Major journals

LANCET

Microvascular outcome risk from ACCORD data

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

1 The authors of this study investigated whether reducing blood glucose would decrease the rate of microvascular complications among people with T2D.

2 Data from the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial – in which people with T2D, an HbA_{1c} level >7.5% (>58 mmol/mol) and cardiovascular disease (CVD) were randomised to either intensive (target HbA_{1c}, <6.0% [<42 mmol/mol]; *n*=5128) or standard (target HbA_{1c}, 7.0–7.9% [53–63 mmol/mol]; *n*=5123) glycaemic therapy – were used.

3 In this analysis, the first prespecified composite outcome was dialysis or renal transplantation, high serum creatinine, or retinal photocoagulation or vitrectomy and the second was peripheral neuropathy plus the first composite outcome.

4 Before study end, those receiving intensive therapy were transferred to standard therapy because of higher mortality. At transition, the first composite outcome was recorded in 443 of 5107 people in the intensive group versus 444 of 5108 in the standard group (*P*=1.00). The second composite outcome was noted in 1591 of 5107 versus 1659 of 5108 (*P*=0.19). The results were similar at study end.

5 The authors concluded that the microvascular benefits of intensive glycaemic therapy should be considered alongside CVD-related mortality, weight gain and hypoglycaemia.

Ismail-Beigi F, Craven T, Banerji MA et al (2010) Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial. *Lancet* **376**: 419–30

ACCORD treatment resulted in microvascular benefit even in people with long-standing type 2 diabetes

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It is well recognised that there is a close link between hyperglycaemia, as measured by HbA_{1c} level, and microvascular complications in people with type 2 diabetes. The glycaemia arm of the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial was an investigation of the effects on cardiovascular events of intensive versus standard glycaemic control therapy for hyperglycaemia in a large population with type 2 diabetes (ACCORD Study Group et al, 2008). Besides the primary composite cardiovascular endpoint, the ACCORD trial had predefined secondary endpoints to assess the effect of intensive glycaemic therapy on incidence and progression of retinopathy, nephropathy, and neuropathy. Near-normal glycaemia was targeted in people with longstanding type 2 diabetes (mean duration, 10 years) and cardiovascular disease or high cardiovascular risk. The intensive therapy aimed to reduce HbA_{1c} values to <6.0% (<42 mmol/mol), with a mean of 6.4% (46 mmol/mol), whereas the standard therapy sought to keep values between 7.0% (53 mmol/mol) and 7.9% (63 mmol/mol), with a mean of 7.5% (58 mmol/mol).

In this study by Ismail-Beigi et al (2010; summarised alongside), no significant effect of intensive glycaemic control was observed on advanced renal and eye complications. The risk of development of macroalbuminuria was 29% lower in association with intensive therapy, while markers of neuropathy – including loss of ankle jerks, loss of vibration sensation and loss of light touch sensation – were all lower in the in the intensive treatment group. In contrast to UKPDS (UK Prospective Diabetes Study; UKPDS Group, 1998) this study did not record a clear benefit of intensive therapy for diabetic retinopathy on the basis of major clinical endpoints (such as necessity of photocoagulation); a result that is consistent with VADT (Veterans Affairs Diabetes Trial; Duckworth et al, 2009) and ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evalution; ADVANCE Collaborative Group et al, 2008).

Collectively, these findings emphasise the benefit of glycaemic control for the reduction of albuminuria. The difference in effect of intensive glycaemic control on the composit retina–renal outcome seen between this study and UKPDS may be related to the fact that the UKPDS cohort was much earlier in the natural history of type 2 diabetes. Thus, the observations of this study further support the concept that achieving intensive control early in the natural history of type 2 diabetes may be associated with optimal outcomes, although intensive glycaemic control also has some microvascular outcome benefits in people with long-standing type 2 diabetes. The benefits of intensive glycaemic control in this context, however, have to be weighed against the necessary prescribing costs, weight gain and hypoglycaemia risk.

Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME et al (2008) Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* **358**: 2545–59

ADVANCE Collaborative Group, Patel A, MacMahon S et al (2008) Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med* **358**: 2560–72

Duckworth W, Abraira C, Moritz T et al (2009) Glucose control and vascular complications in veterans with type 2 diabetes. *N Engl J Med* **360**: 129–39

UKPDS Group (1998) Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. *Lancet* **352**: 837–53

"In older men with mobility limitations and a high prevalence of chronic disease, testosterone gel application was associated with an increased risk of adverse cardiovascular events."

