Major journals

LANCET

Statins lower risk of vascular events in diabetes

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

1 Uncertainty exists about whether statin therapy lowers the risk of occlusive vascular events in people with diabetes, and if effects depend on diabetes type, lipid profile or other factors.

2 A prospective meta-analysis was performed on data from 18 686 people with diabetes (1466 with type 1 and 17 220 with type 2) and 71 370 people without diabetes in 14 statin treatment trials.

3 In a mean follow-up of 4.3 years, the group with diabetes had 3247 major vascular events.

4 The proportional reduction in all-cause mortality per mmol/l reduction in LDL cholesterol was similar in those with and without diabetes (9% vs 13%, respectively), reflecting a significant reduction in vascular mortality and no effect on non-vascular mortality in people with diabetes.

5 A 21% proportional reduction in major vascular events per mmol/l reduction in LDL cholesterol in people with diabetes was similar to the effect seen in those without diabetes; people with diabetes had reduced myocardial infarction or coronary death, coronary revascularistion and stroke.

6 After 5 years, 42 fewer people with diabetes had major vascular events per 1000 allocated statin treatment.

7 For those with diabetes, the effects of treatment with statins was irrespective of history of vascular disease and other baseline characteristics, indicating that statin therapy should be considered for all people with diabetes who are at high risk of vascular events.

Cholesterol Treatment Trialists' (CTT) Collaborators (2008) Efficacy of cholesterol-lowering therapy in 18686 people with diabetes in 14 randomised trials of statins: a meta-analysis. *Lancet* **371**: 117–25

Intensive multifactorial care in high-risk people with type 2 diabetes leads to reduced death and CV morbidity

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The Steno-2 Study (Gaede et al, 2003) was a multiple risk factor intervention in people with type 2 diabetes and microalbuminuria, over a duration of 7.8 years, which assessed the efficacy of tight lipid, glucose and blood pressure regulation along with the use of renin-angiotensin system blockers and aspirin on cardiovascular events. The mean treatment targets achieved in the intensive group were HbA_{1c} 7.9%, blood pressure 131/73mm/Hg, total cholesterol 3.5mmol/l, LDL cholesterol 1.8mmol/l and HDL cholesterol 1.2mmol/l, which were associated with significant reductions in cardiovascular mortality and progression of microvascular complications. The study summarised overleaf presents the observations of the 5.5 year follow up period subsequent to the completion of the initial 7.8 year period of the Steno-2 Study. The primary endpoint at 13.3 years was the time to death from any cause. On completion of the follow up period, HbA_{1c} was similar in both groups (7.7% vs 8.0%) as was blood pressure (140/76 vs 146/74) and total cholesterol (3.8mmol/l vs 4.0mmol/l).

The importance of cholesterol reduction in the management of cardiovascular risk in type 2 diabetes was further illustrated by the results of the cholesterol treatment trialists collaborators (CTTC) meta-analysis of diabetes subgroups in the statin megatrials (abstracted alongside). This analysis demonstrated that for a 1 mmol/l reduction in LDL cholesterol a relative risk reduction of around 21% in risk of cardiovascular morbidity and mortality was achieved. The reduction in risk was uniform across all categories of people with diabetes and was independent of baseline cardiovascular risk. The greatest absolute risk reduction occurred in those with the highest baseline level of absolute cardiovascular risk. it is, therefore, likely that the cholesterol reductions seen in the high cardiovascular risk population exemplified in the Steno-2 cohort may well have been the major contributory factor to the reduction in cardiovascular mortality observed in this study.

Smoking rates, body weight and daily calorie intake were similar in both groups during the 13.3 year period of observation. An absolute risk reduction of 29% and relative risk reduction of 59% of death from any cause was seen among participants who received intensive therapy, with an absolute risk of cardiovascular death of 13%.

During the entire follow-up period, the rate of death in the conventionally treated group was 50%, highlighting the poor prognosis in such patients in the absence of intensive risk factor intervention. The observations of the study suggest that the findings of individual risk factor intervention studies using antihypertensive and lipid lowering agents appear to be additive in the context of a multiple risk factor intervention approach.

