Diabetes journals

DIABETOLOGIA

Metformin reduces CV risk in diabetes

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

1 This study assessed the risk of adverse cardiovascular (CV) outcomes in people with type 2 diabetes who had recently begun treatment with sulphonylureas and metformin alone or in combination.

2 Patient details (n=5730) were taken from the Diabetes Audit and Research in Tayside, Scotland (DARTS), database. Those recently prescribed with oral hypoglycaemic agents were allocated into one of five study groups: metformin only; sulphonylureas only; sulphonylureas plus metformin later; metformin plus sulphonylureas later; and both drugs simultaneously.

3 People in the sulphonylurea monotherapy group had more than three times the risk of mortality and CV mortality than those in the metformin monotherapy group, although there was no increased risk of CV hospital admission.

4 People in the combination groups had increased risks of mortality, CV mortality and CV hospital admission compared with those in the metformin-only group.

5 Adjusting for all potential confounding variables resulted in reduced risk estimates, although people in the sulphonylureas-only group were still at higher risk of mortality and CV mortality than those in the metformin-only group.

6 The study showed that people in the metformin monotherapy group were at lower CV risk than those in the sulphonylureas-only group or those in the combination groups.

Evans JMM, Ogston SA, Emslie-Smith A, Morris AD (2006) Risk of mortality and adverse cardiovascular outcomes in type 2 diabetes: a comparison of patients treated with sulphonylureas and metformin. *Diabetologia* **49**: 930–6

Lower cardiovascular risk with metformin monotherapy

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Evans et al (2006; see left) examine the risk of adverse cardiovascular outcomes in people with type 2 diabetes newly treated with sulphonylureas or metformin. The study is a part of the Diabetes Audit and Research in Tayside, Scotland (DARTS), initiative.

People newly diagnosed with type 2 diabetes and prescribed oral hypoglycaemic agents between 1994 and 2001 were separated into five study groups according to treatment: metformin alone; sulphonylureas alone; sulphonylureas added to metformin; metformin added to sulphonylureas; and both drugs simultaneously. The relative risk for all mortality, cardiovascular mortality and cardiovascular hospital admissions were estimated using Cox regression analysis in the five study cohorts.

The metformin monotherapy group served as the reference group. Of the 5730 people studied, 1000 died during a maximum of 8 years' follow-up. Those in the sulphonylureas-only group had increased risks of mortality and cardiovascular mortality, with unadjusted risks of 3.12 (95 % confidence interval [CI], 2.54–3.84) and 3.71 (95 % CI, 2.64–5.22).

Adjusting for differences between the groups for age, sex, duration of diabetes, blood pressure, cholesterol, glycosylated haemoglobin, smoking, previous hospital admission and treatment with cardiovascular medication still demonstrated an increased mortality (relative risk, 1.43) and cardiovascular mortality (relative risk, 1.70) for the sulphonylureas-only group.

Individuals in the combination groups had significantly increased risk of cardiovascular hospital admission as well as increased risks of mortality and cardiovascular mortality.

Thus, people with diabetes treated with either sulphonylureas alone or sulphonylurea and metformin combinations were at a higher risk of adverse cardiovascular outcomes than those treated with metformin alone.

DIABETIC MEDICINE

Met S linked with NAFLD increases CVD risk in diabetes

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

1 This study determined the prevalence of cardiovascular disease (CVD) in 400 people with type 2 diabetes with non-alcoholic fatty liver disease (NAFLD) and in a matched group of 400 people with type 2 diabetes without NAFLD.

2 Outcome measures included CVD, NAFLD and the presence of the metabolic syndrome (Met S).

3 People with type 2 diabetes and NAFLD had significantly greater rates of coronary (23.0 versus 15.5 %), cerebrovascular (17.2 versus 10.2 %) and peripheral (12.8 versus 7.0 %) vascular disease than those with type 2 diabetes without NAFLD ($P<0.001$).

4 The Met S was independently related to prevalent CVD, whereas NAFLD was not.

5 The presence of Met S was more frequent in those with NAFLD ($P<0.001$), which might explain the increased prevalence of CVD in individuals with type 2 diabetes and NAFLD.

6 Studies are needed to determine whether type 2 diabetes or another component of the Met S is responsible for the increased prevalence of CVD in people with NAFLD.

