Management & prevention of type 2 diabetes

Family history of T2D matters, but in what way?

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I know that by being a Pakistani, male individual with both parents having type 2 diabetes (T2D), my risk for T2D is much higher than average (Hippisley-Cox et al, 2009); but to what extent does family history matter, and can its association with diabetes be explained largely by greater adiposity and known diabetes genes?

This topic is carefully examined in an impressive InterAct paper (summarised alongside), which gathered relevant information on many thousands of individuals over eight countries in Europe. Some of the findings broadly confirm what we know; if one parent has diabetes, risk increases around 2.5-fold, but if both parents have diabetes then risk increases around 5-fold. The results also add further to the concept that if mum (perhaps more so than dad) developed T2D at a younger age, then risks appear even higher (6-fold if mum had diabetes <50 years of age). This of course fits with what one might expect, as the younger one develops diabetes the higher the likely "genetic" loading. Yet the extent to which genetics, programming effects (which continue to be debated), shared environment and adverse lifestyle factors contribute to familial risk remains unclear.

The real novelty of the present paper, however, was to examine to what degree simple adiposity measures or identified genes help to explain family history of T2D; and this is where some surprises come. The researchers determined that adiposity and genes accounted for less than 13% of the family history association with diabetes, with a higher waist circumference being the dominant contributor. As the authors correctly stated, future studies could usefully determine the mechanism by which familial history of diabetes is transmitted, and such work would include both better body compositional studies (e.g. to determine muscle mass and ectopic fat depots) as well as molecular (insulin resistance pathways) and epigenetic work.

Of course, whatever the mechanisms, the clinical relevance of the findings remain strong. Family history of diabetes can be easily ascertained by questioning, and as such will always contribute to any diabetes risk score. Indeed, as diabetes becomes more prevalent, more and more individuals will have a family history of diabetes, making this information potentially even more valuable; and if age of diabetes onset can also be gathered for parents and siblings, more precision in risk scoring may be possible – a testable hypothesis.

Finally, in their supplementary data the authors were able to show that high levels of activity and (perhaps in particular) low BMI lessened diabetes risk regardless of family history. This led the authors to correctly state that "individuals with a family history of diabetes have much to gain from such lifestyle interventions," a message all of us can reiterate to our relevant patients, or indeed try to follow ourselves.

Hippisley-Cox J, Coupland C, Robson J et al (2009) Predicting risk of type 2 diabetes in England and Wales. *BMJ* **338**: b880. Available at: http://dx.doi.org/10.1136/bmj.b880 (accessed 08.03.13)

DIABETES CARE

Bariatric surgery may improve microvascular complications of T2D

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

1 The authors examined whether bariatric surgery is safe for the retinal and renal complications of T2D.

2 In this study, retinal photographs and urine albumin:creatinine ratios (ACRs) were analysed retrospectively in 84 individuals with T2D before and 12–18 months after bariatric surgery.

3 Of the 67 individuals with complete retinal data, five (7.5%) had an improvement in retinal disease, one (1.5%) had deterioration and 61 (91.0%) had no change; in those with preoperative disease, mean retinopathy scores decreased significantly from 4.7±0.6 to 3.3±0.5 (P=0.004).

4 Thirty-two individuals (42.7%) had preoperative albuminuria, and their ACRs improved from 7.6 (4.7–24.5) to 2.2 (1.0–17.3) mg/mmol (P<0.001) 12–18 months after bariatric surgery.

5 Although diabetes-related microvascular complications progressively deteriorate over time, bariatric surgery halted this process and in some cases reversed retinopathy.

Miras AD, Chuah LL, Lascaratos G et al (2012) Bariatric surgery does not exacerbate and may be beneficial for the microvascular complications of type 2 diabetes. *Diabetes Care* **35**: e81

DIABETOLOGIA

Family history is a strong risk factor for T2D

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

1 The InterAct Consortium sought to determine the extent to which genetic, anthropometric and lifestyle risk factors mediated the association between family history and risk of T2D.

2 In this study, 13 869 individuals had family history data available (6168 incident cases of T2D) and 6887 had complete data on all mediators.

3 A family history of diabetes was ascertained by questionnaire at follow-up, lifestyle and anthropometric measurements were performed at baseline and a genetic risk score was constructed by the genotyping of 35 single nucleotide polymorphisms associated with T2D.

4 Individuals with a family history of diabetes in a first-degree family member were at higher risk of T2D (hazard ratio [HR], 2.72; 95% confidence interval [CI], 2.48–2.99); higher risks were seen in those with a biparental history of T2D (HR, 5.14; 95% CI, 3.74–7.07) and those whose parents had been diagnosed with diabetes at a younger age (<50 years; HR, 4.69; 95% CI, 3.35–6.58).

5 Adjustments for established risk factors such as BMI and waist circumference only modestly attenuated this increased risk (HR, 2.44; 95%, CI 2.03–2.95); the genetic score explained only 2% of the family-history-associated risk of T2D.

6 Lifestyle, anthropometric and genetic risk factors explained only a proportion of the excess risk of T2D associated with family history.

