Management of type 2 diabetes

NEJM

Intensive blood glucose control reduces vascular risk due to reduced nephropathy

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

1 This factorial randomised controlled trial was carried out across 20 countries, and the effects on vascular outcomes of lowering HbA_{1c} to a target of ≤6.5% were assessed.

2 Participants in the trial were aged 55 years or older at study entry, diagnosed with type 2 diabetes at 30 years of age or later; and had a history of micro- or macrovascular disease, or had at least one further risk factor for vascular disease.

3 Those who met the inclusion criteria (n=12 877) entered a 6-week run-in period with perindopril and indapamide. Individuals who completed the run-in period (n=11 140) were randomised to receive placebo or continue with the perindopril and indapamide.

4 Participants were also randomised to either intensive blood glucose control (target HbA_{1c}≥6.5%; n=5571) or standard blood glucose control, with HbA_{1c} targets based on local protocols (n=5569).

5 At the end of the follow-up period, the average HbA_{1c} in the intensive arm was 6.5%, and 7.3% in the standard arm. Incidence of combined major vascular events was significantly lower in the intensive arm than the standard arm (P<0.01).

6 The reduction in vascular events in the intensive arm was as a consequence of a significant reduction in incidence of nephropathy in this group (21%; P=0.006).

The ADVANCE Collaborative Group (2008) Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *New England Journal of Medicine* **358**: 2560–72

Setting HbA_{1c} targets: What do the results from the ACCORD and ADVANCE trials tell us?

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

Two new diabetes trials that look at the value of lowering HbA_{1c} to 6.5% or less have been recently published. What do they tell us about the HbA_{1c} targets that we need to agree with people who have type 2 diabetes? In the ADVANCE (Action in Diabetes and Vascular disease: Preterax and Diamicron Modified Release Controlled Evaluation) trial, summarised alongside, 11140 people with type 2 diabetes were randomised to undergo either standard glucose control or intensive glucose control – defined as the use of gliclazide plus other drugs to achieve an HbA_{1c} ≤6.5%.

After a median of 5 years' follow-up, the average HbA_{1c} in the group receiving intensive therapy was 6.5%, and was 7.3% in the group receiving standard therapy.

Intensive therapy reduced the incidence of the combined macrovascular and microvascular endpoint by 10%, primarily as a consequence of a 21% relative reduction in nephropathy. There was no effect on macrovascular events. Severe hypoglycaemia was uncommon overall, but more common in the intensive group.

In the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial, summarised overleaf, 10251 people with type 2 diabetes were randomised to an intensive group targeting an HbA_{1c} of <6%, or a standard group targeting an HbA_{1c} between 7.0 and 7.9%.

At 1 year, the average HbA_{1c} was stable in the intensive group at 6.4%, and in the standard group at 7.5%. During 3.5 years of follow-up, 257 people in the intensive group died, compared with 203 in the standard group, so this arm of the trial was stopped.

The main strength of these two trials is the large number of participants with typical baseline characteristics. About one-third in each trial had pre-existing macrovascular disease, so the trials assessed the benefit of glycaemic control in those with and without pre-existing cardiovascular disease (CVD).

The most compelling message from both studies is that near-normal glucose control (an HbA_{1c} level of between 6.4 and 6.5%) for 3.5 to 5 years does not reduce CVD events. However, the ADVANCE trial reconfirmed the predicted reductions in new-onset nephropathy.

The troubling finding is of an increased death rate in the ACCORD study in the intensive group. The reasons for this are not clear. Of the 41 excess deaths from CVD in the study, 19 were attributed to unexplained or presumed CVD, which could have been related to hypoglycaemia.

The mean weight gain of 3.5kg in the intensive arm of the ACCORD study may be related to use of insulin plus glitazone (28% gained more than 10kg). Weight gain in the ADVANCE trial was negligible.

Although in both trials the intensively treated groups achieved similar HbA_{1c} levels, the rate of reduction in HbA_{1c} was different. In the ACCORD study the intensive group had a very rapid reduction in HbA_{1c}, by 1.4 percentage points within 4 months; in the ADVANCE trial it was 0.6 percentage points at 12 months.

What conclusion can we draw from these two trials about safe HbA_{1c} target levels? These studies can be said to support the conclusion of the NICE guideline for type 2 diabetes (National Collaborating Centre for Chronic Conditions, 2008), which recommends an HbA_{1c} target of 6.5% where this is safely achievable using simple glucose-lowering regimens, such as lifestyle change with metformin and/or sulphonylurea. Where more complex glucose-lowering regimens are required, the threshold for additional treatment should be an HbA_{1c} of 7.5%.

National Collaborating Centre for Chronic Conditions (2008) *Type 2 diabetes: national clinical guideline for management in primary and secondary care (update)*. Royal College of Physicians, London

NEJM

Intensive glucose lowering therapy increases mortality in those at CV risk

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

1 This trial investigated whether intensive therapy (targeting an HbA_{1c} <6.0%) in people with type 2 diabetes who had either established cardiovascular disease or additional cardiovascular risk factors, would reduce cardiovascular events.

2 A total of 10 251 participants (mean age of 62.2 years) with a median HbA_{1c} of 8.1% were randomly assigned to receive intensive therapy (n=5128) or standard therapy (n=5123; targeting an HbA_{1c} between 7.0 and 7.9%).