Targher G, Bertolini L, Padovani R et al (2006) Increased prevalence of cardiovascular disease in type 2 diabetic patients with non-alcoholic fatty liver disease. *Diabetic Medicine* **23**: 403–9

'High cardiovascular disease incidence rates were reached in people with type 1 diabetes at a much younger age than in people in the general population.'

DIABETIC MEDICINE

Pioglitazone decreases diabetes risk in Asian Indian population

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

1 The authors examined the effect of pioglitazone (30 mg once daily for 16 weeks) on insulin sensitivity, inflammatory and cardiovascular risk markers, endothelial function and body fat distribution in 18 Asian Indian people without diabetes and in 17 matched (by age and body mass index) European Caucasians without diabetes.

2 At baseline the Asian Indian group were insulin resistant compared with the Caucasian group ($P<0.0001$).

3 After pioglitazone treatment, insulin sensitivity significantly improved in the Asian Indian group ($P<0.001$).

4 Insulin-mediated vasodilation improved in the Asian Indian group but not in the Caucasian group, which correlated with the change in insulin sensitivity ($P=0.03$).

5 C-reactive protein level was higher in the Asian Indian group compared with the Caucasian group, and was negatively correlated with insulin sensitivity ($P=0.02$).

6 Pioglitazone significantly decreased inflammatory and cardiovascular risk markers in the Asian Indian group but significant changes in visceral or total fat were not observed.

7 Insulin sensitisers, such as pioglitazone, may have a role in reducing diabetes and CV events in the high-risk Asian Indian population.

Raji A, Gerhard-Herman MD, Williams JS et al (2006) Effect of pioglitazone on insulin sensitivity, vascular function and cardiovascular inflammatory markers in insulin-resistant non-diabetic Asian Indians. *Diabetic Medicine* **23**: 537–43

DIABETES CARE

Type 1 diabetes increases CVD risk

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

1 The study aim was to estimate the absolute and relative risk of cardiovascular disease (CVD) in 7479 people with type 1 diabetes and 38 116 people without diabetes.

2 Type 1 diabetes was linked with a four-fold risk of major CVD in men, an eight-fold risk in women and a hazard ratio (HR) of 4.5 in all those with type 1 diabetes compared with those without.

3 People with type 1 diabetes had greatly elevated HRs for acute coronary events, coronary revascularisations and stroke.

4 High CVD incidence rates were reached in people with type 1 diabetes at a much earlier age than in people in the general population.

5 Absolute and relative risks of CVD are increased with type 1 diabetes.

Soedamah-Muthu SS, Fuller JH, Mulnier HE et al (2006) High risk of cardiovascular disease in patients with type 1 diabetes in the UK. *Diabetes Care* **29**: 798–804

DIABETES CARE

Diabetic nephropathy increases CR risk

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

1 The authors investigated the prevalence of cardiorenal (CR) risk factors, their routine clinical management and the achievement of international guideline targets in 847 people with type 2 diabetes and diabetic nephropathy (749 with microalbuminuria and 98 with macroalbuminuria).

2 The percentages of people who reached the guideline targets were 17.5 % for blood pressure, 32.3 % for HbA_{1c}, 30.7 % for LDL-cholesterol, 47 % for HDL-cholesterol and 55.2 % for triglycerides.

3 Chronic renal failure (glomerular filtration rate <60 ml/min) was shown in 41 % and anaemia in 23.8 % of participants.

4 Impaired renal function can often be diagnosed in people with early and moderate diabetic nephropathy.

5 The authors suggest that a correct diagnosis of diabetic nephropathy should always be made and that sodium intake and anaemia evaluated in these patients.

Sasso FC, Nicola LD, Carbonara O et al (2006) Cardiovascular risk factors and disease management in type 2 diabetic patients with diabetic nephropathy. *Diabetes Care* **29**: 498–503

DIABETIC MEDICINE

Weight gain improves HbA_{1c} but has adverse effects on lipids and BP

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

1 The EURODIAB Prospective Complications Study examined 3250 people with type 1 diabetes at baseline, and then re-examined 1800 participants 7–8 years later. The effect of weight gain during this time on HbA_{1c}, plasma lipids and blood pressure (BP) was investigated.

2 The change in HbA_{1c} during the study was more favourable in people who gained 5 kg or more.

3 However, a weight gain of 5 kg or more had adverse effects on plasma lipids and blood pressure.

4 We need a better understanding of how weight gain improves HbA_{1c}.

Ferriss JB, Webb D, Chaturvedit N et al (2006) Weight gain is associated with improved glycaemic control but with adverse changes in plasma lipids and blood pressure in type 1 diabetes. *Diabetic Medicine* **23**: 557–64

'We need a better understanding of how weight gain improves HbA_{1c}.'

