Management & prevention of type 2 diabetes

Smoking: A confirmed new risk factor for type 2 diabetes

Naveed Sattar
Professor of Metabolic Medicine, University of Glasgow, Glasgow

Smoking is one of the major risk factors for chronic diseases, particularly cardiovascular disease (CVD) and cancers. In terms of CVD, it is well established that smoking accelerates risk and increases mortality and fatal events (JBS3 Board, 2014). Smoking affects multiple risk pathways inclusive of, but not limited to, altering blood lipids levels (e.g. lowering HDL-cholesterol concentrations; altering LDL particle adherence or toxicity), increasing thrombotic potential, and promoting oxidative stress and endothelial dysfunction. Smoking, therefore, features as a strong independent risk factor for CVD, and a smoking ban in public places in many countries has helped accelerate a decline in smoking prevalence, leading in turn to a reduction in CVD events. Yet despite considerable efforts, many individuals in the UK continue to smoke, and elsewhere (especially in developing countries) smoking prevalence continues to rise. This is clearly a concern for CVD and cancer rates in such countries, but smoking may now also be a concern for diabetes risk, as very nicely reported by the EPIC-InterAct Study (paper being commented upon alongside).

In this prospective study, former or current smoking as compared to never smoking was associated with an approximate 40% higher risk of type 2 diabetes in men and just less than half this risk (13–18%) in women. The large number of incident diabetes cases led to moderate confidence intervals to lend support to such observations. However, a few questions now emerge including the paradoxical association of smoking with adiposity and explanatory mechanisms. Smoking is normally associated with lower BMI, which one would normally associate with lower diabetes risk, but paradoxically, associations with diabetes risk tended to be stronger in normal weight versus heavier smokers in the EPIC-InterAct study.

One reason for this may be caused by an effect that smoking severity has on adiposity: individuals who smoke more aggressively tend to be lighter than those who smoke more lightly and, speculatively, this observation may also in part account for diabetes risk being greater in men than women. A causal effect of smoking on adiposity has been confirmed by genes that dictate the aggressiveness of smoking in smokers; we recently showed that smokers who carry this "smoking" gene were lighter than smokers without this gene whereas this pattern was not seen in non-smokers (Freathy et al, 2011).

It appears, therefore, that smoking must alter diabetes risk by mechanisms, which are currently not well understood, beyond total adiposity. Several ongoing studies are trying to determine these mechanisms. Smoking may enhance diabetes risk through an effect on beta cells or via altering adiposity location or through insulin resistance, or perhaps by lessening blood flow to muscle beds. All of these suggestions remain speculative and more studies are needed. Nevertheless, in terms of public health messages, it is clear that type 2 diabetes risk should be added to the list of conditions that smoking accelerates, albeit to a lesser extent than its acceleration of CVD and specific cancers.

Furthermore, physicians in the clinics can now also discuss smoking cessation with relevant patients in terms of lowering long-term type 2 diabetes risk. As ever, we must give our patients the facts and hope that these provide the motivation they need to contemplate smoking cessation. We must also encourage and help them, when they are ready, to have repeated attempts since the more they try, the more likely they will eventually succeed. ■

Freathy RM, Kazeem GR, Morris RW et al (2011) Genetic variation at CHRNA5-CHRNA3-CHRNB4 interacts with smoking status to influence body mass index. *Int J Epidemiol* **40**: 1617–28

JBS3 Board (2014) Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3). *Heart* **100** Suppl 2 (ii1–ii67)

Diabetes Care

Association between smoking and long-term T2D risk

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

1 The aim of this analysis was to investigate the association between smoking and incident T2D.

2 Participant data from the European Prospective Investigation into Cancer and Nutrition (EPIC)-InterAct study were used. The study is a prospective case-cohort study which took place in eight countries.

3 After exclusion of missing data, there were 10 327 cases of T2D and 13 863 individuals in the control sub-cohort group.

4 Smoking status was split into three categories: never, former and current, and hazard ratios (HRs) for T2D were calculated.

5 In men, the HRs (95% confidence interval) for T2D were 1.40 (1.26–1.55) and 1.43 (1.27–1.61) for former and current smokers, respectively.

6 Smoking and incident T2D had a weaker association among women than men for former and current female smokers: HR 1.18 (1.07–1.30) and 1.13 (1.03–1.25), respectively.

7 Former and current smoking is associated with a higher risk of incident T2D than never smoking in men and women. This was consistently independent of educational level and lifestyle influences such as physical activity, alcohol consumption and diet.

8 Those who were former smokers from a long time prior to the study start had a slightly elevated risk of T2D compared to those who had never smoked, including after adjustment for BMI and waist circumference. This suggests that the effect of smoking on diabetes is reversible.

