

Review: Lipid-lowering agents reduce cardiovascular events in type 2 diabetes

Vijan S, Hayward RA. Pharmacologic lipid-lowering therapy in type 2 diabetes mellitus: background paper for the American College of Physicians. *Ann Intern Med.* 2004;140:650-8.

QUESTION

In patients with type 2 diabetes mellitus, do lipid-lowering agents reduce cardiovascular disease (CVD) events?

METHODS

Data sources: Cochrane Library, MEDLINE (to September 2002), contacting experts, and references in retrieved studies and reviews.

Study selection and assessment: Randomized controlled trials (RCTs) of lipid-lowering agents that evaluated major CVD events in patients with type 2 diabetes. Studies were categorized for primary prevention (patients with no known coronary artery disease [CAD]) and secondary prevention (patients with known CAD).

Outcomes: Major CVD events (CVD mortality, myocardial infarction, and depending on the trial, other such CV events as stroke, angina, and revascularization).

MAIN RESULTS

12 RCTs met the selection criteria: 4 focused on primary prevention ($n = 6460$), 6 focused on secondary prevention ($n = 2515$), and

2 had data on both ($n = 6586$). The intervention drugs were statins (lovastatin, pravastatin, simvastatin, atorvastatin, and fluvastatin) and fibrates (gemfibrozil). The control treatment was placebo in 11 trials; 1 trial compared aggressive with moderate cholesterol lowering. No significant between-study differences existed among primary-prevention trials; significant and unexplained differences existed among secondary-prevention trials. Lipid-lowering agents reduced the risk for major CVD events in both primary and secondary prevention (Table).

CONCLUSION

In patients with type 2 diabetes mellitus (with or without coronary artery disease), lipid-lowering agents reduce cardiovascular disease events.

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Lipid-lowering agents vs control for cardiovascular disease events in patients with type 2 diabetes*

Category	Number of trials	Weighted event rates		RRR (95% CI)	NNT (CI)
		Lipid-lowering agents	Control†		
Primary prevention‡	6§	10%	13%	22% (11 to 33)	35 (25 to 100) for 4.3 y
Secondary prevention	8	28%	35%	24% (7 to 41)	14 (9 to 36) for 4.9 y

*Abbreviations defined in Glossary; weighted event rates and CI for NNT calculated from data in article.

†Control intervention was placebo in 11 of 12 trials.

‡A fixed-effects model was used.

§Data from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT) are included in the pooled RRR but not weighted event rates or NNT because they were not available.

||A random-effects model was used.

COMMENTARY

Recent guidelines recommended lipid-lowering therapy for all patients with diabetes (1). However, direct evidence to support this recommendation was lacking (2). Vijan and Hayward have incorporated the latest data (some unpublished) in this meta-analysis and provide new and important insights into the role of lipid-lowering agents in these patients.

The meta-analysis is well designed but lacks assessment of publication bias, quality assessments of trials, and adequate subgroup analyses to test explanations for between-trial differences, including characteristics of the trial populations, study drugs and doses, and outcome definitions.

As expected, the meta-analysis confirms the substantial benefit of lipid lowering in patients (diabetic or not) with established CAD. More important, it provides the first pooled data (dominated by the Heart Protection Study [3]) regarding the benefits of primary prevention in diabetic patients. The absolute risk reduction for primary prevention was only 3%. This was because of baseline risks of 4% to 19%, which are considerably lower than the baseline risks of 23% to 45% for diabetic patients in the secondary prevention trials. This discrepancy highlights the fact that diabetes is not simply a "coronary heart disease equivalent" as has been suggested. Rather, diabetic patients should be considered candidates for lipid-lowering agents in a manner similar to that for other patients: on the basis of individual baseline risk for CVD events. The available evidence, summarized by Vijan and Hayward,

suggests that diabetic patients who are at very low risk might not necessarily benefit from lipid-lowering agents. Their data also suggest that treating to achieve arbitrary low-density lipoprotein goals may be less important than just establishing a moderate dose of an agent.

This and other persisting questions, such as whether a specific lipid-lowering agent is superior to another, especially in diabetic patients with low high-density lipoprotein levels, and whether drug combinations provide increased benefit without prohibitive risks, remain unanswered.

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References

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