Medicine by the Numbers
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The NNT Group rating system:

Green:	Benefits greater than harms
Yellow:	Unclear benefits
Red:	No benefits
Black:	Harms greater than benefits

Nicotine Replacement Therapy for Smoking Cessation

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NICOTINE REPLACEMENT THERAPY FOR SMOKING CESSATION

Number needed to treat = 15 for smoking cessation

Benefits	*Harms*
1 in 15 was helped (successfully quit smoking)	1 in 94 was harmed (chest pain or palpitations) None were harmed (cardiovascular event)

Details For This Review

Study Population: Adults who want to quit smoking

Efficacy End Points: Abstinence from smoking at six months and beyond

Harm End Points: Chest pain/palpitations, cardiovascular events

Narrative: Smoking kills more than 5 million individuals worldwide and about 443,000 Americans each year. Cigarette and tobacco use costs the United States $193 billion a year in health care expenditures and productivity losses.[1,2]

Data suggest that up to 70% of current smokers want to quit.[3] Cessation has been shown to lower risks of lung and other smoking-attributable cancers, coronary artery disease, stroke, peripheral vascular disease, chronic obstructive pulmonary disease, and infertility, while improving lung function and symptoms.[4] Yet, despite known health effects, stigma, and costs, 19% of Americans (44 million) still smoke.[5]

Nicotine dependence, the most common form of chemical addiction, may be comparable to that of heroin, cocaine, or alcohol.[6] Nicotine replacement therapy (NRT) has been suggested as a plausible smoking cessation method. NRT is available in a variety of forms, including gums, patches, tablets, inhalers, and sprays.

A Cochrane review, including 150 studies and more than 50,000 participants, compared NRT with placebo. Overall, NRT increased successful cessation rates from 10% with placebo to 17% (number needed to treat [NNT] = 15).[7] The relative benefit of NRT on smoking cessation was independent of delivery method, definition of abstinence, length of treatment, level of support counseling, treatment venue (hospital, clinic, support group), and whether a fixed, variable, or tapered dose was used. Success rates were even higher when NRT was available over the counter.

The use of NRT slightly increased rates of symptomatic chest pain and palpitations (odds ratio = 1.88; number needed to harm = 94), which is similar to results of an earlier study.[8] Other fairly rare adverse effects varied with type of NRT and included gastrointestinal upset, dental problems, and jaw pain (gum); skin irritation (patch); throat/nose irritation, sore throat (inhaler, lozenge, spray); and headache, dizziness, sleep disturbance, hiccups (general). Importantly, the Cochrane review found that NRT is not associated with any significant increase in cardiovascular events and is safe to use during pregnancy, which is in line with previous studies.[9-11]

Caveats: The Cochrane review included thousands of patients in a large number of high-quality, randomized controlled trials. Most studies were supported by public funds and grants, although a large number received free NRT products and a smaller number received direct funding from pharmaceutical companies, which may falsely augment the treatment effect size.[12]

Most trials included only heavy smokers (15 or more cigarettes per day); the average number of cigarettes smoked was about 20 per day. Therefore, it is unclear how this study may apply to lighter smokers. Pregnant women also demonstrated less benefit than other populations.

In general, the authors attempted to produce a conservative estimate by assuming all patients lost to follow-up were treatment failures and by contacting other researchers for unpublished data to limit publication bias. Additionally, only complete cessation, and not smoking reduction, was assessed.[7]

The quit rate in the unassisted (control) group, or self-quit rate, in this Cochrane review (about 10%) was higher than others published (3% to 5%[13]). Applying the same relative benefit of NRT to a baseline quit rate of 3% to 5% would yield an absolute risk reduction of about 2% with an NNT of about 50. If the baseline rate was 15%, the absolute risk reduction would be 8% with an NNT of 11. Thus, although the relative benefit of NRT appeared consistent, the absolute effect may vary with other factors (behavioral support, financial incentives, etc.).

Similarly, although the benefit of NRT continued at 12 months, the absolute rates of abstinence declined. A separate meta-analysis with follow-up beyond one year found that the absolute benefit of NRT declined from 11% at one year to 7% at four years.[14]

Given the quality of research and the lack of serious adverse effects, NRT appears to be a safe and effective option for current smokers who wish to quit.

This series is coordinated by Dean A. Seehusen, MD, MPH, *AFP* Contributing Editor, and Daniel Runde, MD, from the NNT Group.

This review is available from the NNT Group at http://www.thennt.com/nnt/nicotine-replacement-therapy-for-smoking-cessation/.

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REFERENCES

1. World Health Organization. Tobacco fact sheet. May 2015. http://www.who.int/mediacentre/factsheets/fs339/en/. Accessed June 6, 2015.
2. Centers for Disease Control and Prevention. Smoking-attributable mortality, years of potential life lost, and productivity losses—United States, 2000-2004. *MMWR Morb Mortal Wkly Rep.* 2008;57(45):1226-1228.
3. Centers for Disease Control and Prevention. Quitting smoking among adults—United States, 2001-2010. *MMWR Morb Mortal Wkly Rep.* 2011;60(44):1513-1519.
4. *The Health Benefits of Smoking Cessation: A Report of the Surgeon General.* Rockville, Md.: U.S. Department of Health and Human Services; 1990.
5. Centers for Disease Control and Prevention. Current cigarette smoking among adults—United States, 2011. *MMWR Morb Mortal Wkly Rep.* 2012;61(44):889-894.
6. Amerian Society of Addiction Medicine. Nicotine addiction and tobacco. October 1, 2008. http://www.asam.org/advocacy/find-a-policy-statement/view-policy-statement/public-policy-statements/2011/12/15/nicotine-addiction-and-tobacco. Accessed April 8, 2015.
7. Stead LF, Perera R, Bullen C, et al. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev.* 2012;(11):CD000146.
8. Mills EJ, Wu P, Lockhart I, Wilson K, Ebbert JO. Adverse events associated with nicotine replacement therapy for smoking cessation. A systematic review and meta-analysis of one hundred and twenty studies involving 177,390 individuals. *Tob Induc Dis.* 2010;8:8.
9. Greenland S, Satterfield MH, Lanes SF. A meta-analysis to assess the incidence of adverse effects associated with the transdermal nicotine patch. *Drug Saf.* 1998;18(4):297-308.
10. Joseph AM, Fu SS. Safety issues in pharmacotherapy for smoking in patients with cardiovascular disease. *Prog Cardiovasc Dis.* 2003;45(6):429-441.
11. Meine TJ, Patel MR, Washam JB, Pappas PA, Jollis JG. Safety and effectiveness of transdermal nicotine patch in smokers admitted with acute coronary syndromes. *Am J Cardiol.* 2005;95(8):976-978.
12. Etter JF, Burri M, Stapleton J. The impact of pharmaceutical company funding on results of randomized trials of nicotine replacement therapy for smoking cessation: a meta-analysis. 2007;102(5):815-822.
13. Hughes JR, Keely J, Naud S. Shape of the relapse curve and long-term abstinence among untreated smokers. *Addiction.* 2004;99(1):29-38.
14. Etter JF, Stapleton JA. Nicotine replacement therapy for long-term smoking cessation: a meta-analysis. *Tob Control.* 2006;15(4):280-285. ■