Review: Cholesterol-lowering treatment with statins reduces all-cause mortality in persons at risk


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

Question
In persons at risk, do cholesterol-lowering interventions reduce mortality?

Methods
Data sources: [Computer databases, relevant journals, bibliographies of relevant articles, lists of conference abstracts, the trial register of the International Committee on Thrombosis and Haemostasis, researchers in the field, and manufacturers of lipid-modifying drugs]*.

Study selection and assessment: Unconfounded randomized controlled trials (RCTs) that compared a statin with a control condition (placebo or usual care) for ≥2 years, and enrolled ≥1000 participants.

Outcomes: All-cause mortality, coronary heart disease (CHD) mortality, and non-CHD mortality. Secondary outcomes included major coronary events (a composite outcome of nonfatal myocardial infarction [MI] or CHD death), major vascular events (a composite outcome of major coronary events, nonfatal or fatal stroke, or coronary revascularization), and incidence of cancer.

Main results
14 RCTs (n = 90,056, age range 18 to 82 y, 76% men) met the selection criteria. Meta-analyses assessed the effects on clinical outcomes in each trial weighted by the absolute risk reduction (ARR) for MI or coronary death was 3.8% (95% CI 2.9 to 4.7), suggesting diminishing, although still important, benefits at lower LDL cholesterol levels.

Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Statins</th>
<th>Control</th>
<th>RRR ‡ (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>8.5%</td>
<td>9.7%</td>
<td>12% (9 to 16)</td>
<td>87 (65 to 115)</td>
</tr>
<tr>
<td>Coronary heart disease (CHD)</td>
<td>3.4%</td>
<td>4.4%</td>
<td>19% (15 to 24)</td>
<td>121 (96 to 154)</td>
</tr>
<tr>
<td>Non-CHD vascular mortality</td>
<td>1.2%</td>
<td>1.3%</td>
<td>7% (3 to 7)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Nonvascular mortality</td>
<td>3.8%</td>
<td>4.0%</td>
<td>5% (1 to 11)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Any major coronary event</td>
<td>7.4%</td>
<td>9.8%</td>
<td>23% (20 to 26)</td>
<td>45 (40 to 51)</td>
</tr>
<tr>
<td>Any major vascular event</td>
<td>14.1%</td>
<td>17.8%</td>
<td>21% (19 to 23)</td>
<td>27 (25 to 30)</td>
</tr>
<tr>
<td>Cancer incidence</td>
<td>6.4%</td>
<td>6.4%</td>
<td>0% (1 to 10)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

★Any major coronary event = nonfatal myocardial infarction or CHD mortality; any major vascular event = a major coronary event, nonfatal or fatal stroke, or coronary revascularization. Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

Hydroxymethylglutaryl-CoA reductase inhibitors (statins) vs control (e.g., placebo or usual care) in persons at risk at 5 years†

Commentary
The meta-analysis by the Cholesterol Treatment Trials’ Collaboration confirms that lowering LDL cholesterol with statins significantly reduces CHD mortality, MI stroke, and coronary revascularization without increasing nonvascular mortality or cancer incidence.

Statins had a good toxic-to-therapeutic ratio: For every patient with a statin-induced excess case of rhabdomyolysis, 174 persons did not die and 361 people did not have an MI or coronary death.

Regardless of starting LDL cholesterol level, the authors found that each 39 mg/dL (1.0 mmol/L) statin-induced reduction in LDL cholesterol was associated with a one-eighth relative reduction in all-cause mortality and a one-fifth relative reduction in major vascular events. While this was true for relative risk, it was not true for absolute risk. The absolute risk reduction (ARR) for MI or coronary death was 3.8% for LDL cholesterol > 173 mg/dL (> 4.47 mmol/L) (number needed to treat [NNT] = 28), 2.3% for LDL cholesterol 135 to 173 mg/dL (3.49 to 4.47 mmol/L) (NNT = 43), and 1.9% for LDL cholesterol < 135 mg/dL (< 3.49 mmol/L) (NNT = 53), suggesting diminishing, although still important, benefits at lower LDL cholesterol levels.

When LDL cholesterol is high, statins are clearly indicated. The When LDL cholesterol is high, statins are clearly indicated. The absolute risk reduction (ARR) for MI or coronary death was 3.8% for LDL cholesterol > 173 mg/dL (> 4.47 mmol/L) (number needed to treat [NNT] = 28), 2.3% for LDL cholesterol 135 to 173 mg/dL (3.49 to 4.47 mmol/L) (NNT = 43), and 1.9% for LDL cholesterol < 135 mg/dL (< 3.49 mmol/L) (NNT = 53), suggesting diminishing, although still important, benefits at lower LDL cholesterol levels.

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References