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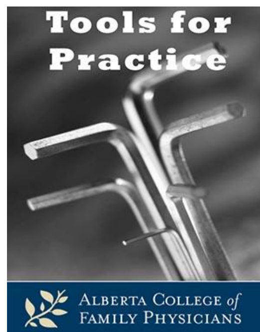
Reviewed: December 17, 2017
Evidence Updated: Updated varenicline Cochrane & safety reviews safety and context updated
Bottom Line: Increased confidence in varenicline superiority
First Published: May 26, 2010



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, with varenicline more-so. Adverse events vary and may in part relate to quitting smoking, and require monitoring.

Evidence:
See Part 1 for nicotine replacement therapy (NRT).

- Antidepressants: Cochrane review of bupropion 65 and nortriptyline 10 randomized controlled trials (RCTs).[1]
  - Risk Ratio (RR) for cessation over placebo,
    - Bupropion (at 6-12 months): 1.62 (1.49-1.76)
    - Nortriptyline (at 6 months): 2.03 (1.48-2.78)
  - Serious adverse events:
    - Bupropion: Seizure (about 1/1000) and suicidal thoughts/behavior (association unclear) are rare.
  - SSRI (6 RCTs) and venlafaxine (1 RCTs): not effective.
- Varenicline:
  - Cochrane review[2] of 39 RCTs: RR for cessation at 6-12 months over placebo= 2.24 (2.06-2.43)
    - RR over bupropion= 1.39 (1.25-1.54)
    - RR over NRT = 1.25 (1.14-1.37)
  - Serious Adverse Events: RR 1.25 (1.05-1.49)
  - Neuropsychiatric safety: Early studies[2,3] suggested possible increase in depression, irritability, and suicidal thoughts/attempts, however:
    - Systematic review[4] of 39 RCTs: No increase versus placebo
    - RCT[5] 0f 8,144 (50% with psychiatric disorder): No difference versus placebo, NRT or bupropion

        - Cohort[6] of ~120,000 patients: No difference between varenicline, bupropion or NRT.
    - Cardiovascular events: No increase (see updated Tools for Practice #71).
- Assuming 10% placebo cessation rates (mean across studies), number needed to treat: Varenicline 8, Nortriptyline 10 and Buproprion 10.

Context:

- Risk of bias in varenicline evidence:
    - Superiority of varenicline > buproprion is at risk of funding bias
    - Previously noted publication bias: In 2011, 75% of varenicline trials were unpublished.[7]
- Health Canada recommends "thorough consideration" of NRT before varenicline or bupropion.[8]
- Dosing:
    - Lower doses are effective:
        - Bupropion 150 mg is equivalent to 300 mg[1,9]
        - Varenicline 0.5 mg BID may be slightly less effective than 1 mg BID (with fewer adverse events)[2,10]
    - Nortriptyline: Can start at 25 mg qhs and increase by 25 mg every 3-4 days, if needed, to a maximum of 75-100 mg. Encouraged quit date 10 days in (or so) and continue for 10-12 weeks.

Original Authors:
G Michael Allan MD CCFP & Charl Els MBChB, FCPsych (Psychiatry)

Updated:
Ricky D Turgeon BSc(Pharm), ACPR, PharmD

Reviewed:
G Michael Allan MD CCFP

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