Using a risk calculator derived from the UK Prospective Diabetes Study (UKPDS), statins and antihypertensive drugs appeared to have the largest effect on cardiovascular outcomes during the 7.8 years of intervention with hypoglycaemic agents and aspirin the next most important. Reductions in the progression of microvascular complications occurred after a mean period of 3.8 years of intensified intervention, changes that were maintained at 13.3 years. This translated into a highly significant absolute risk reduction of 6.3% in the need for dialysis. Adverse events were not continuously monitored, but few were reported during the course of the study.

When adopting such an intensive approach to therapy, however, it is important to balance the risk–benefit ratio of such an approach. Many analyses demonstrate slow progress of multiple therapeutic targets in people with type 2 diabetes.

The follow up results of the Steno-2 Study demonstrate that intensive multifactorial care in high risk people with type 2 diabetes leads to a marked reduction on death and cardiovascular morbidity, so early and meticulous implementation of such a strategy remains crucial.

Gæde 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

AMERICAN JOURNAL OF MEDICINE

Metformin can reduce onset of diabetes

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

1 A meta-analysis was conducted to assess the effect of metformin on metabolic parameters and the incidence of the development of diabetes in people at risk of diabetes.

2 Searches of three databases from 1966–2006 included randomised trials that compared metfomin with placebo or no treatment in people without diabetes.

3 Results of 31 trials with 4570 participants indicated that, compared with placebo or no treatment, metformin reduced BMI, fasting glucose, fasting insulin, calculated insulin resistance, triglycerides and LDL cholesterol, and increased HDL cholesterol.

4 During a mean trial duration of 1.8 years, the incidence of the development of diabetes was reduced by 40% (with an absolute risk reduction of 6%).

Salpeter SR, Buckley NS, Kahn JA, Salpeter EE (2008) Meta-analysis: metformin treatment in persons at risk for diabetes mellitus. *American Journal of Medicine* **121**: 149–57

BMJ

Anti-obesity drugs differ in CV risk profiles

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

1 A meta-analysis of 30 double-blind randomised placebo-controlled trials summarised the long-term efficacy of anti-obesity drugs in improving health status and reducing weight.

2 People receiving drug therapies were more likely to achieve 5–10% weight loss; compared with placebo, orlistat reduced weight by 2.9kg, sibutramine by 4.2kg and rimonabant by 4.7kg.

3 Orlistat reduced diabetes incidence and improved total and LDL cholesterol, blood pressure and glycaemic control in people with diabetes, but increased rates of gastrointestinal side effects and slightly lowered HDL cholesterol.

4 Sibutramine lowered HDL cholesterol and triglycerides, but raised blood pressure and pulse rate.

5 Rimonabant improved HDL cholesterol, triglycerides, blood pressure and glycaemic control in people with diabetes, but increased the risk of mood disorders.

Rucker D, Padwal R, Li SK, et al (2008) Long term pharmacotherapy for obesity and overweight: updated meta-analysis. *British Medical Journal* **335**: 1194–99

‘Rimonabant improved HDL cholesterol, triglycerides, blood pressure and glycaemic control in people with diabetes.’

ARCHIVES OF INTERNAL MEDICINE

The burden of diabetes increases with age

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

1 Trends were examined in the occurrence of diabetes and its complications in people older than 65 years in the US.

2 Analyses of medical claims and data for people diagnosed with diabetes in 1994 (n=33 164), 1999 (n=31 722) and 2003 (n=40 058) were compared with control groups without diabetes.

3 Annual incidence of diabetes increased by 23% between 1994 and 95, and 2003 and 04, prevalence increased by 62%, and mortality rate post-diagnosis decreased by 8.3% compared with controls.

4 Complication rates in those diagnosed increased or stayed the same as controls (except for ophthalmic diseases) and rates for some major complications were high; therefore, the cost of caring for older people with diabetes is growing.

Sloan FA, Bethel MA, Ruiz Jr D et al (2008) The growing burden of diabetes mellitus in the US elderly population. *Archives of Internal Medicine* **168**: 192–99

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.

