










Atorvastatin reduced major cardiovascular disease events in type 2 diabetes mellitus

Colhoun HM, Betteridge DJ, Durrington PN, *et al.* Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 2004;**364**:685–96.

Clinical impact ratings GP/FP/Primary care ★★★★★☆ IM/Ambulatory care ★★★★★☆ Endocrine ★★★★★★
Cardiology ★★★★★☆

Q In patients with type 2 diabetes mellitus, is atorvastatin better than placebo for primary prevention of major cardiovascular disease (CVD) events?

METHODS

-  **Design:** randomised placebo controlled trial (Collaborative Atorvastatin Diabetes Study [CARDS]).
-  **Allocation:** concealed.*
-  **Blinding:** blinded (clinicians, patients, pharmacists, data collectors, outcome assessors, monitoring committee, and data analysts).*
-  **Follow-up period:** median 3.9 years.
-  **Setting:** 132 clinical centres in the UK and Ireland.
-  **Patients:** 2838 patients 40–75 years of age (mean age 62 y, 68% men) with type 2 diabetes mellitus (met 1985 World Health Organization criteria) who had ≥1 of the following: a history of hypertension, retinopathy, microalbuminuria or macroalbuminuria, or a current smoking habit. Exclusion criteria included a history of CVD, plasma creatinine >150 µmol/l (1.7 mg/dl), glycated haemoglobin >12%, and <80% compliance with placebo during the baseline phase.
-  **Intervention:** atorvastatin, 10 mg daily (n = 1429), or placebo (n = 1412).
-  **Outcomes:** a composite endpoint consisting of an acute coronary heart disease event (myocardial infarction including silent infarction, unstable angina, acute coronary heart disease death, or resuscitated cardiac arrest), coronary revascularisation procedures, or stroke.
-  **Patient follow up:** 99% (intention to treat analysis).

*See glossary.

MAIN RESULTS

The atorvastatin group had a lower rate of the composite endpoint than the placebo group (table). When assessed individually, the atorvastatin group had lower rates for acute coronary events and stroke, but not for coronary revascularisation (table).

CONCLUSION

In patients with type 2 diabetes mellitus, atorvastatin reduced major cardiovascular disease events.

Abstract and commentary also appear in ACP Journal Club

Commentary

Before the trial by Colhoun *et al.*, evidence for lipid lowering for primary prevention of CVD in patients with diabetes came only from the Heart Protection Study (HPS)¹ and subgroup analyses from trials in which treatment allocation was not stratified by diabetes status.^{2,3} In CARDS, patients with type 2 diabetes and 1 other risk factor for coronary artery disease or retinopathy had a 35% relative risk reduction in CVD attributed to atorvastatin, 10 mg daily, similar to a 33% relative risk reduction in CVD with simvastatin, 40 mg daily in the HPS.¹

Participants' baseline mean low density lipoprotein (LDL) level (3.0 mmol/L [117 mg/dL]) was unchanged in the placebo group but decreased by 31% in the atorvastatin group after 4 years. Prevention of CVD attributed to atorvastatin was of a similar magnitude regardless of participants' baseline lipid levels, which suggests that a threshold level below which statin therapy should be withheld does not exist.

These data show that substantial CVD risk reductions can be realised by achieving relative reductions in LDL levels with 1 drug at a fixed dose, but neither the CARDS nor the HPS addressed the risk or benefit for further LDL reduction with increasing doses of drugs or combinations of drugs to target "goal" lipid concentrations.

In CARDS and HPS, adverse events including rhabdomyolysis did not increase with statin therapy. Although participants in randomised controlled trials may not represent all patients seen in clinical practice, participants in CARDS had comorbid conditions similar to most patients with diabetes. The CARDS and HPS provide conservative estimates of 25–27% for 10 year risk of CVD in untreated patients with diabetes and direct evidence of the substantial benefit and low risk of statin therapy for primary prevention of CVD.

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1 Collins R, Armitage J, Parish S, *et al.* *Lancet* 2003;**361**:2005–16.

2 Gami AS, Montori VM, Erwin PJ, *et al.* *BMJ* 2003;**326**:528–9.

3 Sever PS, Dahlöf B, Poulter NR, *et al.* *Lancet* 2003;**361**:1149–58.

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Sources of funding: Diabetes UK; UK Department of Health; Pfizer UK; Pfizer Inc.

Atorvastatin v placebo in patients with type 2 diabetes mellitus at median 3.9 years†

Outcomes	Atorvastatin	Placebo	RRR (95% CI)	NNT (CI)
Composite endpoint	5.8%	9.0%	35% (16 to 51)	32 (20 to 79)
Acute coronary events	3.6%	5.5%	35% (8 to 54)	53 (29 to 273)
Stroke	1.5%	2.8%	47% (11 to 68)	78 (42 to 411)
Coronary revascularisation	1.7%	2.4%	30% (–16 to 58)	Not significant

†Composite endpoint = an acute coronary heart disease event, coronary revascularisation, or stroke. Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article.