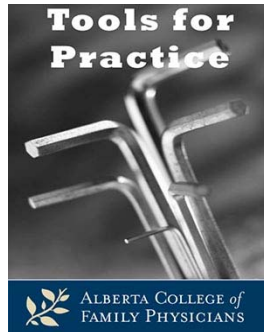


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## **Pharmacotherapy for Smoking: Which work and what to consider (Part II)?**

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

### **Evidence:**

Part II continues with antidepressants and varenicline.

- Antidepressants: Cochrane review of bupropion 49 and nortriptyline 9 randomized controlled trials (RCT).<sup>1</sup>
  - o Risk Ratio (RR) for cessation over placebo,
    - Bupropion (at 6-12 months): 1.69 (1.53-1.85)
    - Nortriptyline (at 6 months): 2.03 (1.48-2.78)
  - o Adverse events (AE):
    - Bupropion: Primarily insomnia and dry mouth. 7-12% drop-out due to AE. Seizure (about 1/1000) and suicidal thoughts/behavior (association unclear) are rare.
    - Nortriptyline: Primarily dry mouth, drowsiness, light-headed, and constipation (less at lower doses). 4-12% drop-out due to AE.
  - o SSRI (6 RCT) and venlafaxine (1 RCT): not effective. There is no evidence for tricyclic antidepressants other than nortriptyline.
- Varenicline: 9 RCT.<sup>2</sup>
  - o RR for cessation rate at 6 months over placebo= 2.33 (1.95-2.80)
    - RR for cessation over bupropion= 1.52 (1.22-1.88)
  - o AE: Primarily nausea, insomnia, and abnormal dreams. Approximately 10% drop-out due to AE.<sup>3</sup>
  - o Neuropsychiatric AE like depression, agitation and suicidal thoughts/behavior are infrequent but require monitoring.
    - Debate around causation and actual numbers continues.<sup>4</sup>
- Assuming 10% placebo cessation rates (mean across studies), number needed to treat (NNT): Varenicline 8, Nortriptyline 10 and Bupropion 15 (at 6 months, from meta-analysis, NNT 10).
  - o Benefit of varenicline may partially be influenced by industry funding and lack of pragmatic design (it's earlier in varenicline research).

### **Context:**

- Dosing:
  - o Lower doses may be as effective in cessation.

- Bupropion 150mg is equivalent to 300mg<sup>1,5</sup>
- Compared to Varenicline 1 mg BID, Varenicline 0.5 mg BID is also effective (but perhaps slightly less)<sup>6,7</sup> with less adverse events<sup>2</sup>
- Nortriptyline: Can start at 25mg qhs and increase by 25mg every 3-4 days, if the desire to smoke persists, to a maximum of 75-100mg. Encouraged quit date 10 days in (or so) and continue for 10-12 weeks.

**Bottom-line: In addition to nicotine replacement, bupropion, nortriptyline (off-label) and varenicline are all effective in smoking cessation, perhaps the latter more so. Adverse events vary and may in part relate to quitting smoking, but are important and require monitoring.**

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