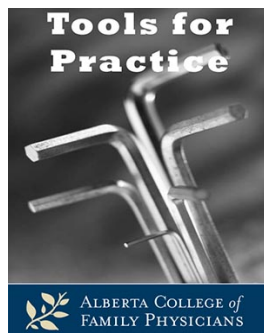


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**Reviewed: October 28, 2013**  
**Evidence Updated: Cochrane review, varenicline safety and context updated**  
**Bottom Line: Unchanged**  
**First Published: May 26, 2010**



## **Pharmacotherapy for Smoking: Which work and what to consider (Part II)?**

**Clinical Question: In patients ready to make a smoking cessation attempt, how effective are registered first-line medications and what are the potential concerns?**

**Bottom-line: Bupropion, nortriptyline, and varenicline are all effective in smoking cessation, perhaps varenicline more so. Adverse events vary and may in part relate to quitting smoking, but are important in drug selection and require monitoring.**

See Part 1 for nicotine replacement therapy.

### **Evidence:**

- Antidepressants: Cochrane review of bupropion (49) and nortriptyline (nine) Randomized Controlled Trials (RCT).<sup>1</sup>
  - Risk Ratio (RR) for cessation over placebo,
    - Bupropion (at 6–12 months): 1.69 (1.53–1.85)
    - Nortriptyline (at six months): 2.03 (1.48–2.78)
  - Serious adverse events:
    - Bupropion: Seizure (about 1/1000) and suicidal thoughts/behaviour (association unclear) are rare.
  - SSRI (six RCTs) and venlafaxine (one RCT): not effective.
- Varenicline: 14 RCTs.<sup>2</sup>
  - RR for cessation at six months over placebo: 2.27 (2.02–2.55).
    - RR over bupropion: 1.52 (1.22–1.88).
  - Serious adverse events:
    - Neuropsychiatric events like depression, agitation and suicidal thoughts/behaviour require monitoring but causation and actual numbers are uncertain.<sup>2-6</sup>
    - Increased risk of cardiovascular events, [number needed to harm over one year ranges from 34 (immediately after myocardial infarction) to 1667 (in low-risk individuals)].<sup>7,8</sup>
- Assuming 10% placebo cessation rates (mean across studies), number needed to treat: Varenicline 8, Nortriptyline 10 and Bupropion 10.

**Context:**

- Varenicline evidence has at risk of bias.
  - Superiority of varenicline > bupropion is:
    - At risk of funding bias.
    - Both are equivalent to nicotine replacement therapy. Therefore superiority is questionable.<sup>2,9</sup>
  - Almost 75% of varenicline trials are unpublished.<sup>10</sup>
- Health Canada recommends “thorough consideration” of nicotine replacement therapy before varenicline or bupropion.<sup>11</sup>
- Dosing:
  - Lower doses are effective:
    - Bupropion 150mg is equivalent to 300mg<sup>1,12</sup>
    - Varenicline 0.5mg BID is equivalent to 1mg BID (with less adverse events)<sup>2</sup>
  - Nortriptyline: Can start at 25mg qhs and increase by 25mg every 3–4 days, if needed, to a maximum of 75–100mg. Encouraged quit date 10 days in (or so) and continue for 10–12 weeks.

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