Primary prevention with pravastatin for 5 years continued to prevent coronary events in the following 10 years

Ford I, Murray H, Packard CJ, et al. **Long-term follow-up of the West of Scotland Coronary Prevention Study.** N Engl J Med. 2007;357:1477-86.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Cardiology ★★★★★☆☆

QUESTION

In middle-aged men with hypercholesterolemia and no history of myocardial infarction (MI), does 5 years of pravastatin treatment have long-term benefits for prevention of coronary heart disease (CHD)?

METHODS

Design: Long-term, posttrial follow-up of a 5-year, randomized, placebo-controlled trial.
Allocation: Unclear allocation concealment.*
Blinding: Blinded during the trial period {clinicians, patients, data collectors, and outcome adjudication committees}†.*
Follow-up period: Original trial follow-up was 5 years; this study followed surviving patients (96%) for another 10 years.
Setting: {Coronary screening clinics throughout West Scotland, United Kingdom}†.
Patients: 6595 men {45 to 64 y of age}† (mean age 55 y) with no history of MI and low-density lipoprotein cholesterol levels ≥ 155 mg/dL (4.01 mmol/L) on 2 occasions {mean 192 mg/dL (4.97 mmol/L)}†.
Intervention: Pravastatin, 40 mg daily (n = 3302), or placebo (n = 3293) for 5 years. When the trial ended in 1995, {70% of men in each group}† were still taking the study drug. After this time, treatment with statins was at the discretion of each man's primary care physician.
Outcomes: Death from any cause, CHD, cardiovascular disease, or cancer; CHD-related death or MI; CHD-related death or hospitalization; stroke; and cancer.
Patient follow-up: 100% (intention-to-treat analysis).

MAIN RESULTS

5 years after the end of the trial, 39% of men in the pravastatin group and 35% in the placebo group were receiving statin therapy (P < 0.001). Results of the posttrial period, including sustained relative risk reductions in cardiovascular events for the total follow-up, are shown in the Table. Groups did not differ during any period for overall incidence of cancer or death from cancer. The only difference in risk for specific types of cancer was an increase in prostate cancer in the pravastatin group (hazard ratio 1.5, 95% CI 1.1 to 2.0).

CONCLUSION

In middle-aged men with hypercholesterolemia and no history of myocardial infarction, 5 years of pravastatin treatment continued to prevent coronary heart disease events in the following 10 years.

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*See Glossary.

†**Shepherd J, Cobbe SM, Ford I, et al.** N Engl J Med. 1995;333:1301-7.

Pravastatin vs placebo for 5 years for primary prevention of coronary heart disease (CHD) in middle-aged men with hypercholesterolemia‡

Outcomes	Trial period (5 y)	Posttrial period (10y)				Total follow-up period (15 y)
	RRR (95% CI)	Pravastatin	Placebo	RRR (CI)	NNT (CI)	RRR (CI)
Death from CHD or nonfatal MI	39% (24 to 51)	8.6%	10%	17% (4 to 30)	57 (33 to 256)	25% (16 to 35)
CHD-related death or hospitalization	33% (19 to 43)	16%	19%	18% (9 to 27)	29 (20 to 58)	22% (15 to 29)
Death from CHD	34% (2 to 56)	4.1%	4.7%	17% (–5 to 33)	Not significant	21% (4 to 35)
Death from cardiovascular disease	34% (5 to 54)	6.4%	7.2%	14% (–4 to 28)	Not significant	18% (4 to 31)
Death from all causes	24% (2 to 40)	16%	17%	8% (–3 to 18)	Not significant	11% (1 to 19)
Stroke	33% (–4 to 57)	5.1%	5.6%	12% (–8 to 28)	Not significant	17% (–1 to 31)

‡MI = myocardial infarction; other abbreviations defined in Glossary. RRR, NNT, and CI calculated from hazard ratios in article, adjusted for other risk factors.

COMMENTARY

This analysis of the long-term follow-up of the West of Scotland Coronary Prevention Study aimed to assess the ongoing safety and efficacy of 5 years of pravastatin therapy in moderately high-risk men without previous MI (average 10-year Framingham risk score 17%). Despite only 39% of the intervention group receiving statin therapy compared with 35% of the control group 5 years after the end of the trial, the intervention group showed a clinically and statistically significant 25% reduction in CHD-related death or MI over the total follow-up period (trial period plus posttrial period). The absolute risk reduction was 3.7% (11.8% in the intervention group vs 15.5% in the placebo group), which translates into a number needed to treat of 27. In terms of safety, the study showed an 11% relative reduction in overall mortality in the intervention group and no increased risk for death from cancer; however, the authors observed an increase in prostate cancer incidence (2.7% vs 1.8%).

This evidence should help clinicians concerned about the efficacy and safety of long-term statin use for primary prevention in high-risk, middle-aged men. However, certain caveats should be considered when interpreting the data. The benefits of a placebo-controlled randomized trial in blinding outcome assessments were abandoned once the formal trial ended. The low level of continued use of statins in the intervention group (39%), and concomitant use of statins in the control group (35%), probably led to underestimation of the long-term benefits of statin therapy in this study. Future studies should determine if these benefits apply to younger cohorts, those with lower overall CHD risk, and women.

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