Atorvastatin reduced coronary and stroke events in patients with hypertension and without dyslipidemia


**Question**
In patients with hypertension and no dyslipidemia, is atorvastatin effective for primary prevention of coronary heart disease (CHD)?

**Design**
Randomized (allocation concealed*)†‡, blinded {patients, health care providers, data collectors, outcome assessors, and data analysts}†,* placebo-controlled trial with median follow-up of 3.3 years (ASCOT-LLA).

**Setting**
Centers in 8 countries.

**Patients**
10 305 patients who were 40 to 79 years of age (mean age 63 y; 81% men) with uncontrolled hypertension, nonfasting total cholesterol level ≤ 6.5 mmol/L, and ≥ 3 other cardiovascular (CV) disease risk factors who were not taking a statin or fibrate. Exclusion criteria were previous myocardial infarction (MI), angina, cerebrovascular event in the previous 3 months, fasting triglyceride levels > 1.7 mmol/L, ≤ 65 mmHg for those with diabetes.

**Intervention**
Patients were allocated to atorvastatin, 10 mg/d (n = 5168), or placebo (n = 5137). Patients were part of 19 342 participants in the ASCOT trial allocated to 1 of 2 antihypertensive regimens aimed at achieving target blood pressures < 140/90 mm Hg for those without diabetes and < 130/80 mm Hg for those with diabetes.

**Main outcome measures**
Primary outcome was the combined endpoint of nonfatal MI and fatal CHD. Secondary endpoints were the primary outcome without silent events, total CV events, total coronary events, all-cause mortality, total CV mortality, fatal and nonfatal stroke, and fatal and nonfatal heart failure.

**Main results**
Analysis was by intention to treat. Compared with placebo, atorvastatin was associated with lower risk for the primary endpoint, the primary outcome excluding silent events, total CV events including revascularization procedures, total coronary events, and fatal and nonfatal stroke (Table). Groups did not differ for all-cause mortality, total CV mortality, fatal and nonfatal heart failure, or serious adverse events.

**Conclusion**
In patients with hypertension and other cardiovascular risk factors and without dyslipidemia, atorvastatin reduced coronary and stroke events at a median follow-up of 3.3 years.

*See Glossary.
†Information provided by author.
‡MI = myocardial infarction; CHD = coronary heart disease. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article using Cox proportional-hazards model.

**Outcomes**
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Atorvastatin</th>
<th>Placebo</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonfatal All and fatal CHD</td>
<td>1.9%</td>
<td>3.0%</td>
<td>36% (17 to 50)</td>
<td>94 (68 to 200)</td>
</tr>
<tr>
<td>Nonfatal All and fatal CHD without silent events</td>
<td>1.7%</td>
<td>2.7%</td>
<td>38% (19 to 58)</td>
<td>99 (65 to 198)</td>
</tr>
<tr>
<td>Total cardiovascular events</td>
<td>7.5%</td>
<td>9.5%</td>
<td>20% (10 to 30)</td>
<td>53 (36 to 111)</td>
</tr>
<tr>
<td>Total coronary events</td>
<td>3.4%</td>
<td>4.8%</td>
<td>28% (14 to 40)</td>
<td>74 (52 to 153)</td>
</tr>
<tr>
<td>Fatal and nonfatal stroke</td>
<td>1.7%</td>
<td>2.4%</td>
<td>27% (4 to 44)</td>
<td>156 (96 to 1054)</td>
</tr>
</tbody>
</table>


**Commentary**
Except for the ALLHAT, which was nonblinded and suffered from the frequent use of statins among participants who were allocated to placebo (1), ASCOT-LLA joins other primary and secondary CHD prevention studies showing that lowering low-density lipoprotein cholesterol (LDL-C) with statins prevents CHD events among persons at higher CHD risk. Primary CHD-prevention statin trials, including ASCOT-LLA, when taken together have additionally shown a trend toward lower all-cause mortality. The reduction in events seems to be a class-effect (i.e., not restricted to certain statins). Although benefit correlates with the magnitude of cholesterol lowering, statins have important effects on inflammatory markers, plaque stabilization, nitric oxide production, and thrombosis that probably add to their effectiveness.

Participants in ASCOT-LLA had a mean baseline LDL-C level of 3.4 mmol/L but were at higher risk based on their CHD risk factor profile. A 10-mg dose of atorvastatin decreased LDL-C levels by approximately 1.0 mmol/L, and with the notable exception of women, all subgroups benefited from treatment. However, even among this higher-risk cohort, 94 patients had to receive statins for over 3 years to prevent 1 additional nonfatal MI or fatal CHD event. Although the benefits of statins are apparent across a wide range of LDL-C levels, as shown by similar relative risk reductions, the number needed to treat to prevent 1 additional event increases as the absolute CHD risk decreases. In persons at high risk, current guidelines are not being met (2); hence, treating persons likely to accrue the greatest benefit from statins still remains an unachieved goal.

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**References**