JAMA

Tight BP control does not improve CV outcomes

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

1 The authors aimed to determine the association of systolic blood pressure (BP) control and cardiovascular outcomes in people >50 years of age, with diabetes and coronary artery disease (CAD).

2 This was an observational subgroup analysis of 6400 of the 22 576 participants in INVEST (International Verapamil SR-Trandolapril Study), where the subgroup received either a calcium antagonist or a beta-blocker first-line, followed by an angiotensin-converting enzyme (ACE) inhibitor, a diuretic or both. The treatment target was to reach a systolic BP of <130 mmHg and diastolic of <85 mmHg.

3 Participants were classified as having good control if their systolic BP was <130 mmHg; usual control if it was between 130 mmHg and <140 mmHg and uncontrolled if it was ≥140 mmHg.

4 The primary outcome was the occurrence of all-cause mortality, non-fatal myocardial infarction or non-fatal stroke.

5 During 16 893 person-years of follow-up, a primary outcome event was reached by 286 (12.7%) of those who had tight control, 249 (12.6%) of those who had usual control and 431 (19.8%) who had uncontrolled systolic BP.

6 There was little difference in cardiovascular event rate between people with usual control and people with tight control (P=0.24).

7 Compared with usual control, tight control of systolic blood pressure in people with diabetes and CAD was not associated with improved cardiovascular outcomes in this cohort.

Cooper-DeHoff RM, Gong Y, Handberg EM et al (2010) Tight blood pressure control and cardiovascular outcomes among hypertensive patients with diabetes and coronary artery disease. *JAMA* **304**: 61–8

ARCHIVES OF INTERNAL MEDICINE

Net benefit of aggressive CV risk factor modification

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

1 This study assessed the variability in the benefit and harm of aiming for LDL-cholesterol and blood pressure (BP) targets.

2 Participants underwent treatment intensification to achieve targets of 5.56 mmol/L for LDL-cholesterol and 130/80 mmHg for BP using titration of statin and antihypertensive treatment, respectively.

3 Participants gained 1.50 quality-adjusted life-years (QALYs) of lifetime treatment-related benefit for LDL-cholesterol and 1.35 QALYs for BP, which declined to 1.42 and 1.16 QALYs after accounting for treatment-related harm.

4 It was found that benefit and harm from aggressive treatment of cardiovascular risk factors varies widely depending on underlying risk profile.

Timbie JW, Hayward RA, Vijan S (2010) Variation in the net benefit of aggressive cardiovascular risk factor control across the US population of patients with diabetes mellitus. *Arch Intern Med* **170**: 1037–44

NEW ENGLAND JOURNAL OF MEDICINE

Testosterone gel associated with increased CV risk

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

1 The authors of this study aimed to assess the safety and efficacy of testosterone treatment in men over the age of 65 years who have limited mobility and a total serum testosterone level of 3.5–12.1 nmol/L.

2 A total of 209 men were randomly assigned to receive placebo gel or testosterone gel, once-daily for 6 months.

3 The trial was stopped early because of significantly more adverse cardiovascular (CV) events occurring in the testosterone group.

4 A total of 23 people in the testosterone group had CV-related adverse events compared with five in the placebo group. The testosterone group also had significantly greater improvements in leg-press and chest-press strength and in stair-climbing while carrying a load.

5 In these older men with mobility limitations and a high prevalence of chronic disease, testosterone gel application was associated with an increased risk of adverse CV events.

Basaria S, Coviello AD, Travison TG et al (2010) Adverse events associated with testosterone administration. *N Engl J Med* **363**: 109–22

LANCET

Fasting BG and vascular disease

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

1 This meta-analysis looked at the association of diabetes and fasting blood glucose (BG) concentration with coronary heart disease and stroke risk.

2 Data were drawn from 698 782 participants in 102 published prospective studies.

3 Adjusted hazard ratios (HRs) with diabetes were 2.00 for coronary heart disease, 2.27 for ischaemic stroke, 1.56 for haemorrhagic stroke, 1.84 for unclassified stroke and 1.73 for the aggregate of other vascular death.

4 Diabetes was estimated to account for 11% of vascular deaths.

5 The authors concluded that fasting BG concentration was modestly associated with risk of cardiovascular disease in people with diabetes.

Emerging Risk Factors Collaboration, Sarwar N, Gao P et al (2010) Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet* **375**: 2215–22