Gæde 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

BMJ

Positive benefits of group education on type 2 do not include HbA_{1c}

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

1 A multicentre cluster randomised controlled trial evaluated the effectiveness of structured group education on biomedical, psychosocial and lifestyle measures in people with newly diagnosed type 2 diabetes.

2 Participants comprised 824 adults, of whom 437 took part in structured group education for 6 hours were compared with 387 who received usual care.

3 At 12 months, the intervention group showed more weight loss, better odds of not smoking, greater changes in illness belief scores and a lower depression score than the control group, but while HbA_{1c} levels had decreased, the difference was not statistically significant.

Davies MJ, Heller S, Skinner TC et al (2008) Effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. *BMJ* **336**: 491–95

ARCHIVES OF INTERNAL MEDICINE

Early death risk for those with stroke and obstructive sleep apnoea

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

1 This study investigated if obstructive or central sleep apnoea is related to reduced survival in people with stroke.

2 A total of 132 people admitted for stroke rehabilitation from 1995–97 had overnight sleep apnoea recordings at a mean of 23 days after stroke onset, and were followed up for a mean of 10 years, with death as the primary outcome.

3 Of 132 participants, 116 had died at follow up, and it was found that the risk of death was higher among the 23 people with obstructive sleep apnoea than controls.

4 No difference in mortality was found between participants with central sleep apnoea and controls.

Sahlin CS, Sandberg O, Gustafson Y et al (2008) Obstructive sleep apnea is a risk factor for death in patients with stroke. *Archives of Internal Medicine* **168**: 297–301

ANNALS OF INTERNAL MEDICINE

ARBs and ACE inhibitors are better together

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

1 The effect of angiotensin-receptor blockers (ARBs) vs placebo and alternative treatments, and the effect of combined treatment with ARBs and angiotensin-converting enzyme (ACE) inhibitors on proteinuria were assessed in this meta-analysis.

2 From 49 studies involving 6181 participants, it was found that ARBs reduced proteinuria compared with placebo or calcium-channel blockers; ARBs and ACE inhibitors reduced proteinuria to a similar degree.

3 Combining ARBs and ACE inhibitors reduced proteinuria more than either agent alone.

4 Most studies were small, of varied quality and did not give reliable data on adverse side effects and outcomes.

Kunz R, Friedrich C, Wolbers M, Mann JFE (2008) Meta-analysis: effect of monotherapy and combination therapy with inhibitors of the rennin-angiotensin system on proteinuria in renal disease. *Annals of Internal Medicine* **148**: 30–48

ARCHIVES OF INTERNAL MEDICINE

Prognostic risk index developed for management strategies of PAD

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

1 The aim of this study was to develop a prognostic risk index for long-term mortality in people with peripheral arterial disease (PAD).

2 A total of 2642 people with an ankle-brachial index (ABI) of 0.9 or less were divided into derivation (n=1332) and validation (n=1310) groups.

3 In 10 years of follow up, 42.2% and 40.4% of people died in the derivation and validation groups, respectively.

4 The risk index for 10-year mortality included renal dysfunction, heart failure, ST-segment changes, age over 65 years, hypercholesterolaemia, ABI less than 0.6, Q-waves, diabetes, cerebrovascular disease and pulmonary disease.

5 Statins, aspirin and β-blockers were associated with reduced 10-year mortality.

6 Participants were stratified into differing categories according to risk score (low, low–intermediate, high–intermediate and high), and 10-year mortality rates were 22.1%, 32.2%, 45.8% and 70.4%, respectively, and were comparable to mortality in the validation group.

7 This prognostic risk index for long-term mortality may be useful for risk stratification, counselling and medical decision-making.

Feringa HH, Bax JJ, Hoeks S et al (2007) A prognostic risk index for long-term mortality in patients with peripheral arterial disease. *Archives of Internal Medicine* **167**: 2482–89

'Combining ARBs and ACE inhibitors reduced proteinuria more than either agent alone.'