

Review: Lipid-lowering drugs decrease CAD events but not all-cause or CAD mortality in men with no history of CAD

Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. *BMJ*. 2000 Oct 21;321:983-6.

QUESTION

In patients with no history of coronary artery disease (CAD), does a lipid-lowering drug (cholestyramine, gemfibrozil, pravastatin, or lovastatin) decrease the risk for CAD events, CAD mortality, or all-cause mortality?

DATA SOURCES

English-language studies were identified by searching MEDLINE (1994 to June 1999) with the Medical Subject Headings (MeSH) hyperlipidemia and anti-cholesterolemic agents and with MeSH or keywords identifying randomized controlled trials and individual drug names, the Cochrane Clinical Trials Registry, and bibliographies of systematic reviews and clinical practice guidelines.

STUDY SELECTION

Randomized controlled trials were selected if they had ≥ 1 year of duration and measured CAD events, CAD mortality, and all-cause mortality. Exclusion criteria were studies of secondary prevention or studies published in abstract form only.

DATA EXTRACTION

Data were extracted on each drug and its dosage, study duration, population characteristics and size, initial and mean reduction

in cholesterol levels, CAD events, CAD mortality, and all-cause mortality.

MAIN RESULTS

4 randomized controlled trials met the inclusion criteria. 21 087 patients (mean age 53 y, 95% men) received a lipid-lowering drug (50%) or placebo (50%). Duration was 7 years (1 study) or 5 years (3 studies). The mean initial total cholesterol level was ≥ 7.0 mmol/L in 3 of the 4 trials. Mean reductions in cholesterol levels were 8.5% for cholestyramine, 10% for gemfibrozil, and 18% to 20% for high-dose statins. Treatment decreased CAD events but not CAD mortality or all-cause mortality (Table). When analysis was

limited to the 2 trials that used statins, the results were similar.

CONCLUSION

In patients with no history of coronary artery disease (CAD), lipid-lowering drugs decrease the risk for CAD events but not CAD mortality or all-cause mortality.

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Lipid-lowering drugs (LLDs) vs placebo for decrease of coronary artery disease (CAD) events and mortality and all-cause mortality in patients with no history of CAD*

Outcomes at median 5 y	Unweighted event rates		RRR (95% CI) weighted	NNT (CI) weighted
	LLDs	Placebo		
CAD events in all 4 studies	4.2%	5.8%	28% (19 to 36)	69 (49 to 120)
CAD events in 2 statin studies	3.5%	5.2%	33% (21 to 43)	69 (49 to 120)
CAD mortality in all 4 studies	0.9%	1.2%	25% (2 to 43)	Not significant
CAD mortality in 2 statin studies	0.7%	1%	27% (-5 to 49)	Not significant
All-cause mortality in all 4 studies	2.8%	3.1%	8% (-7 to 21)	Not significant
All-cause mortality in 2 statin studies	2.8%	3.2%	12% (-6 to 28)	Not significant

*Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data provided by author.

COMMENTARY

The meta-analysis by Pignone and colleagues reinforces the first rule of primary prevention for CAD: Absolute reduction in mortality is proportional to overall risk for CAD. Although the authors conclude that "treatment with lipid lowering drugs . . . reduces CHD [sic] events but not all-cause mortality in people with no known cardiovascular disease," they also point out that the West of Scotland Coronary Prevention Study (1), whose participants had a relatively high risk for CAD (8%), had a reduction in all-cause mortality with pravastatin. Furthermore, a previous meta-analysis that did not include a trial whose participants were at very low risk also suggested that lipid lowering reduces all-cause mortality (2).

The meta-analysis by Pignone and colleagues relies on high-quality studies but does not give us reliable information on adverse event rates. The results of these studies may not be generalizable to other populations, particularly the elderly and women, because these demographic groups were underrepresented in the trials considered in the meta-analysis.

Lipid lowering was not shown to reduce all-cause or CAD mortality in patients at low risk for CAD probably because it takes larger num-

bers of patients or longer trials to show small, statistically significant absolute reductions in mortality. We have no reason to believe that lipid lowering increases noncoronary mortality. Physicians should continue to consider lipid lowering for primary prevention. As pointed out by the authors, overall CAD risk should be calculated and used to select higher-risk patients for treatment with lipid-lowering drugs (3). For low-risk patients, issues of cost-effectiveness may predominate.

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References

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3. Jackson R Guidelines on preventing cardiovascular disease in clinical practice. *BMJ*. 2000;320:659-61.