InterAct Consortium, Spijkerman AM, van der A DL et al (2014) Smoking and long-term risk of type 2 diabetes: the EPIC-InterAct study in European populations. *Diabetes Care* **37**: 3164–71

Diabetes Care

Lifestyle intervention reduces use and cost of medical services

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

1 The Look AHEAD (Action for Health in Diabetes) study compared the impact of intensive lifestyle intervention (ILI) with diabetes support and education (DSE) among overweight and obese individuals with T2D in the US. Although the trial was terminated early due to "statistical futility", collected data are still being analysed.

2 The use and costs of health services for both participant cohorts were compared over an average of 10 years.

3 Follow-up data were available for 99.5% of the original 5121 Look AHEAD participants.

4 The ILI resulted in an 11% reduction in hospitalisations per year compared to the DSE intervention (P=0.004), and there was also a 15% reduction in average annual days in hospital among ILI compared to DSE participants (P=0.01).

5 Average annual prescriptions were also significantly lower in the ILI group compared to the DSE group (4.65 vs 4.96 prescription medications respectively; P<0.0001).

6 The per-participant average annual cost of health services and medications were also lower among ILI participants: the annual cost was 7% lower ($8321 for ILI and $8926 for DSE; P=0.002).

7 Cumulatively, these effects resulted in an annual saving of almost $600 per participant relative to DSE.

8 The authors note the intervention costs were not taken into account in this analysis; a cost-benefit analysis is reserved for future studies.

Espeland MA, Glick HA, Bertoni A et al (2014) Impact of an intensive lifestyle intervention on use and cost of medical services among overweight and obese adults with type 2 diabetes: the action for health in diabetes. *Diabetes Care* **37**: 2548–56

Diabetic Medicine

Adolescents with T2D: Their views and experiences

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

1 In-depth interviews were conducted with adolescents with T2D to gain an understanding of their views and experiences of different treatments for T2D, in order to improve current treatment pathways.

2 A sample of 100 adolescents from a UK cohort study varying in age, gender, ethnicity and geographical location were specifically invited to achieve a broad demographic. In total, 12 adolescents responded and were interviewed on the telephone. Interviews typically lasted 30 minutes.

3 Interviews were audio recorded, fully transcribed and data were analysed thematically.

4 All adolescents were aged between 14 and 19 years and had been diagnosed with T2D for at least 2 years. Based on self-reports, 11 had received metformin at one stage, four had received insulin, four had received liraglutide and two had undergone weight loss surgery.

5 It was apparent from the interviews that very few adolescents had made sufficient lifestyle changes to result in weight loss, and there was evidence that some adolescents were not concerned about having T2D, especially if other members of family also had the condition.

6 The results from the interviews highlighted a level of stigma associated with having T2D, as interviewees feared how others would react if they knew they had the condition. There was also a stigma surrounding weight loss surgery (interviewees regarding it as a last resort or for "lazy people") although there was a willingness to consider surgery in specific situations.

Turner KM, Percival J, Dunger DB et al (2015) Adolescents' views and experiences of treatments for type 2 diabetes: a qualitative study. *Diabet Med* **32**: 250–6

Diabetes Care

From the DPP study: Baseline HbA_{1c} as a predictor for diabetes incidence

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

1 The DPP (Diabetes Prevention Program) study was a 3.2-year randomised clinical trial investigating diabetes prevention in people at high risk of T2D by comparing diabetes treatments. The DPPOS (DPP Outcomes Study) then followed participants for another 10 years.

2 In the original study, 3234 people at high risk of T2D were randomised to placebo, metformin or intensive lifestyle intervention, and diabetes was diagnosed by fasting plasma glucose (FPG) and 2-hour postload glucose (2hPG) concentrations. HbA_{1c} was not used as a study measure.

3 In this article, the authors evaluated baseline HbA_{1c} as a predictor of diabetes incidence, and evaluated the effect of treatments on T2D, which was defined as an HbA_{1c} ≥48 mmol/mol (6.5%).

4 From 2765 people who had baseline recordings for FPG, 2hPG and HbA_{1c}, baseline HbA_{1c} predicted incident diabetes in all the treatment groups of the DPP study (defined as ≥48 mmol/mol [6.5%]).

5 HbA_{1c} at baseline was a strong predictor of incident T2D during the DPP study and total follow-up period.

6 Diabetes incidence was reduced by metformin versus placebo (P<0.001) and by lifestyle versus placebo (P<0.001), and the reduction by lifestyle was greater than that of metformin (P<0.001).

Diabetes Prevention Program Research Group (2015) HbA_{1c} as a predictor of diabetes and as an outcome in the diabetes prevention program: a randomized clinical trial. *Diabetes Care* **38**: 51–8

> *"The results from the interviews highlighted a level of stigma associated with having T2D, as young interviewees feared how others would react if they knew they had the condition."*