

Pravastatin lowered coronary disease risk in elderly persons with or at risk for vascular disease

Shepherd J, Blauw GJ, Murphy MB, et al. **Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial.** *Lancet.* 2002;360:1623-30.

QUESTION

In elderly persons with or at risk for vascular disease, what is the effectiveness and safety of pravastatin?

DESIGN

Randomized (allocation concealed*), blinded (clinicians, participants, data collectors, outcome assessors),* placebo-controlled trial with mean follow-up of 3.2 years (Prospective Study of Pravastatin in the Elderly at Risk [PROSPER]).

SETTING

Scotland, Ireland, and the Netherlands.

PARTICIPANTS

5804 participants between 70 and 82 years (mean age 75 y, 52% women) who had a history of vascular disease (coronary, cerebral, or peripheral) or risk factors for vascular disease (e.g., smoking, hypertension, or diabetes), a total plasma cholesterol level between 4.0 and 9.0 mmol/L, and a triglyceride level < 6.0 mmol/L. Participants with poor cognitive function (Mini Mental State Examination score < 24) were excluded. Follow-up was 100%.

INTERVENTION

Participants were allocated to pravastatin, 40 mg/d ($n = 2891$), or placebo ($n = 2913$).

MAIN OUTCOME MEASURES

Composite endpoint of coronary death, nonfatal myocardial infarction (MI), or fatal or nonfatal stroke (primary composite endpoint); composite endpoint of coronary death or nonfatal MI; composite endpoint of fatal or nonfatal stroke; and adverse events.

MAIN RESULTS

Analysis was by intention to treat. Pravastatin lowered the risk for the primary composite endpoint and the composite endpoint of coronary death or nonfatal MI (Table). The

pravastatin and placebo groups did not differ for the composite endpoint of fatal or nonfatal stroke, but pravastatin was associated with a greater risk for having a new cancer diagnosis (Table).

CONCLUSION

In elderly persons with or at risk for vascular disease, pravastatin lowered the risk for coronary disease events.

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*See Glossary.

Pravastatin vs placebo in elderly persons with or at risk for vascular disease at mean 3.2 years†

Outcomes	Pravastatin	Placebo	RRR (95% CI)	NNT (CI)
Primary composite endpoint‡	14%	16%	13% (1.8 to 23)	47 (25 to 359)
Coronary death or nonfatal MI	10%	12%	17% (4 to 29)	47 (27 to 199)
			RRI (CI)	NNH
Fatal or nonfatal stroke	4.7%	4.5%	4% (-18 to 31)	Not significant
New cancer diagnoses	8.5%	6.8%	24% (4 to 48)	61 (33 to 362)

†MI = myocardial infarction. Other abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

‡Primary composite endpoint = coronary death, nonfatal MI, or fatal or nonfatal stroke.

COMMENTARY

With proof that lowering cholesterol levels decreases mortality in high-risk, middle-aged patients, it is appropriate to focus attention on the elderly. Beyond about 75 years of age, serum cholesterol levels contribute less to the risk for coronary heart disease than they do between the ages of 55 and 75 years, but coronary mortality is higher.

The results of the PROSPER study extend the results of a subgroup analysis of the Heart Protection Study (1) that showed significant effects of statin therapy on cardiovascular events in older patients. PROSPER failed to confirm decreased stroke rates with statin therapy, probably because of short follow-up and a lower-than-expected background stroke rate. Many participants in the study, however, had systolic hypertension at baseline (mean systolic blood pressure 155 mm Hg), and control of this risk factor might have lessened the effect of statin therapy on stroke (and MI) even more. The finding of increased malignancy rates in patients treated with statins should not be viewed as credible. This finding contradicts a larger body of evidence showing that no such increased risk exists and is more likely the result of chance.

Elderly patients and their caregivers often choose therapies that preserve functional status rather than those that decrease mortality. PROSPER failed to show reductions in cognitive and functional decline, but the measures used in the study were insensitive to change in persons with high levels of function.

On the whole, the results of PROSPER give providers and elderly patients data on which to individualize therapeutic decisions. Elderly patients who are highly functional, have vascular disease or high cholesterol levels and 1 other risk factor, and wish to maximize life span will probably choose statin therapy. Similar patients whose only goal is to preserve their current functional level will probably forgo therapy.

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Reference

1. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet.* 2002;360:7-22.