3 The primary outcome was the occurrence of non-fatal myocardial infarction, non-fatal stroke or death from cardiovascular causes. There were several prespecified secondary outcomes, including death from any cause.

4 When higher mortality was found in the intensive-therapy group after a mean of 3.5 years follow-up, therapy was discontinued.

5 In the intensive therapy group, 257 participants died, compared with 203 participants in the standard therapy group (P=0.04).

6 The intensive therapy group achieved median HbA_{1c} levels of 6.4%, compared with 7.5% in the standard therapy group. The primary outcome occurred in 352 participants in the intensive therapy group compared with 371 in the standard therapy group (P=0.16).

7 After 3.5 years, the use of intensive therapy to target normal HbA_{1c} levels increased mortality and did not reduce major cardiovascular events.

The Action to Control Cardiovascular Risk in Diabetes Study Group (2008) Effects of intensive glucose lowering in type 2 diabetes. *New England Journal of Medicine* **358**: 2545–59

DIABETIC MEDICINE

Long-term adherence to statins in diabetes is poor

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

1 The authors of this retrospective longitudinal observational study aimed to determine the patterns and predictors of long-term adherence to statin therapy in people with diabetes.

2 A total of 6462 people with diabetes who had begun statin treatment during the period from 1 January 1989 to 31 May 2003 in Tayside, Scotland, were studied.

3 Predictors of suboptimal adherence (percentage of days covered by a statin [PDC] <80%) were identified using generalised linear models for repeated measures.

4 Mean PDC in the first year was 87% in the first quarter and 61% in the second quarter. It was 65% after 13 years.

5 These results suggest that long-term adherence is poor overall, and is affected early on in statin treatment.

Donnelly LA, Doney AS, Morris AD et al (2008) Long-term adherence to statin treatment in diabetes. *Diabetic Medicine* **25**: 850–5

DIABETES, OBESITY AND METABOLISM

Glycaemic control in people with type 2 diabetes across Europe

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

1 Glycaemic control in 2023 people with type 2 diabetes in seven European countries was assessed.

2 The main study outcome was the number of people with adequate glycaemic control (HbA_{1c} <6.5%). Goal attainment and treatment changes over time were also assessed.

3 All participants were treated with metformin and either a sulphonylurea or a thiazolinedione, and 25.5% had adequate glycaemic control after a mean of 2.6 years following initiation of these agents.

Álvarez Guisasola F, Mavros P, Nocea G (2008) Glycaemic control among patients with type 2 diabetes mellitus in seven European countries: findings from the Real-Life Effectiveness and Care Patterns of Diabetes Management (RECAP-DM) study. *Diabetes, Obesity and Metabolism* **10** (Suppl 1): 8–15

JOURNAL OF EVALUATION IN CLINICAL PRACTICE

Mobile phone technology improves self-care in people with type 2 diabetes

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

1 This US-based study was undertaken to ascertain whether the self-care of people with type 2 diabetes can be improved through the use of mobile phone technology, and to evaluate the impact of this technology on clinical outcomes.

2 The authors randomised 30 individuals with type 2 diabetes from two community health centres to an intervention group and a control group for 3 months.

3 The intervention group (n=15) attended a training workshop, at which they were educated in the use of Novel Interactive Cell-phone Technology for Health Enhancement (NICHE). They were then required to test their blood glucose levels on waking, and to wear a pedometer; data were uploaded to the NICHE server daily, and tailored text messages were sent based on the results.

4 Participants in the control group carried on with their usual self-care, but also wore a pedometer.

5 An improvement in mean HbA_{1c} levels was seen in the control group, although this was not statistically significant. Self-efficacy scores, assessed using the Diabetes Self-Efficacy Scale were significantly improved in the intervention group (P=0.008)

6 The authors conclude that NICHE has a positive impact on self-care in type 2 diabetes, but that the technology needs to be improved.

Faridi Z, Liberti L, Shuval K et al (2008) Evaluating the impact of mobile telephone technology on type 2 diabetic patients' self-management: the NICHE pilot study. *Journal of Evaluation in Clinical Practice* **14**: 465–9

CURRENT MEDICAL RESEARCH AND OPINION

Factors affecting the perceptions of physicians regarding the use of insulin pens in people with type 2 diabetes

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

1 Physicians' perceptions of insulin pens and factors that affect their recommendations and their patients' pen initiation or use were studied in the US.

2 An internet survey was carried out among primary care physicians and endocrinologists.

3 Five dependent variables were measured (for example, extent of their patients' pen initation and use) and several potential correlates (for example, practice characteristics, therapeutic philosophy or perceptions of insulin pens) investigated.

4 Physicians reported significantly more patient pen use or successful pen initiation (P<0.05 for both) if they were: a) more involved in clinical practice, adopted clinical innovations early, or educated their patients regarding insulin use; b) reported less insulin mixing or therapeutic inertia; c) perceived pens as efficacious and facilitating self-care; and d) presented and recommended pens to their patients.

5 The pen-related actions of physicians are most strongly associated with the perception of clinically relevant attributes of the pen.

Peyrot M, Rubin R (2008) Physician perception and recommendation of insulin pens for patients with type 2 diabetes mellitus. *Current Medical Research and Opinion* **24**: 2413–22