

## Management & prevention of type 2 diabetes

### **Intensive multifactorial intervention lowers mortality risk from cardiovascular disease**



Roger Gadsby, GP and Senior Lecturer, Centre for Primary Healthcare Studies, University of Warwick

The paper from Gaede et al (abstracted alongside) is a follow up of the original Steno-2 Study population (Gaede et al, 2003), in which 160 people with type 2 diabetes and microalbuminuria were randomised to intensive multifactorial or conventional therapy. The mean follow up was 7.8 years. Intensive therapy resulted in a reduction of around 50% in vascular complications. Participants were subsequently observed for a further average of 5.5 years, and this paper reports the findings of this follow up.

The primary end point at 13.3 years of follow up was death from any cause. Twenty-four individuals in the intensive treatment group died, compared with 40 in the conventional therapy group. Intensive therapy was associated with a lower risk of death from cardiovascular disease and cardiovascular-related events. One person in the intensive group progressed to end-stage renal disease, compared with six in the conventional group; there was a reduction in the number of individuals requiring retinal photocoagulation.

The mean HbA<sub>1c</sub> in the intensive treatment group after 7.8 years was 7.9% and 7.7% after 13.3 years. The mean HbA<sub>1c</sub> in the conventional therapy group was 9% and 8%, respectively: the target HbA<sub>1c</sub> for both groups was 6.5%.

Blood pressure values were 131/73mmHg after 7.8 years and 140/74mmHg after 13.3 years in the intensive treatment arm. Blood pressure values in the conventional therapy group were 146/78mmHg and 146/73mmHg, respectively: the target blood pressure was 130/80mmHg for both groups.

The percentage of people on statin therapy was 85% after 7.8 years and 84% after 13.3 years in the intensive treatment group. In the conventional therapy arm, it was 22% and 85%, respectively.

The percentage of individuals on insulin was 57% after 7.8 years and 73% after 13.3 years in the intensive treatment group. In the conventional therapy arm, it was 54% and 92%, respectively.

In terms of control parameters, the conventional group have approached the intensive group in parameters of control during the follow up – as the lessons learned from the initial study were, presumably, applied to the conventional group. Blood pressure appears to be the easiest risk factor to control to target. Most participants were on statin therapy, and few – even in the intensive treatment group – achieved near-target HbA<sub>1c</sub> figures, in spite of widespread use of insulin.

The Steno-2 study (Gaede et al, 2003) showed that interventions directed to give good blood pressure control, good glycaemic control and good control of cholesterol resulted in significant reductions in vascular complications. This follow-up study confirms this finding, even though the blood pressure, HbA<sub>1c</sub> and statin treatment in the two groups converged during the follow up period. It also showed that control of these risk factors reduces microvascular complications.

The ideals of most people on statin therapy, blood pressure at or below 130/80mmHg in people with microalbuminuria, and HbA<sub>1c</sub> <7.5% have been incorporated into the Quality and Outcomes Framework and NICE guidance: therefore, similar levels of mortality reduction from cardiovascular disease should be expected in the UK.

Gaede P, Vedel P, Larsen N, Jensen GVH, Parving H-H, Pedersen O (2003) Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *New England Journal of Medicine* **348**: 383–93

NEW ENGLAND  
JOURNAL OF MEDICINE

### **Multifactorial diabetes intervention reduces risk of CVD**

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

**1** Trials of interventions for single risk factors in people with type 2 diabetes have shown their efficacy in reducing complications related to cardiovascular disease (CVD) and diabetes.

**2** The Steno-2 Study showed that intensive, multifactorial intervention (using aspirin, antihypertensive treatments and lipid-lowering drugs, for example), reduced the risk of non-fatal CVD among patients with type 2 diabetes and microalbuminuria.

**3** In this follow up to the Steno-2 Study, the authors determined whether this multifactorial intervention affected mortality rates from any cause and from cardiovascular causes, as well as whether risk reductions already achieved were sustained during follow up.

**4** The Steno-2 Study comprised 160 people with type 2 diabetes and microalbuminuria who received either intensive diabetes therapy or conventional therapy for an average of 7.8 years; participants were then followed up for an average of 5.5 years.

**5** During the total follow up of 13.3 years, the mortality rate was 30% for the intensive-therapy group and 50% for the conventional-therapy group.

