial evaluating drug and lifestyle intervention treatments in USA children recently diagnosed with type 2 diabetes. This article describes the baseline characteristics of the cohort, and there are already important messages for public health and primary care teams.

This multicentre study screened 1211 children for entry, 927 entered the run-in phase to assess adherence and tolerance of metformin, and 704 were finally included and randomised to metformin alone, metformin plus rosiglitazone, or metformin plus a family-based behavioural lifestyle change programme aimed at promoting weight loss.

This is a very carefully selected group of children. There was a range of exclusion criteria, including autoantibody positivity (10%) despite a clinical diagnosis of type 2 diabetes, low levels of C-peptide and raised liver enzymes. Autoantibody positivity is common in children with type 2 diabetes and its significance controversial, although the rationale for this exclusion was to exclude those with autoimmune type 1 diabetes. The mean age was 14 years and almost all were pubertal, with 59.6% having a first degree family history of diabetes, rising to 89.4% with inclusion of grandparents. A disproportionate 64.9% were female and the majority were from ethnic minority groups and from socioeconomically and educationally disadvantaged backgrounds. There was a high apparent prevalence of family breakdown. The metabolic syndrome was rife.

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There is much to discuss in these data, which seem to describe a collision between genetic risk, obesity and social breakdown. The TODAY study should add significantly to our understanding of the relative efficacy of the main potential treatment options, although the control of type 2 diabetes in this population may require political and social, as much as medical, interventions.

Ehtisham S, Barrett TG, Shaw NJ (2000) Type 2 diabetes mellitus in UK children--an emerging problem. *Diabet Med* **17**: 867–71

J CLINICAL ENDOCRINOLOGY AND METABOLISM

Comorbidities present within 2 years of T2D diagnosis in youth

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

1 The TODAY (Treatment Options for Type 2 Diabetes in Adolescents and Youth) cohort represents the largest and best-characterised national sample of young people in the USA with recent-onset T2D.

2 Participants (n=704) were recruited at 15 clinical centres. Eligible participants were aged 10–17 years, had diagnosed T2D for a duration of <2 years and had a BMI in the 85th percentile or greater.

3 Participants were randomised to receive: (i) metformin alone; (ii) metformin plus rosiglitazone; or (iii) metformin plus a lifestyle programme of weight management. In this study, the authors present baseline data.

4 The cohort was 64.9% female and mean age was 14.0 years; mean T2D duration was 7.8 months; 89.4% had a family history of diabetes; 72.6% were black or Hispanic and 41.5% had a household annual income of <US$25 000.

5 Blood pressure was in the 90th percentile or greater for 26.3% of the cohort; 13.6% had a blood pressure at the 95th percentile or greater; 13.0% had microalbuminuria; 79.8% had a low HDL-cholesterol level; and 10.2% had high triglycerides.

6 The authors concluded that the TODAY cohort is predominantly made up of ethnic minority groups with low socioeconomic status, in whom clinical and biochemical abnormalities and comorbidities are prevalent within 2 years of T2D diagnosis.

Copeland KC, Zeitler P, Geffner M et al (2011) Characteristics of adolescents and youth with recent-onset type 2 diabetes: the TODAY cohort at baseline. *J Clin Endocrinol Metab* **96**: 159–67

PUBLIC HEALTH AND NUTRITION

Obesity duration is a risk factor for T2D, independent of degree of BMI

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

1 The role of the duration of obesity as an independent risk for T2D has not been fully explored and the authors sought to investigate this association in a prospective cohort study as part of the Framingham Heart Study (follow-up 1948–1998).

2 A total of 1256 participants, free from T2D at baseline but obese on at least two of the study's consecutive twenty-four biennial examinations, were included.

3 T2D status was collected throughout the 48 years of follow-up and the relationship between duration of obesity and T2D was analysed using time-dependent Cox models, adjusting for a number of covariates.

4 Unadjusted hazard ratio (HR) for the risk of T2D was 1.13 (95% confidence interval [CI], 1.09–1.17) for men and 1.12 (95% CI, 1.08–1.16) for women per additional 2-year increase in the duration of obesity.

5 The dose–response relationship was less clear for female participants than male; compared with men who were obese for ≤5 years, men who were obese for 15–24 years had a 3-times higher risk of T2D, which rose to approximately 6-times higher in those who were obese for ≥25 years. However, there were no clear dose–response relationships for women.

6 It was concluded that duration of obesity is a relevant risk factor for T2D, independent of the degree of BMI.

Abdullah A, Stoelwinder J, Shortreed S et al (2011) The duration of obesity and the risk of type 2 diabetes. *Public Health Nutr* **14**: 119–26

DIABETOLOGIA

Regional variations in adipocyte size associated with metabolic complications

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

1 The authors aimed to determine whether the mean size of fat cells (in visceral or subcutaneous adipose tissue) in morbidly obese women (n=80) has an impact on metabolic and inflammatory profiles.

2 Visceral, but not subcutaneous, adipocyte size was significantly associated with plasma apolipoprotein B, total cholesterol, LDL-cholesterol and triglycerides (P=0.002–0.015).

3 Subcutaneous adipocyte size was significantly associated with plasma insulin and glucose, insulin-induced glucose disposal and insulin sensitivity (P=0.002–0.005); visceral adipocyte size was not.

4 The authors concluded that region-specific variations in mean adipocyte size was associated with metabolic complications, but not systemic or adipose inflammation, in morbidly obese women.

Hoffstedt J, Arner E, Wahrenberg H et al (2010) Regional impact of adipose tissue morphology on the metabolic profile in morbid obesity. *Diabetologia* **53**: 2496–503

DIABETOLOGIA

Leisure-time physical activity protects from T2D

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

1 The authors aimed to determine whether physical activity levels at baseline influence later T2D.

2 At baseline in 1975, same-sex Finnish twin pairs (born before 1958) were sent a questionnaire including questions on physical activity.

3 The participants (20 487 individuals, 8182 complete twin pairs) were divided into quintiles by leisure-time physical activity metabolic equivalent (MET). T2D during the 29-year follow-up period was monitored by national register.

4 After controlling for childhood environment and genetic predisposition, participants in MET quintiles III–V were at significantly decreased risk of T2D when compared with sedentary individuals (quintile I). Similar results were obtained for both dizygotic and monozygotic pairs.

5 The authors concluded that leisure-time physical activity protects from T2D after taking familial and genetic effects into account.

Waller K, Kaprio J, Lehtovirta M et al (2010) Leisure-time physical activity and type 2 diabetes during a 28 year follow-up in twins. *Diabetologia* **53**: 2531–7

DIABETOLOGIA

Low level of education linked to T2D, mediated by health behaviours

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

1 The authors aimed to identify the impact of socioeconomic status on incident impaired glucose metabolism and T2D.

2 A total of 4405 participants completed baseline (1999–2000) and 5-year follow-up data relevant for these analyses.

3 Highest level of education was a stronger predictor of incident impaired glucose tolerance and T2D (P=0.002). However, smoking and physical activity partly mediated the relationship between low education and T2D.

Williams ED, Tapp RJ, Magliano DJ et al (2010) Health behaviours, socioeconomic status and diabetes incidence: the Australian Diabetes Obesity and Lifestyle Study (AusDiab). *Diabetologia* **53**: 2538–45

"... duration of obesity is a relevant risk factor for T2D, independent of the degree of BMI."