

Diabetes journals

DIABETES CARE



Type 2 diabetes is a 'CHD equivalent'

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

1 This study investigated the hypothesis that coronary heart disease (CHD) mortality in people with diabetes without prior evidence of CHD is equal to that in people without diabetes with prior myocardial infarction (MI) or any prior evidence of CHD.

2 A random Finnish sample of 1373 people without diabetes and 1059 people with diabetes participated in the baseline study in 1982–4. All people were aged 45–6 years. The 18-year follow-up end points were total mortality, cardiovascular disease (CVD) mortality and CHD mortality.

3 Adjusted multivariate Cox hazard models indicated that people with diabetes without prior MI, compared with people without diabetes with prior MI, had a hazard ratio (HR) of 0.9 for the risk of CHD death; the corresponding HR was 0.9 in men and 1.9 in women.

4 People with diabetes without any prior evidence of CHD, compared with people without diabetes with prior evidence of CHD, had an HR of 1.9 for CHD death (men 1.5; women 3.5); the results for CVD and total mortality were similar to those for CHD mortality.

5 The study indicates that type 2 diabetes is a 'CHD equivalent' during an 18-year follow-up, when the criterion for CHD is prior MI. However, diabetes without any prior evidence of CHD indicates a higher risk than prior evidence of CHD in people without diabetes, especially in women.

Juutilainen A, Lehto S, Rönnemaa T, Pyörälä K, Laakso M (2005) Type 2 diabetes as a 'coronary heart disease equivalent': an 18-year prospective population-based study in Finnish subjects. *Diabetes Care* **28**: 2901–7

Two further studies find that type 2 diabetes is a coronary heart disease equivalent in men and women



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In 1998 Steven Haffner and co-workers published a now highly cited paper reporting that people with type 2 diabetes who had not suffered an earlier myocardial infarction (MI) had the same risk of coronary heart disease (CHD) mortality as a person without diabetes who had previously sustained an MI (Haffner et al, 1998). This paper has subsequently been questioned and the wisdom of the statement that type 2 diabetes is a coronary artery disease equivalent also questioned (Evans et al, 2002). Two recent papers add important information to this debate, and have also explored further the effect of type 2 diabetes on CHD in women.

In a follow-up of the original report by Haffner et al, Juutilainen et al (see left) report 18-year follow-up of the original cohort of two groups (>1000 people with type 2 diabetes and >1000 people without diabetes). The findings support the original report.

Juutilainen et al demonstrated that type 2 diabetes is a CHD equivalent; moreover, the use of previous MI as a criterion for CHD underestimates

the significance of diabetes status with respect to mortality from CHD. Additionally, the combination of diabetes and prior CHD was a particularly dangerous combination, particularly in women.

In another report, from the FINAMI study, Pajunen et al (see below) explored the same question in a different population. These workers demonstrated complementary findings to those of Juutilainen et al. Pajunen et al showed that in older men type 2 diabetes was a CHD equivalent. In keeping with the findings of Juutilainen et al they showed that women who had type 2 diabetes had a similar risk of suffering a first MI to that in women without diabetes with a prior MI for suffering a recurrent MI.

These two important manuscripts further consolidate our understanding of risk of coronary events in people with type 2 diabetes. Type 2 diabetes should be considered a CHD equivalent in both men and women. There is an urgent need to reduce this risk, as once a person with diabetes has sustained an MI his or her prognosis is very poor.

Evans JM, Wang J, Morris AD (2002) Comparison of cardiovascular risk between patients with type 2 diabetes and those who had had a myocardial infarction. *British Medical Journal* **324**: 939–42

Haffner SM, Lehto S, Ronnemaa T, Pyörälä K, Laakso M (1998) Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *New England Journal of Medicine* **339**: 229–34

DIABETOLOGIA



Diabetes with no prior MI increases risk of CHD

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

1 It remains controversial whether people with diabetes have a similar risk of developing acute coronary heart disease (CHD) events to those without diabetes who have suffered a prior myocardial infarction (MI).

2 This study compared the risk of acute coronary events in people with and without diabetes and with and

without a prior MI, stratified by age and sex. Participants were taken from the Finnish MI register (FINAMI) study (n=6988) and FINRISK population surveys.

3 People with diabetes but no prior MI, and people with a prior MI but no diabetes were found to be high-risk individuals for CHD.

4 Among men, a prior MI conferred a higher risk of a coronary event than diabetes in the 45- to 54-year age group, but the situation was reversed in older people. Among women with diabetes, the risk of suffering a first MI was similar to the risk that women without diabetes with prior MI had of suffering a recurrent MI.