**6** People receiving intensive, multifactorial intervention had sustained benefits resulting in a lower risk of death from CV causes, and of CV events.

Gaede P, Lund-Andersen H, Parving H-H, Pedersen O (2008) Effect of a multifactorial intervention on mortality in type 2 diabetes. *New England Journal of Medicine* **358**: 580–91

# Type 2 diabetes

## DIABETES CARE

### Premixed analogue insulin regimen non-inferior to basal-bolus regimen

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

**1** The study compared an analogue, prandial premixed insulin (PPT) regimen with an analogue, basal-bolus insulin (BBT) regimen in people with type 2 diabetes who

had previously been taking insulin glargine ( $\geq 30$  units/day) plus oral agents.

**2** In total, 187 people with type 2 diabetes were assigned to the PPT regimen and 187 to the BBT regimen for this 24-week, comparative study.

**3** At 24 weeks, mean HbA<sub>1c</sub> was significantly reduced in both groups, but was lower in the BBT group.

**4** The difference in HbA<sub>1c</sub> change from baseline to end point (BBT minus PPT) was  $-0.22\%$ ; as the prespecified non-inferiority margin was  $0.3\%$ , non-inferiority of PPT to BBT was not shown.

Rosenstock J, Ahmann AJ, Colon G et al (2008) Advancing insulin therapy in type 2 diabetes previously treated with glargine plus oral agents. *Diabetes Care* **31**: 20–5

## DIABETES CARE

### Many adolescents with diabetes do not perceive obesity

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

**1** As more than 80% of children with type 2 diabetes are overweight, it is critical that children and their parents are aware of the negative health risk.

**2** In total, 104 adolescents with type 2 diabetes and one of their parents

were interviewed about their views on the adolescents' weight, diet and level of physical activity, as well as their perceived barriers to healthy behaviour.

**3** Typically, most adolescents and their parents underestimated the adolescents' weight, and were more likely to have a poorer diet and level of physical activity; they also had perceived barriers to healthy behaviour.

**4** Clinicians should be aware that overweight adolescents with type 2 diabetes and their parents may not always recognise the presence of a weight problem and may not understand the related adverse risk to the adolescents' health.

Skinner AC, Weinberger M, Mulvaney S, Schlundt D, Rothman RL (2008) Accuracy of perceptions of overweight and relation to self-care behaviours among adolescents with type 2 diabetes and their parents. *Diabetes Care* **31**: 227–9

## DIABETES CARE

### Vildagliptin effective for elderly people with type 2 diabetes

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

**1** The study aim was to determine the efficacy and tolerability of vildagliptin (a dipeptidyl peptidase IV inhibitor that improves glycaemic control with a low risk of hypoglycaemia) in elderly people with type 2 diabetes using pooled data from trials of vildagliptin monotherapy.

**2** The effects of vildagliptin monotherapy (100 mg/day) for 24 weeks were compared in 1231 people with type 2 diabetes less than 65 years-old and 238 people with type 2 diabetes and older than 65 years.

**3** Vildagliptin significantly decreased HbA<sub>1c</sub> in both groups; the older group showed a greater decrease in HbA<sub>1c</sub> with a significant decrease in weight and a low incidence of hypoglycaemia.

**4** Vildagliptin monotherapy was shown to be effective and well tolerated in people older than 65 years with type 2 diabetes.

Pratley RE, Rosenstock J, Pi-Sunyer FX et al (2007) Management of type 2 diabetes in treatment-naïve elderly patients. *Diabetes Care* **30**: 3017–22

# Type 2 diabetes

LANCET

## Statin therapy is effective in diabetes

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

- 1 A prospective meta-analysis was undertaken to resolve the uncertainties about the effects of statin therapy in people with diabetes.
- 2 Data from 1466 people with type 1 diabetes, 17 220 people with type 2 diabetes and

71 370 people without diabetes in trials of statin therapy were analysed.

3 Over a mean of 4.3 years, people with diabetes had a 9% reduction in all-cause mortality and a 21% reduction in the incidence of major vascular events per mmol/l reduction in low-density lipoprotein cholesterol (13% and 21%, respectively, in people without diabetes).