7 Family history remains a strong, independent and easily assessed risk factor for T2D.

The InterAct Consortium (2012) The link between family history and risk of type 2 diabetes is not explained by anthropometric, lifestyle or genetic risk factors: the EPIC-InterAct study. *Diabetologia* 28 Sep [Epub ahead of print]

"Younger adults with T2D have impaired emotional well-being and physical health."

DIABETIC MEDICINE

Young adults with T2D have impaired emotional well-being

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

1 A survey was performed to ascertain the needs and concerns of young Australian adults with T2D; 1417 were invited to complete the online survey, and 149 responses were eligible for inclusion in the study.

2 It was found that 63% of respondents had diabetes-related stress, 27% had impaired emotional well-being, 82% were overweight or obese and 77% had at least one other comorbidity.

3 Many respondents perceived their health needs as different to older people with T2D (68%), and that most information or services were aimed at older adults (62%).

4 Younger adults with T2D have impaired emotional well-being and physical health.

Browne JL, Scibilia R, Speight J (2012) The needs, concerns and characteristics of younger Australian adults with type 2 diabetes. *Diabet Med* 26 Nov [Epub ahead of print]

DIABETES CARE

Insulin resistance and obesity explain T2D risk in ethnic minority women but not men

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

1 Previously the authors reported a three-fold prevalence of diabetes in Indian Asian and African Caribbean people compared with Europeans.

2 In this study the authors examined potential explanations for ethnic differences in diabetes incidence in a cohort with a 20-year follow-up to ages 60–89 years; incident diabetes was identified in 14% of Europeans (196/1356), 33% of Indian Asians (282/842) and 30% of African Caribbeans (100/335).

3 Compared with Europeans, age-adjusted subhazard ratios (95% confidence interval) for men and women, respectively, were 2.88 (2.36–3.53; $P<0.001$) and 1.91 (1.18–3.10; $P=0.008$) in Indian Asians, and 2.23 (1.64–3.03; $P<0.001$) and 2.51 (1.63–3.87; $P<0.001$) in African Caribbeans.

4 Insulin resistance and truncal obesity account for the two-fold excess diabetes incidence in Indian Asian and African Caribbean women, but not for the excess diabetes risk in ethnic minority men.

Tillin T, Hughes AD, Godsland IF et al (2012) Insulin resistance and truncal obesity as important determinants of the greater incidence of diabetes in Indian Asians and African Caribbeans. *Diabetes Care* 27 Nov [Epub ahead of print]

ENDOCRINE PRACTICE

Bromocriptine-QR can improve glycaemia

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

1 The authors examined the effect of timed bromocriptine-QR therapy on glycaemic control in individuals with T2D poorly controlled by one or two oral antidiabetes (OAD) agents.

2 In total, 515 individuals with an HbA_{1c} ≥58 mmol/mol (7.5%) on one or two OADs at baseline were randomised 2:1 to bromocriptine-QR (1.6–4.8 mg/day) or placebo for 24 weeks.

3 Significantly more individuals (approximately 1.5- to 2-fold more; $P<0.05$) intensified concomitant antidiabetes medication during the study in the placebo versus the bromocriptine-QR arm; bromocriptine-QR treatment significantly improved glycaemic control across all analyses (reductions ranged from 7.5 to 9.1 mmol/mol [0.69% to 0.83%], depending on baseline therapy). There were no serious adverse events.

4 Bromocriptine-QR therapy for 24 weeks can improve glycaemia in those with poorly controlled T2D.

Vinik AI, Cincotta AH, Scranton RE et al (2012) Effect of bromocriptine-QR on glycaemic control in subjects with uncontrolled hyperglycaemia on one or two oral anti-diabetes agents. *Endocr Pract* **18**: 931–43

DIABETOLOGIA

Low BW does not affect adult glucose metabolism in BW-discordant MZ twins

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

1 Although studies in twins has shown that T2D can be inherited, factors in early life, such as low birth weight (BW) may also predispose to the development of diabetes; the authors investigated the association between BW and indices of glucose metabolism in adult, extremely BW-discordant monozygotic (MZ) twins.

2 The hypothesis was that if BW is associated with health in adulthood independent of genes and rearing environment, significant differences in markers of glucose metabolism would be expected in this study group.

3 The study comprised 155 of the most BW-discordant MZ twin pairs identified from the 77 885 twins in the Danish Twin Registry; individuals were assessed using a 2-hour oral glucose tolerance test (OGTT) with sampling of plasma glucose, insulin, C-peptide, glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1.

4 HOMAs of beta-cell function and insulin resistance (HOMA-beta and HOMA-IR, respectively), the OGTT-derived insulin sensitivity index (BIGTT-SI) and OGTT-derived index of acute insulin response (BIGTT-AIR) were calculated.

5 There were no between-twin differences in plasma glucose, insulin, C-peptide, incretin hormones, HOMA-beta, HOMA-IR or BIGTT-SI identified.

6 BW-discordant MZ twins provide no evidence for a detrimental effect of low BW on glucose metabolism in adulthood once genetic factors and rearing environment are controlled for.

Frost M, Petersen I, Brixen K et al (2012) Adult glucose metabolism in extremely birthweight-discordant monozygotic twins. *Diabetologia* **55**: 3204–12