Management & prevention of type 2 diabetes

Understanding statin use in diabetes: Who, why and where are we going?

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Around 15 years ago, a landmark study was used to support type 2 diabetes as a potential cardiovascular disease (CVD) risk equivalent (Haffner et al, 1998). Subsequently, guideline committees recommended that all patients with type 2 diabetes above 40 years of age received statins, leading in turn to a substantial escalation of statin use. The consequence was that average cholesterol levels in people with diabetes declined from around 5.8 mmol/L in the 1990s to around 4.2 mmol/L by 2008 (Oluwatowoju et al, 2010), changes that have contributed to a remarkable improvement in CVD risk levels in our diabetes population. Despite these impressive statistics, the question remains whether we can, or should, aim to do better, and whether the case is the same for people with type 1 diabetes. Such questions were partially addressed by Jones et al in their study of primary prevention in patients over 40 with a recent diabetes diagnosis (summarised alongside).

In this population, 68% had been prescribed a statin, leaving 32% without. At first glance this looks like a glaring missed opportunity, but closer inspection reveals a mixed picture. First, it appears that confusion reigns over statin recommendations in people with type 1 diabetes, since these patients were 58% less likely to receive statins compared to those with type 2 diabetes. Secondly, higher total cholesterol, higher BMI and being a current smoker were associated with greater odds of statin prescription, as would be expected. Finally, much older patients (>85 years of age) had very low statin prescription rates (odds ratio, 0.25 compared with the 40–54-year-old age bracket). This finding is perhaps not surprising given that at this age statins may have limited time to yield any discernible benefit. Statin usage was also lower in people aged 75–84 years, and this may also be unsurprising as the current evidence base of the benefits of commencing statins in this group is limited. Such findings suggest that doctors are exercising their judgement in ways that reflect the lack of robust evidence in some areas (e.g. statin use in elderly people newly diagnosed with diabetes) and the uncertainty in others (e.g. people with type 1 diabetes with short disease duration). Of course, guidelines should never be indisputable, and clinical judgement applied on a patient-by-patient basis remains valuable.

There are, however, new challenges ahead. NICE have recently recommended that, rather than prescribing statins for all people with type 2 diabetes above 40 years of age, a risk score, based on 10-year risk thresholds on the QRISK2 model, should first be conducted (NICE, 2014). Whilst this change is consistent with recent evidence that diabetes is not a CVD risk equivalent, the downside is that many younger people (i.e. those aged 40–55 years) with type 2 diabetes may not receive statins straight away, despite recent data suggesting that these people are the heaviest and have the highest relative risk for diabetes complications (Constantino et al, 2013). This is also the group with a considerable lifetime risk given their future exposure to decades of hyperglycaemia. For these reasons, it may have been better to maintain the 40-year age threshold, as the US guidelines have recently done (Goff et al, 2014). Such a move would have simplified matters and helped maintain the excellent average cholesterol levels currently achieved in diabetes. It would also have led to a consistent recommendation for people with type 1 or type 2 diabetes, thus making the educational message simpler.

With recent evidence from NICE that LDL-cholesterol reduction is cost-effective at much lower thresholds than previously thought (NICE, 2014), and that cholesterol reduction adds more disease-free years if it is applied earlier in life (JBS3 Board, 2014), there is genuine cause for debate. With emergence of big data sets, more rigorous risk scores in type 1 and type 2 diabetes may emerge that could theoretically help in deciding which younger patients should receive statins and who should receive them at higher doses. In the meantime, we should remember that cholesterol reduction remains an important cornerstone of cardiovascular risk reduction in diabetes, and that relevant guidance, if pragmatic, can have merits. ■

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Diabet Med

Statin prescribing rates in people with diabetes in Scotland

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

1 In this study, statin prescribing patterns in Scotland were investigated to determine the proportion of people with diabetes who receive these agents.

2 A total of 7157 men and 5601 women aged ≥40 years with incident T1D or T2D and no history of cardiovascular disease or statin treatment were evaluated.

3 Although all of these people were recommended to receive statins according to national guidelines, only 68% of men and 69% of women received these agents in the 2 years following diabetes diagnosis.

4 People aged 55–64 years were more likely to receive statins compared with other age groups, and those aged ≥75 years were less likely to receive them.

5 Current and former smokers, people with cholesterol levels ≥5 mmol/L, those who were overweight or obese, those with T2D rather than T1D and those with lower socioeconomic status were more likely to receive statins.

6 These findings indicate that doctors were more likely to offer statins to people with increased cardiovascular risk rather than diabetes *per se*. The fact that prescription rates were lower in people with T1D may reflect uncertainty about the effectiveness of statins in this patient group.

7 The authors conclude that, while it appears that clinical judgement is being used, there could be a missed opportunity to reduce cardiovascular risk in people with diabetes in Scotland.

Jones NR, Fischbacher CM, Guthrie B et al (2014) Factors associated with statin treatment for the primary prevention of cardiovascular disease in people within 2 years following diagnosis of diabetes in Scotland, 2006–2008. *Diabet Med* **31**: 640–6

Diabetes Care

Effects of intensive lifestyle modification on depression and QoL in T2D

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

1 In this analysis of the Look AHEAD (Action for Health in Diabetes) study, the effects of intensive lifestyle modification on depression and health-related quality of life (QoL) were evaluated over 8 years of follow-up.