4 Results confirm that the benefits of statin therapy on major vascular events were similar in a wide range of people with and without diabetes.

Cholesterol Treatment Trialists' Collaborators (2008) Efficacy of cholesterol-lowering therapy in 18 686 people with diabetes in 14 randomised trials of statins. *Lancet* **371**: 117–25

FAMILY PRACTICE

## Population screening for diabetes was low

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

1 Because many cases of type 2 diabetes remain undiagnosed, this study from the Netherlands sought to determine whether screening the general population for diabetes would be effective.

2 In total, 56 978 people not known to have diabetes (aged 50–70 years) were screened for

diabetes.

3 The four-step procedure comprised a questionnaire, random glucose measurements, fasting glucose measurement and oral glucose tolerance test; the three-step procedure was without random glucose measurement.

4 Type 2 diabetes was diagnosed in 285 people using the four-step procedure and in 301 people using the three-step procedure; as the dropout rate was high, opportunistic screening may be more appropriate than population-based screening.

Janssen PGH, Gorter KJ, Stolk RP, Rutten GEHM (2007) Low-yield of population-based screening for type 2 diabetes in the Netherlands: the ADDITION Netherlands study. *Family Practice* **24**: 555–61

FAMILY PRACTICE

## Personalised goals improve BP control in type 2 diabetes

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

1 Studies have shown that the risk of diabetic complications is strongly linked with raised blood pressure (BP) in people with type 2 diabetes; however, little is known about practice and patient factors that are linked with good BP control in this population.

2 A cross-sectional study was undertaken to quantify the relationships between a range of patient and practice factors and BP control in people with type 2 diabetes.

3 In total, 1534 people with type 2 diabetes from 42 general practices in Nottingham

were assessed, and systolic and diastolic BPs measured.

4 Only 46% of people had well-controlled BP ( $\leq 145/85$  mmHg).

5 Systolic and diastolic BP were higher in men overall, in people with a body mass index  $\geq 25$  kg/m<sup>2</sup> and in people with increased alcohol consumption.

6 Systolic BP increased with increasing duration of diabetes, whereas diastolic BP decreased.

7 Diastolic BP was lower in smokers and ex-smokers than in those who had never smoked.

8 People from practices where individual BP targets were negotiated had significantly lower systolic and diastolic BPs than those from practices that had not set personal goals.

9 Negotiating individually personalised goals for BP may be important to achieve good BP control for all patients with type 2 diabetes.

Bebb C, Coupland C, Stewart J et al (2007) Practice and patient characteristics related to blood pressure in patients with type 2 diabetes in primary care: a cross-sectional study. *Family Practice* **24**: 547–54

*'Bone fracture risk should, therefore, also be considered as a possible outcome when deciding upon antihyperglycaemic therapy, especially in older people with type 2 diabetes.'*

## DIABETES CARE

### Antihyperglycaemic agents can affect bone fracture risk

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

**1** Although people with diabetes have an increased risk for bone fractures, antihyperglycaemic agents could modulate this risk.

**2** This case-control study nested within a retrospective cohort assessed the risk for bone fractures associated with exposure to insulin or individual oral antihyperglycaemic treatments.

**3** In total, 1945 people with diabetes were followed for an average of 4.1 years; the 83 new cases of bone fractures were compared with a matched sample of 249 control people.

**4** Exposure to antihyperglycaemic treatment was determined for the 10-year period preceding the fracture in the case-control group and prior to matching index dates in the control group.

**5** As many people had used more than one antihyperglycaemic agent, a multivariate analysis was performed to assess the effect of each treatment on fracture risk.

**6** Treatment with insulin secretagogues, metformin and insulin for at least 3 years during the previous 10 years had no significant association between bone fracture risk and medication used.

**7** In an alternative analysis of treatments at the time of fracture or matched index date, insulin treatment was significantly associated with bone fractures in men but not in women, although long-term insulin use does not appear to affect bone frailty.

**8** Bone fracture risk should therefore also be considered as a possible outcome when deciding upon antihyperglycaemic therapy, especially in older people with type 2 diabetes.

Monami M, Cresci B, Colombini A et al (2008) Bone fractures and hypoglycaemic treatment in type 2 diabetic patients. *Diabetes Care* **31**: 199–203