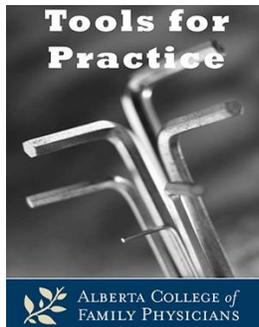


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## **Statin-Induced Diabetes: Too Sweet a Deal?**

**Clinical Question: Do statins increase the risk of diabetes, and does this worsen outcomes?**

**Bottom-line: Statins modestly increase blood glucose, which leads to 1 in 250 or so patients crossing the “diabetic threshold” over 5 years. Pre-existing elevated sugars, other diabetes risk factors or higher doses may slightly increase the risk. This should not change statin prescribing as they reduce cardiovascular events and all-cause mortality in appropriate patients.**

### **Evidence:**

- Statin versus no statin: Meta-analysis<sup>1</sup> of 13 randomized controlled trials (RCTs), with 91,140 patients with, or at high risk, of cardiovascular disease:
  - New diabetes over mean 4 years: Statins 4.9% versus control 4.5%, Number Needed to Harm (NNH) 250.
- High versus moderate/low dose statin (e.g. atorvastatin 80 mg versus 10 mg): Meta-analysis<sup>2</sup> of 5 RCTs, with 32,752 patients with cardiovascular disease:
  - New diabetes over mean 5 years: High 8.8% versus moderate/low 8%, NNH 125.

### **Context:**

- Diagnosis of type II diabetes is largely based on crossing an arbitrary laboratory threshold, like Fasting Plasma Glucose (FPG)  $\geq 7.0$  mmol/L:<sup>3</sup>
  - Elevated baseline FPG is a risk factor for developing diabetes with statins.<sup>4</sup>
  - In an observational study, FPG increased by 0.1 mmol/L at 2 years in non-diabetics taking statins.<sup>5</sup>
  - Thus, the increase in diabetes diagnoses in statin users is likely in good part from patients with borderline glucose levels crossing the diagnostic cutoff.
- Despite the increases in blood glucose, statins reduce important clinical outcomes including mortality in patients with an appropriate indication:<sup>6</sup>
  - In the Heart Protection Study,<sup>7</sup> for every 1 person newly diagnosed with diabetes due to statin use, 5 deaths, 6 non-fatal myocardial infarctions and 4 strokes were prevented over 5 years.

- Similar pooled RCT evidence shows an increased risk of diabetes with thiazides and beta-blockers versus placebo or other antihypertensives:<sup>8</sup>
  - Thiazides<sup>9</sup> and beta-blockers (in appropriate patients)<sup>10</sup> also provide net benefit.

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