2 A total of 5145 people with T2D who were overweight or obese were randomised to an intensive lifestyle regimen designed to reduce weight or to basic diabetes support and education. They were assessed with QoL questionnaires and the Beck Depression Inventory (BDI) at baseline, after 1–4 years and after 8 years.

3 At the 8-year follow-up, in addition to superior weight loss, the lifestyle group had a significantly reduced incidence of mild or greater depression (BDI score, ≥10 points) than the control group (hazard ratio, 0.85; $P=0.015$).

4 Among the 82% of participants who were not depressed at baseline, the lifestyle group were 15% less likely to develop depression. Among those with depression at baseline, neither remission nor progression rates were different between the groups.

5 Physical QoL scores decreased in both groups over time, consistent with the previously observed effects of ageing; however, the scores remained significantly higher in the lifestyle group over the follow-up.

6 The authors conclude that this intensive lifestyle intervention to reduce weight lowered the risk of depression as well as age-related deterioration of physical QoL in these overweight people with T2D.

Rubin RR, Wadden TA, Bahnson JL et al (2014) Impact of intensive lifestyle intervention on depression and health-related quality of life in type 2 diabetes: the Look AHEAD Trial. *Diabetes Care* **37**: 1544–53

Diabetes Care

Need for antidiabetes medications delayed by a low-carbohydrate Mediterranean diet

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

1 This was the 8-year follow-up of a study comparing a low-carbohydrate Mediterranean diet (LCMD) with a low-fat diet in terms of their effect on T2D progression.

2 In total, 215 overweight, middle-aged people with T2D who had never been treated with antihypoglycaemics were randomised to one of the two diets and evaluated at baseline, 4 years and 8 years.

3 The LCMD had a target of ≤50% of calorie intake from carbohydrates and ≥30% from fat, replacing red meat with poultry and fish. The low-fat diet restricted fat intake to ≤30% of calories, no more than 10% coming from saturated fat. Both restricted caloric intake to 1500 kcal/day in women and 1800 kcal/day in men.

4 Baseline demographics, clinical characteristics and study withdrawal rates were similar in the two groups. After 4 years, the proportion of people requiring antidiabetes drugs (the primary endpoint) was lower in the LCMD group than the low-fat group (44% vs 70%; hazard ratio, 0.63).

5 At final follow-up, all participants required medication; however, the LCMD delayed this by 2 years compared with the low-fat diet.

6 Weight loss was significantly greater (mean difference, 2 kg) in the LCMD group at 4 years; however, at 8 years the mean difference was a non-significant 0.4 kg.

7 The LCMD also resulted in a greater reduction in HbA_{1c}.

Esposito K, Maiorino MI, Petrizzo M et al (2014) The effects of a Mediterranean diet on the need for diabetes drugs and remission of newly diagnosed type 2 diabetes: follow-up of a randomized trial. *Diabetes Care* **37**: 1824–30

Diabet Med

Effect of diabetes duration and weight loss on remission of T2D following bariatric surgery

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

1 The authors examined the effects of diabetes duration and the amount of weight loss achieved after surgery on diabetes remission in 89 people with T2D who underwent bariatric surgery.

2 Diabetes duration was <4 years in 26 participants, 4–8 years in 36 and >8 years in 27.

3 Overall, 48% of the total cohort achieved diabetes remission (HbA_{1c}, <43 mmol/mol [6.1%]) within 2.5 years of surgery. Percentage weight loss was significantly correlated with diabetes remission (Spearman $r_s=0.53$; $P<0.0001$).

4 Diabetes remission was achieved in 62%, 56% and 26% of people with short, medium and long diabetes duration, respectively.

5 In regression analysis, the degree of weight loss, but not diabetes duration, was associated with remission. However, there was an interaction between weight loss and diabetes duration, such that people with long-lasting T2D who lost <25 kg of weight rarely achieved diabetes remission.

6 These results show that weight loss is the key predictor of diabetes remission following bariatric surgery. Normoglycaemia can be achieved in people with a long diabetes duration but requires more weight loss.

7 The authors suggest that remission may be a result of improved beta-cell function owing to lower levels of the toxic metabolites of fat following weight loss.

Steven S, Carey PE, Small PK, Taylor R (2014) Reversal of type 2 diabetes after bariatric surgery is determined by the degree of achieved weight loss in both short- and long-duration diabetes. *Diabet Med* 16 Aug [Epub ahead of print]

> *"The authors conclude that this intensive lifestyle intervention to reduce weight lowered the risk of depression as well as age-related deterioration of physical quality of life in these overweight people with T2D."*

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Haffner SM, Lehto S, Rönnemaa T et al (1998) Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* **339**: 229–34

JBS3 Board (2014) Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3). *Heart* **100**(Suppl 2): ii1–67

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Oluwatowoju I, Abu E, Wild SH, Byrne CD (2010) Improvements in glycaemic control and cholesterol concentrations associated with the Quality and Outcomes Framework: a regional 2-year audit of diabetes care in the UK. *Diabet Med* **27**: 354–9