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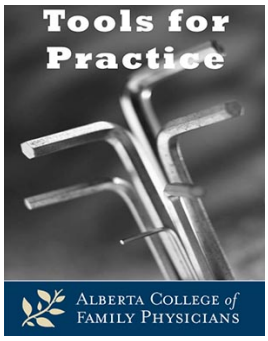
Reviewed: July 26, 2016
Evidence Updated: New evidence
Bottom Line: Large change
First Published: August 13, 2012



Varenicline and Cardiovascular Risk – Is the Cure Worse than the Affliction?

Clinical Question: Does smoking cessation with varenicline (Champix®) increase the risk of cardiovascular disease (CVD)?

Bottom Line: Varenicline does not appear to increase the risk of cardiovascular events over placebo or other smoking cessation drugs. Smoking cessation is the most effective intervention to reduce CVD risk. Varenicline is at least as good as other medications for cessation and may be slightly better.

Evidence:

- CMAJ:[1] First meta-analysis of 14 Randomized Controlled Trials (RCTs) of 8,216 patients found statistically significant increase in CVD (Peto odds ratio 1.72, 95% CI 1.09-2.71).
  - Pooled event rates: Varenicline 1.06%, placebo 0.82%.
- Subsequent meta-analyses[2-5] including more studies found no statistically significant increase in CVD:
  - Meta-analysis of 38 RCTs (12,706 patients):[4] Relative risk 1.03, 0.72-1.49.
    - Pooled event rates: Varenicline 0.79% versus placebo 0.78%.
  - Meta-analysis[5] of CVD risk with smoking cessation therapies found:
    - No increase in major CVD events with bupropion, nicotine replacement therapy (NRT), or varenicline versus placebo.
    - An increased risk of CVD events of any severity with NRT (mostly low-risk events like transient tachycardia): NRT 2.8% versus placebo 1.6%.
- All meta-analyses limited by included studies:
  - Few CVD events limiting power.
  - CVD outcomes not systematically recorded in most RCTs.
  - High drop-out rates (up to 30%).
- Three large observational studies[6-8] (total 278,596 patients on varenicline) found no difference in CVD risk between smokers taking varenicline versus bupropion.

Context:

- RCT of smoking cessation (counselling plus bupropion or nicotine replacement) after coronary care unit admission:[9]
  - 9% absolute reduction in mortality at two years despite ≤40% abstinent.
- Varenicline may be the most effective smoking cessation drug.[10] Number Needed to Treat (NNT) for different meds after one year, based on 10% cessation with placebo.
  - Varenicline NNT=8, Nortriptyline NNT=10, bupropion NNT=10.
- Concerns were also raised about an association between varenicline and an increased risk of depression and self-harm.
  - Multiple RCTs and observational studies, including patients with stable psychiatric disoders,[11] show no increased risk of adverse neuropsychiatric events.[12,13]

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