

Cardiovascular disease

The MRC/BHF Heart Protection Study: lowering cholesterol with simvastatin



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The benefit of statins in people with diabetes is well established. Significant numbers of patients with diabetes were included in the 4S, CARE and LIPID studies, and separate sub-group analysis has been published for 4S and CARE.

So what does the MRC/BHF Heart Protection Study (HPS) tell us about cholesterol lowering with simvastatin in people with diabetes?

Inclusion criteria for the HPS were coronary heart disease (CHD), cerebrovascular or peripheral vascular disease, diabetes, or treated hypertension. Patients were excluded on run-in if their GP thought there was a clear indication for statin therapy (e.g. they fulfilled criteria for treatment based on the results of previous studies).

Patients with prior myocardial infarction (MI) or CHD and diabetes had the highest

event rate in the study, with an event rate of 38% in 5 years in the placebo group, which was reduced to 33% with simvastatin, extending the results of the 4S, CARE and LIPID studies to patients with lower cholesterol concentrations.

For patients with diabetes and no prior CHD, an event rate of 19% was reduced to 16% with simvastatin. These subjects included a significant proportion who also had cerebrovascular or peripheral vascular disease; information on the number of diabetic patients without any prior vascular disease (i.e. true primary prevention) was not provided in the principal publication. Furthermore, lipid levels before and after simvastatin treatment are not provided separately for subjects with diabetes. Without this information it is difficult to place the results of the HPS in context for people with diabetes. Let us hope that a separate publication of the full diabetes data is not long in coming.

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Angina pectoris: a protective role?

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

1 To investigate whether patients with preinfarction angina pectoris have smaller myocardial infarcts and a better prognosis than those without angina, the authors of this study reviewed 290 patients with a diagnosis of first acute myocardial infarction (AMI).

2 Preinfarction angina was present in 27 patients with, and 80 patients without, diabetes.

3 The absence of preinfarction angina was an independent predictor of in-hospital death and congestive heart failure in diabetic and nondiabetic patients.

4 Malignant arrhythmias were more frequent in subjects with diabetes without previous angina than in those with previous angina.

5 In conclusion, angina pectoris within 1 week of a first AMI is associated with a lower incidence of in-hospital complications in patients with diabetes, but it does not preserve left ventricular ejection fraction.

Jiménez-Navarro M, Gomez-Doblas JJ, Garci JMH, Alonso-Briales J et al (2002) Does angina pectoris the week before protect against first acute myocardial infarction in patients with diabetes mellitus? *The American Journal of Cardiology* 90: 160–2

5 Results suggest that it might be worth considering statin therapy in people at lower risk of major vascular events.

6 Treatment with simvastatin for 5 years should prevent about 70–100 people per 1000 from suffering at least one of the major vascular events, largely irrespective of age, sex or presenting cholesterol concentrations.

Heart Protection Study Collaborative Group (2002) MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20536 high-risk individuals: a randomised placebo-controlled trial. *The Lancet* 360: 7–22

THE LANCET



Simvastatin

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

1 This study aimed to assess the long-term effects of cholesterol-lowering therapy on vascular and non-vascular mortality and major morbidity in a wide range of circumstances.

2 Over a 5-year treatment period, 20536 adults (aged 40–80 years) with coronary disease, other occlusive

arterial disease, or diabetes, received 40mg simvastatin daily or placebo.

3 All-cause mortality was reduced by 12.9% with simvastatin and by 14.7% with placebo. Simvastatin produced reductions of about 25% in the first event rate for non-fatal myocardial infarction (MI) or coronary death, for non-fatal or fatal stroke, and for coronary or non-coronary revascularisation.

4 Lowering LDL cholesterol with 40mg simvastatin daily substantially reduced the incidence of MI, stroke and revascularisation by about 25% among a wide range of high-risk individuals, irrespective of their initial cholesterol concentrations. These benefits are additional to those of other treatments.

‘Coronary stent implantation reduces the rate of occlusive restenosis in diabetics treated with balloon angioplasty.’

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Coronary stenting

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

1 This study aimed to compare coronary stent implantation with balloon angioplasty (BA) in 314 patients with diabetes undergoing percutaneous coronary revascularisation (PCR) without any pharmacological adjunct.

