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## Q / Which smoking cessation interventions work best?

### EVIDENCE-BASED ANSWER

**A** / **NICOTINE REPLACEMENT THERAPY (NRT)**, bupropion, nortriptyline, clonidine, and varenicline are all effective, although insufficient evidence exists to recommend one intervention over another (SOR: A, systematic reviews).

Effective nonpharmacologic interventions include brief physician advice and more intensive counseling, such as proactive telephone counseling, group and individual counseling, and use of quit lines (SOR: A, systematic reviews).

### Evidence summary

**NRT.** A Cochrane review of 111 randomized controlled trials (RCTs) with a total of >40,000 subjects evaluated abstinence rates after 6 months of NRT and placebo or no treatment.<sup>1</sup> All forms of NRT increased abstinence vs placebo or no treatment, independent of setting, duration of treatment, and intensity of nonpharmacologic therapies. Overlapping confidence intervals suggested that no one form of NRT was superior. (The **TABLE** summarizes all the studies discussed here.)

■ **Bupropion.** A Cochrane review of 36 RCTs (N=11,140) showed higher abstinence rates with bupropion than placebo after ≥6 months of follow-up (average quit rate 17% vs 9%). Duration (6 vs 12 months) and intensity (150 vs 300 mg) of therapy didn't influence the results.<sup>2</sup> Six separate RCTs comparing bupropion plus NRT with NRT alone showed significant heterogeneity, but found no significant differences using a mixed-effects model.<sup>2</sup>

■ **Nortriptyline.** A Cochrane review that pooled results from 6 RCTs (N=975) showed superior 6-month abstinence rates for nortriptyline compared with placebo.<sup>2</sup> Adding nicotine patches in other RCTs (N=1219) didn't change abstinence rates.<sup>2</sup> No long-term studies have examined other tricyclic antidepressants.

■ **Clonidine.** A pooled analysis of 6 RCTs found clonidine superior to placebo after ≥12 weeks of follow-up.<sup>3</sup> Results were heavily

influenced by one trial limited to heavy smokers and poor tolerability due to adverse effects of therapy, especially sedation and dry mouth.

■ **Nicotine receptor partial agonists and antagonists.** Standard dose varenicline was more than twice as likely as placebo to produce abstinence at 6 months in a Cochrane review of 10 RCTs.<sup>4</sup> Lower doses were slightly less effective, but had fewer side effects. Adverse effects included mild to moderate nausea and sleep disorders; causation has not been established between varenicline and rare postmarketing reports of severe psychiatric disturbances.<sup>4,5</sup>

The pooled results of 3 RCTs suggested that varenicline was superior to bupropion, but different abstinence rates for bupropion users in other placebo-controlled trials necessitate caution in interpreting these results.<sup>4</sup> Varenicline was not superior to NRT.<sup>4</sup>

One RCT (N=48) comparing nicotine patches plus the nicotine antagonist mecamylamine with patches plus placebo found improved abstinence rates at 6 and 12 months; a larger RCT didn't support these findings.<sup>6</sup>

### These interventions are not supported

A review of placebo-controlled RCTs found no evidence of improved abstinence at 6 to 12 months with fluoxetine, paroxetine, sertraline, venlafaxine, citalopram, or monoamine oxidase inhibitors, alone or as adjuncts to NRT.<sup>2</sup>

No good evidence supports using anxi-

TABLE

## How effective are smoking cessation interventions?

Intervention	No. of studies	Effect size* (95% confidence interval)	Total N
NRT vs placebo or no treatment <sup>1</sup>	111	1.58 (1.50-1.66)	>40,000
Bupropion vs placebo <sup>2</sup>	36	1.69 (1.53-1.85)	11,140
Bupropion 300 mg/d vs 150 mg/d <sup>2</sup>	3	1.08 (0.93-1.26)	2042
Bupropion + NRT vs NRT <sup>2</sup>	6	1.23 (0.67-2.26)	1106
Nortriptyline vs placebo <sup>2</sup>	6	2.03 (1.48-2.78)	975
Nortriptyline + NRT vs NRT <sup>2</sup>	4	1.29 (0.97-1.72)	1219
Clonidine vs placebo <sup>3</sup>	6	1.63 (1.22-2.18)	776
Varenicline vs placebo, standard dose <sup>4</sup>	10	2.31 (2.01-2.66)	4443
Varenicline vs placebo, low dose <sup>4</sup>	4	2.09 (1.56-2.78)	1272
Varenicline vs bupropion <sup>4</sup>	3	1.52 (1.22-1.88)	1622
Varenicline vs NRT <sup>4</sup>	2	1.13 (0.94-1.35)	778
Mecamylamine + NRT vs NRT+ placebo <sup>6</sup>	1	37.5% vs 12.5%	48
Simple advice vs usual care <sup>10-13</sup>	17	1.66 (1.42-1.94)	15,930
Patient-initiated telephone quit line vs usual care <sup>14</sup>	9	1.37 (1.26-1.50)	24,000