DIABETES

Change in acute insulin response determines glucose tolerance status

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

1 In the UK Prospective Diabetes Study a continuous decline in beta-cell function was found in people with type 2 diabetes.

2 The authors studied longitudinal changes in beta-cell function over 5.2 years in people with normal glucose tolerance (NGT), impaired glucose tolerance (IGT) and type 2 diabetes.

3 Acute insulin response (AIR) relative to the insulin sensitivity index (S_I) was assessed from a frequently sampled intravenous glucose tolerance test among African-American, Hispanic and non-Hispanic white people aged 40–69 years.

4 At baseline, decreasing levels of both S_I and AIR reflected deteriorating glucose tolerance status at baseline and at follow-up.

5 Regarding longitudinal changes, S_I declined in each glucose tolerance category; this was significantly different between NGT at baseline and NGT at follow-up (NGT/NGT) and NGT/IGT.

6 However, AIR increased in all categories, except for a small decline in NGT/diabetes and diabetes/diabetes.

7 Results were similar for each ethnic group.

8 The change in AIR principally determined glucose tolerance status at follow-up; NGT was maintained by a compensatory increase in insulin secretion.

9 Failure to increase insulin secretion led to IGT, and a decrease in insulin secretion led to overt diabetes.

Festa A, Williams K, D'Agnostino R et al (2006) The natural course of ß-cell function in non-diabetic and diabetic individuals. The Insulin Resistance Atherosclerosis Study. *Diabetes* **55**: 1114–20

DIABETIC MEDICINE

IDF defines Met S

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

1 There is a strong need for one simple definition of the metabolic syndrome (Met S) that can be used easily in clinical practice and in any country to identify people at risk of cardiovascular disease and diabetes.

2 In May 2004 the International Diabetes Federation (IDF) held a workshop comprising 21 experts who examined how the Met S could be better defined and unified.

3 The resultant consensus statement includes a new set of criteria to identify people with the Met S in order to reduce the long-term risk of cardiovascular disease.

4 The IDF has also identified where more studies are needed.

Alberti KGMM, Zimmet P, Shaw J (2006) Metabolic syndrome — a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabetic Medicine* **23:** 469–80

DIABETES CARE

Elevated glucose increases CAD risk

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

1 The study objective was to determine whether elevated blood glucose in the absence of diabetes increases the risk for coronary artery disease (CAD).

2 Records from 24 160 people without diabetes were studied, and baseline morning blood glucose determinations were evaluated with respect to subsequent CAD.

3 In total, 3282 patients developed CAD over a total analysis time at risk of 77 048 years.

4 Higher baseline morning glucose (100–126 versus <100 mg/dl [5.6–7 versus <5.6 mmol/l]) was linked with a 53.9 %-greater incidence rate of myocardial infarction, an 18.6 %-greater incidence rate of coronary syndrome and a 26.4 %-greater number of new prescriptions for nitrates (all $P<0.05$).

5 Results indicate that elevated glucose in the absence of diabetes is associated with a greater incidence of CAD independent of other recognised risk factors, such as age, weight, hyperlipidaemia, renal failure and hypertension.

Nielson C, Lange T, Hadjokas N (2006) Blood glucose and coronary artery disease in non-diabetic patients. *Diabetes Care* **29**: 998–1001

DIABETES CARE

Albuminuria relates to CV outcomes

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

1 Urinary albumin-to-creatinine ratio (UACR) was measured for a mean of 4.7 years in 1063 people with diabetes, hypertension and left ventricular hypertrophy to see if it predicted cardiovascular (CV) outcomes.

2 Increasing levels of baseline albuminuria were related to increased risk for CV morbidity and mortality.

3 Reductions in UACR at years 1 and 2 were approximately 33 % with losartan treatment versus 15 % for atenolol ($P<0.001$).

4 Benefits of losartan were most prominent in people with the highest level of baseline UACR.

5 A lowering of albuminuria in these individuals translated to a reduction in CV events.

Ibsen H, Olsen MH, Wachtell K et al (2006) Does albuminuria predict cardiovascular outcomes on treatment with losartan vs atenolol in patients with diabetes, hypertension and left ventricular hypertrophy? *Diabetes Care* **29**: 595–600

'The change in acute insulin response principally determined glucose tolerance status at follow-up.'