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 10 systematic reviews evaluate fibrates on CV disease with similar findings.\textsuperscript{1-10}

Focusing on the most up-to-date and complete:

- Meta-analysis\textsuperscript{1} of 18 trials (45,058 patients) of fibrates versus placebo over 1-6 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\textsuperscript{11}) 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:

- The latest Canadian dyslipidemia guidelines\textsuperscript{12} recommend against routine use of fibrates in patients taking statins.
- 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\%;\textsuperscript{1}
    - Statins reduce CV risk to 7.5\%;\textsuperscript{13}
    - Thiazides reduce CV risk to 7\%.\textsuperscript{14}
  - 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\textsuperscript{15} suggests they do the opposite:

- Fibrates increase pancreatitis (Number Needed to Harm (NNH) = 935) at five years.
- Statins reduce pancreatitis (Number Needed to Treat (NNT) = 1,200) at five years.

Additional potential adverse effects associated with fibrates include:

- Venous thromboembolism (NNH ~ 110)\textsuperscript{16} over five years;
- Acute kidney injury (NNH ~ 450)\textsuperscript{17} during first three months of initiation;
- Rhabdomyolysis over five years for fibrates (NNH ~ 5,050) and for fibrates with statins (NNH ~ 1,975)\textsuperscript{18}.

**References:**