2 At 6 months, the rates of restenosis (27% vs 62%) and occlusion (4% vs 13%) were lower in the stent group than in the BA group. These were associated with a significant decrease in ejection fraction at 6 months in the BA group, but no change in the stent group.

3 At 4 years, the combined clinical endpoint of cardiac death and non-fatal myocardial infarction was lower in the stent group (14.8% vs 26%), as was the need for repeat revascularisation (35.4% vs 52.1%).

4 Coronary stent implantation reduces the rate of occlusive restenosis and partly prevents the deterioration of left ventricular function observed at 6 months in diabetics treated with BA.

5 This study demonstrates that the use of coronary stents might improve the long-term clinical outcome of diabetic patients who have had PCR.

6 It also suggests that coronary stents, alone or in combination with glycoprotein IIb/IIIa blockade, should be used as a standard therapy for PCR in this group of patients, particularly when single-vessel revascularisation needs to be performed.

van Belle E, Perie M, Braune D, Chmait A et al (2002) Effects of coronary stenting on vessel patency and long-term clinical outcome after percutaneous coronary revascularization in diabetic patients. *Journal of the American College of Cardiology* 40(3): 410–17

‘The presence of baseline silent myocardial infarction and microalbuminuria are associated with future CHD events in asymptomatic patients with type 2 diabetes.’

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Coronary artery bypass grafts

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

1 To determine the impact of diabetes on short-term mortality and morbidity in patients undergoing coronary artery bypass surgery (CABG), the authors studied 146786 patients, with and without diabetes.

2 Cardiac disease was the most common mode of death, although neurological, pulmonary and infectious disorders were also common causes.

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Predicting coronary events

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

1 Patients with type 2 diabetes, with or without microalbuminuria (MA), and free from known CHD, were followed up for 2.8 years to investigate the relationships between future CHD events and baseline silent myocardial ischaemia (SMI) and MA.

Intracoronary radiation

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

1 Outcomes of intracoronary radiation therapy (IRT) and placebo were compared in diabetic and nondiabetic patients with in-stent restenosis (ISR).

2 For diabetics, in-hospital outcomes were similar whether treated with radiation or placebo. At 6-month clinical and angiographic follow-up, radiation reduced binary restenosis (76%), target lesion revascularisation (74%) and target vessel revascularisation (68%).

3 In diabetics with ISR, intracoronary radiation significantly reduced the

3 morbidity, infections and the composite outcomes occurred more commonly in diabetic patients than in nondiabetics, and were associated with an adjusted risk about 35% higher in diabetics than in nondiabetics.

4 Increased risk of death or postoperative complications occurred most commonly in patients treated with insulin.

5 The study concludes that diabetes is an important risk factor for mortality and morbidity among those undergoing CABG.

Carson JL, Scholz PM, Chen AY, Peterson ED et al (2002) Diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery. *Journal of the American College of Cardiology* 40(3): 418–23

2 Of the 86 patients studied, 15 had CHD events; these were significantly related to baseline ankle brachial index (ABI), SMI, MA, 10-year Framingham CHD risk >30%, and fibrinogen.

3 SMI was the strongest independent predictor of CHD events.

4 The presence of baseline SMI and MA is associated with future CHD events in asymptomatic patients with type 2 diabetes. The study suggests that SMI, MA and ABI could be of practical value in risk stratification.

Rutter MK, Wahid ST, McComb JM, Marshall SM (2002) Significance of silent ischemia and microalbuminuria in predicting coronary events in asymptomatic patients with type 2 diabetes. *Journal of the American College of Cardiology* 40(1): 56–61

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recurrence of ISR compared with placebo.

4 In-hospital outcomes were similar in diabetics and nondiabetics, with or without radiation. Comparison of the placebo arms detected a trend towards higher restenosis and target vessel revascularisation in diabetics vs nondiabetics. By contrast, the groups treated with IRT had similar rates of restenosis and revascularisation procedures.

Gruberg L, Waksman R, Ajani AE, Kim, H-S et al (2002) The effect of intracoronary radiation for the treatment of recurrent in-stent restenosis in patients with diabetes mellitus. *Journal of the American College of Cardiology* 39(12): 1930–6

‘In diabetics with in-stent restenosis, intracoronary radiation significantly reduced the recurrence of in-stent restenosis compared with placebo.’