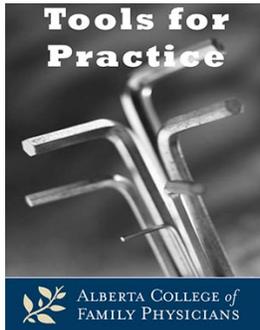


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## Fibrates: Statin's Trusty Sidekick or Lackluster Fallback?

**Clinical Question: Do fibrates reduce cardiovascular (CV) events?**

**Bottom-line: When used alone, fibrates reduce non-fatal coronary events, but have no effect on mortality or other CV events, including stroke. Current evidence suggests fibrates provide no advantage when added to statin therapy.**

### **Evidence:**

At least eight systematic reviews evaluate fibrates on CV disease with similar findings.<sup>1-8</sup> Focusing on the most up-to-date and complete:

- Meta-analysis<sup>1</sup> of 18 trials (45,058 patients) of fibrates versus placebo over one to six years:
  - 10% (confidence interval 0-18%) relative risk reduction (RRR) in CV events.
    - Primarily due to a 19% RRR in non-fatal coronary events.
  - No significant effect on all-cause mortality, vascular mortality or stroke.
  - Coronary benefits seen in both primary and secondary prevention trials.
- Only one trial (ACCORD<sup>9</sup>) evaluated a fibrate or placebo added to statin therapy:
  - No statistically significant difference in cardiovascular events over 4.7 years.
    - Fenofibrate 10.5%, placebo 11.3% (p=0.32).

### **Context:**

- Canadian dyslipidemia guidelines<sup>10</sup> offer little guidance for appropriate fibrate use.
- Before initiating a fibrate, consider optimizing other CV interventions that provide a better value, for example:
  - In a primary prevention patient with 10% risk of CV disease over 10 years:
    - Fibrates reduce CV risk to 9%.<sup>1</sup>
    - Statins reduce CV risk to 7.5%.<sup>11</sup>
    - Thiazides reduce CV risk to 7%.<sup>12</sup>
  - Whereas fibrate benefits are limited to non-fatal coronary events, statins and thiazides also reduce stroke and mortality risk.
- Theoretically fibrates could reduce the risk of pancreatitis (by reducing triglycerides). The best evidence<sup>13</sup> suggests they do the opposite:

- Fibrates increase pancreatitis (Numbers Needed to Harm (NNH)=935) at five years.
- Statins reduce pancreatitis (Numbers Needed to Treat (NNT)=1200) at five years.
- Additional potential adverse effects associated with fibrates include:
  - Venous thromboembolism (NNH ~110)<sup>14</sup> over five years.
  - Acute kidney injury (NNH ~450)<sup>15</sup> during first three months of initiation.
  - Rhabdomyolysis over five years for fibrates (NNH ~5050) and for fibrates with statins (NNH ~1975).<sup>16</sup>

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