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How does high dose statin compare to low dose in people with heart disease

Clinical Question: In patients with coronary heart disease (like previous myocardial infarction), what are the benefits and harms of prescribing high dose compared to low dose statins?

Evidence: There at least 6 meta-analyses1-6:

- Most recent: 10 trials, 41,778 patients with coronary heart disease (CHD). Mean trial duration 2.5 years.
  - High dose is usually atorvastatin 80mg. Low-moderate dose varies: pravastatin 40 mg to lovastatin 5mg.
  - Outcomes:
    - No difference in death, cardiovascular death, or fatal MI.
    - High dose reduced the combined endpoint of non-fatal MI and coronary heart disease death (CHD): 9.4% vs 10.5%, Number Needed to Treat (NNT) 91 over 2.5 years.

- Other meta-analyses have similar results. High dose statins:
  - Reduced mortality in patients with acute coronary syndrome:1,3 NNT 91 over 2 years.
  - Increased adverse events leading to stopping therapy: Number Needed to Harm (NNH) 47

Context:

- In patients with CHD, low-moderate dose statin (like 40mg pravastatin or 20-40mg simvastatin) compared to placebo:7
  - Reduced CHD: NNT 27
  - Reduced mortality: NNT 56
- Benefits of low-moderate dose over placebo (relative benefit 25% for CHD7) are larger than the benefits of high dose over low-moderate dose (only 10% incremental benefit1).
- Adherence to statin therapy in the community is poor (worse than trials):
Up to 50% discontinue statin by 3 years with adverse events often cited as a reason for stopping.\textsuperscript{8-10}

Post-marketing data\textsuperscript{11,12} indicates muscle-related side effects and transaminase abnormalities increase 4-5 fold when increasing atorvastatin from 40 mg to 80 mg.

**Bottom-line:** In patients with coronary heart disease, using high dose statins (compared to low-moderate dose) prevents one CHD event for every 91 patients but results in one in 47 patients discontinuing therapy due to adverse events. However, low-moderate dose statin (compared to placebo) provides 2-3 times greater benefit than increasing to high dose statin. Therefore, getting and keeping patients on any statin is key, with dose adjusted up to tolerable levels.

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**Tools for Practice** is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. If you are not a member of the ACFP and would like to receive the TFP emails, please contact subscribetfp@acfp.ca to be added to the distribution list. Archived articles are available on the ACFP website.

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