NRT, nicotine replacement therapy.

\*An effect size >1.0 means that patients using this intervention are more likely not to smoke at 6 to 12 months; larger numbers correlate with greater effectiveness.

lytics, silver acetate, Nicobrevin (a nicotine-free smoking cessation aid), lobeline, or naltrexone for smoking cessation.<sup>7-9</sup>

### Simple advice and quit lines help

A Cochrane review of 17 RCTs found that simple advice improved quit rates and maintenance of abstinence at 12 months.<sup>10-13</sup>

A review of 9 RCTs (N>24,000) found that telephone quit lines increased abstinence, particularly after more than 2 sessions.<sup>14</sup>

No high-quality studies demonstrate the

effectiveness of acupuncture, hypnotherapy, or acupressure for smoking cessation.<sup>15,16</sup>

### Recommendations

The Agency for Health Care Research and Quality recommends counseling (including individual, group, and telephone sessions and brief physician advice) in addition to sustained-release bupropion, NRT, and varenicline as first-line agents. It considers clonidine and nortriptyline second-line therapies.<sup>17</sup>

JFP



**Smoking cessation:  
Help patients stop  
(and get paid for it)**

Elliot Wineburg, MD,  
Director, Stop  
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### References

- Silagy C, et al. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev.* 2008;(3):CD000146.
- Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database Syst Rev.* 2010;(4):CD000031.
- Gourlay SG, Stead LF, Benowitz NL. Clonidine for smoking cessation. *Cochrane Database Syst Rev.* 2008;(3):CD000058.
- Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev.* 2011;(2):CD006103.
- Product Information for Chantix. New York, NY: Pfizer; 2006.
- Lancaster T, Stead LF. Mecamylamine for smoking cessation. *Cochrane Database Syst Rev.* 2009;(1):CD001009.
- Hughes JR, Stead LF, Lancaster T. Anxiolytics for smoking cessation. *Cochrane Database Syst Rev.* 2010;(1):CD002849.
- Lancaster T, Stead LF. Silver acetate for smoking cessation. *Cochrane Database Syst Rev.* 2009;(2):CD000191.
- David S, Lancaster T, Stead LF, et al. Opioid antagonists for smoking cessation. *Cochrane Database Syst Rev.* 2009;(4):CD003086.
- Lancaster T, Stead LF. Self-help interventions for smoking cessation. *Cochrane Database Syst Rev.* 2009;(2):CD001118.
- Lancaster T, Stead LF. Physician advice for smoking cessation. *Cochrane Database Syst Rev.* 2008;(2):CD000165.
- Lancaster T, Stead LF. Individual behavioral counseling for smoking cessation. *Cochrane Database Syst Rev.* 2008;(4):CD001292.
- Stead LF, Lancaster T. Group behavior therapy programs for smoking cessation. *Cochrane Database Syst Rev.* 2009;(2):CD001007.
- Stead LF, Perera R, Lancaster T. Telephone counseling for smoking cessation. *Cochrane Database Syst Rev.* 2009;(3):CD002850.
- White AR, Rampes H, Campbell JL. Acupuncture and related interventions for smoking cessation. *Cochrane Database Syst Rev.* 2008;(4):CD000009.
- Abbot NC, Stead LF, White AR, et al. Hypnotherapy for smoking cessation. *Cochrane Database Syst Rev.* 2010;(10):CD001008.
- Fiore MC, Jaén CR, Baker TB, et al. *Treating Tobacco Use and Dependence: 2008 Update.* Rockville, MD: US Department of Health and Human Services, Public Health Service; May 2008.