Pajunen P, Koukkuinen H, Ketonen M et al (2005) Myocardial infarction in diabetic and non-diabetic persons with and without prior myocardial infarction: the FINAMI Study. *Diabetologia* **48**: 2519–24

‘In addition to its metabolic effects, insulin may improve endothelial function and increase the threshold for ischaemia in people with diabetes.’

JOURNAL OF DIABETES AND ITS COMPLICATIONS

Diabetes treatment has different effects on CVD risk

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

- The aim of this study was to determine the effect of basal insulin, alone or with a sensitiser, or a combination of oral agents on non-traditional risk factors for cardiovascular disease (CVD).
- Fifty-seven people with type 2 diabetes were randomised to continuous subcutaneous basal insulin, basal insulin and oral pioglitazone (Pio) or a sulfonylurea and metformin (SU+M). Measures were taken at baseline and after 20 weeks of treatment.
- HbA_{1c} decreased by ≥2% and to comparable levels in all groups. Despite improved glycaemia, plasma high-sensitivity C-reactive protein levels did not change in any group, whereas plasma plasminogen activator inhibitor-1 (PAI-1) fell with basal insulin+Pio and with SU+M.
- Levels of 8-epi-prostaglandin F_{2α} (PGF_{2α}) declined with basal insulin and with SU+M.
- High-density lipoprotein cholesterol (HDL-c) increased only with basal insulin+Pio.
- Serum lipoprotein (a) increased with basal insulin therapy alone.
- Data were pooled from all groups to determine the overall effect of glycaemic control – there was a significant decline in HbA_{1c}, PAI-1 and PGF_{2α} and an increase in HDL-c.
- Excellent glycaemic control does not impact on non-traditional risk factors for CVD equally, but various medications for diabetes have different effects on these risk factors.

Fonseca VA, Theuma P, Mudaliar S, Leissinger CA, Clejan S, Henry RR (2006) Diabetes treatments have differential effects on nontraditional cardiovascular risk factors. *Journal of Diabetes and its Complications* **20**: 14–20

‘Mesenteric fat thickness had significant correlations with various metabolic variables. It was an independent determinant of all components of the metabolic syndrome.’

DIABETES

Insulin improves MBF in people with diabetes and CAD

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

- This study determined whether insulin is able to increase myocardial blood flow (MBF) in the regions of compromised myocardial perfusion in people with type 2 diabetes and ischaemic coronary artery disease (CAD).

- Forty-three people (aged 63 ± 7 years) with type 2 diabetes underwent single-photon emission computed tomography and coronary angiography to determine the effects of insulin on MBF in ischaemic and non-ischaemic regions.
- At rest, insulin infusion increased MBF by 13% in ischaemic regions and 22% in non-ischaemic regions.
- In addition to its metabolic effects, insulin may improve endothelial function and increase the threshold for ischaemia in people with diabetes.

Lautamäki R, Airaksinen KE, Seppänen M et al (2006) Insulin improves myocardial blood flow in patients with type 2 diabetes and coronary artery disease. *Diabetes* **55**: 511–16

DIABETIC MEDICINE

Aggressive management of diabetes needed in South Asian people

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

- The authors sought to determine whether 210 South Asian people with diabetes had similar or greater year-on-year deterioration in metabolic parameters compared with 1557 European people consecutively attending the same diabetes clinic over 5.3 years.

- South Asian people were younger than European people at first-recorded diagnosis of diabetes and had significantly lower body mass index and blood pressure.
- Mean HbA_{1c} was not different across ethnic groups at first visit, but with time was worse in South Asian people than in European people. South Asian people had significantly smaller improvements in blood pressure and cholesterol over the follow-up period.
- Results suggest the need to be more aggressive in the management of diabetes and related risk factors in South Asian people.

Mukhopadhyay B, Forouhi NG, Fisher BM et al (2006) A comparison of glycaemic and metabolic control over time among South Asian and European patients with type 2 diabetes. *Diabetic Medicine* **23**: 94–8

DIABETES CARE

Mesenteric fat thickness linked to metabolic syndrome

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

- This study determined whether mesenteric fat thickness was an independent determinant of the metabolic syndrome. Of 290 Chinese people who underwent ultrasound examination for mesenteric fat thickness measurements, 20 had the metabolic syndrome.

- Mesenteric fat thickness had significant correlations with various metabolic variables. It was an independent determinant of all components of the metabolic syndrome.
- The odds ratio of metabolic syndrome was increased by 1.35-fold for every 1 mm increase in mesenteric fat thickness. Mesenteric fat thickness of ≥ 10 mm was the optimal cutoff value to identify the metabolic syndrome.

Liu KH, Chan YL, Chan WB, Chan JCN, Chu CWW (2006) Mesenteric fat thickness is an independent determinant of metabolic syndrome and identifies subjects with increased carotid intima-media thickness. *Diabetes Care* **29**: 379–84

DIABETES CARE

Metabolic syndrome increases risk of mortality

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

1 The objective of this study was to examine the long-term association of the metabolic syndrome with mortality among those at high risk for cardiovascular disease (CVD).

2 A total of 10 950 Multiple Risk Factor Intervention Trial (MRFIT) survivors were additionally followed for mortality for a median of 18.4 years.

3 Proportional hazards models examined multivariate-adjusted risks associated with Adult Treatment Panel III-defined metabolic syndrome conditions.

4 Of 10 950 men, 4588 had the metabolic syndrome at MRFIT annual visit 6, while 6362 did not.

5 Comparing men with the metabolic syndrome with men without, adjusted hazard ratios (HRs) were 1.21, 1.49 and 1.51 for 18-year total, CVD and coronary heart disease mortality, respectively.

6 Among men with the metabolic syndrome, elevated glucose and low high-density lipoprotein-cholesterol were most predictive of CVD mortality, followed by elevated body mass index, elevated blood pressure and elevated triglycerides.

7 For men without the metabolic syndrome, the HR for low high-density lipoprotein-cholesterol was 1.02.

8 The metabolic syndrome is associated with an increased risk of mortality. Among those with the metabolic syndrome, risk is further increased by smoking and by elevated low-density lipoprotein-cholesterol.

Eberly LE, Prineas R, Cohen JD et al (2006) Metabolic syndrome: risk factor distribution and 18-year mortality in the multiple risk factor intervention trial. *Diabetes Care* **29**:123–30

DIABETES CARE

Pioglitazone reduces leptin

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

1 This study elucidated the mechanism of the efficacy of pioglitazone for preventing in-stent restenosis. Fifty-four people with type 2 diabetes referred for coronary stenting were randomly assigned to either the control (n=28) or pioglitazone (n=28) group.

2 There were no significant differences in glycaemic control levels or in lipid levels in the two groups at baseline or at 6-month follow-up.

3 Insulin, homeostasis model assessment of insulin resistance, endothelial nitric oxide synthase and leptin at follow-up were significantly reduced in the pioglitazone group.

4 The authors concluded that decreased leptin improves endothelial function, thus affecting the reduction of in-stent restenosis.

Nishio K, Sakurai M, Kusuyama T et al (2006) A randomized comparison of pioglitazone to inhibit restenosis after coronary stenting in patients with type 2 diabetes. *Diabetes Care* **29**: 101–6

DIABETES CARE

Microalbuminuria and impaired vasodilation

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

1 The authors sought to determine whether microalbuminuria correlates with coronary endothelium-dependent vasodilation by evaluating 84 people with type 2 diabetes without angiographic coronary stenosis and without major cardiovascular (CV) risk factors.

2 Endothelium-dependent vasodilation differed in the people

with and without microalbuminuria and correlated with urinary albumin excretion rate, diastolic blood pressure and left ventricular mass index.

3 Independent predictors for endothelium-dependent vasodilation were urinary albumin excretion rate and left ventricular mass index. Endothelium-independent vasodilation was similar in both groups.

4 People with type 2 diabetes and microalbuminuria have a more severely impaired coronary endothelium-dependent vasodilation than those without microalbuminuria.

Cosson E, Pham I, Valensi P, Paries J, Attali JR, Nitenberg A (2006) Impaired coronary endothelium-dependent vasodilation is associated with microalbuminuria in patients with type 2 diabetes and angiographically normal coronary arteries. *Diabetes Care* **29**: 107–12

DIABETES CARE

hs-CRP predicts CHD in people with diabetes

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

1 This 7-year follow-up study investigated whether high-sensitivity C-reactive protein (hs-CRP) predicted coronary heart disease (CHD) events in 1059 people with type 2 diabetes. CRP values were available

from 1045 people, of whom 878 were free of myocardial infarction (MI) at baseline.

2 Altogether, 157 people died from CHD and 254 had a non-fatal or fatal CHD event. People with hs-CRP >3 mg/l had a higher risk for CHD death than people with hs-CRP ≤3 mg/l.

3 People with high hs-CRP had a relative risk of 1.72 for CHD death.

4 In this large cohort of people with type 2 diabetes, hs-CRP was an independent risk factor for CHD deaths.

Soinio M, Marniemi J, Laakso M, Lehto S, Ronnema T (2006) High-sensitivity C-reactive protein and coronary heart disease mortality in patients with type 2 diabetes: a 7-year follow-up study. *Diabetes Care* **29**: 329–33

‘The authors concluded that decreased leptin improves endothelial function, thus affecting the reduction of in-stent restenosis.’

‘In this large cohort of people with type 2 diabetes, high-sensitivity C-reactive protein was an independent risk factor for coronary heart disease deaths.’