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Nicotine Replacement Therapy as a Maintenance Treatment

Judith J. Prochaska, PhD, MPH

Stanford Prevention Research Center, Department of Medicine, Stanford University, Stanford, California.

Abstract

IMPORTANCE—The US Food and Drug Administration adopted labeling for nicotine patches to allow use beyond the standard 8 weeks. This decision was based in part on data showing increased efficacy for 24 weeks of treatment. Few studies have examined whether the use of nicotine patches beyond 24 weeks provides additional therapeutic benefit.

OBJECTIVE—To compare 8 (standard), 24 (extended), and 52 (maintenance) weeks of nicotine patch treatment for promoting tobacco abstinence.

DESIGN, SETTING, AND PARTICIPANTS—We recruited 525 treatment-seeking smokers for a randomized clinical trial conducted from June 22, 2009, through April 15, 2014, through 2 universities.

INTERVENTIONS—Smokers received 12 smoking cessation behavioral counseling sessions and were randomized to 8, 24, or 52 weeks of nicotine patch treatment.

MAIN OUTCOMES AND MEASURES—The primary outcome was 7-day point prevalence abstinence, confirmed with breath levels of carbon monoxide at 6 and 12 months (intention to treat).

RESULTS—At 24 weeks, 21.7% of participants in the standard treatment arm were abstinent, compared with 27.2% of participants in the extended and maintenance treatment arms ($\chi^2_1=1.98$; P = .17). In a multivariate model controlled for covariates, participants in the extended and maintenance treatment arms reported significantly greater abstinence rates at 24 weeks compared with participants in the standard treatment arm (odds ratio [OR], 1.70 [95% CI, 1.03-2.81]; P = .04), had a longer duration of abstinence until relapse (β = 21.30 [95% CI, 10.30-32.25]; P < .001), reported smoking fewer cigarettes per day if not abstinent (mean [SD], 5.8 [5.3] vs 6.4 [5.1] cigarettes per day; β = 0.43 [95% CI, 0.06-0.82]; P = .02), and reported more abstinent days (mean [SD], 80.5 [38.1] vs 68.2 [43.7] days; OR, 1.55 [95% CI, 1.06-2.26]; P = .02). At 52 weeks, participants in the maintenance treatment arm did not report significantly greater abstinence rates

Corresponding Author: Judith J. Prochaska, PhD, MPH, Stanford University, MSOB X316, 1265 Welch Rd, Stanford, CA 94305 (jpro@stanford.edu).

Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Prochaska reported serving as an expert witness against tobacco companies in lawsuits for which she received fees for the work and providing consultation to Pfizer, which makes smoking cessation medications.

JAMA INTERNAL MEDICINE

Long-term Nicotine Replacement Therapy: A Randomized Clinical Trial

Robert A. Schnoll, PhD; Patricia M. Goelz, MPH; Anna Veluz-Wilkins, MA; Sonja Blazekovic, BA; Lindsay Powers, MA; Frank T. Leone, MD; Peter Gariti, PhD; E. Paul Wileyto, PhD; Brian Hitsman, PhD

compared with participants in the standard and extended treatment arms (20.3% vs 23.8%; OR, 1.17 [95% CI, 0.69-1.98]; $P = .57$). Similarly, we found no difference in week 52 abstinence rates between participants in the extended and standard treatment arms (26.0% vs 21.7%; OR, 1.33 [95% CI, 0.72-2.45]; $P = .36$). Treatment duration was not associated with any adverse effects or adherence to the counseling regimen, but participants in the maintenance treatment arm reported lower adherence to the nicotine patch regimen compared with those in the standard and extended treatment arms (mean [SD], 3.94 [2.5], 4.61 [2.0], and 4.7 [2.4] patches/wk, respectively; $F_{2,522} = 6.03$; $P = .003$).

CONCLUSIONS AND RELEVANCE—The findings support the safety of long-term use of nicotine patch treatment, although they do not support efficacy beyond 24 weeks of treatment in a broad group of smokers.

Tobacco use remains the leading preventable cause of morbidity and mortality, each year causing an estimated 480 000 deaths in the United States and more than 6 million deaths globally.[1] Nicotine addiction is a chronic, relapsing disorder. Prolonged tobacco use results in physiologic dependence and a behavioral compulsion to use tobacco. Most smokers (>70%) want to quit, and 40% attempt to do so each year.[1] Even though cessation medication and counseling approaches are relatively straightforward, most quit attempts are unassisted (with a 2%-5% success rate), undertreatment is common, and relapse is the norm.

Generally, cessation medications approved by the US Food and Drug Administration (FDA), if used properly and with physician support, increase smoking abstinence 2-fold relative to placebo (approximately 20% vs 10%).[2] With different mechanisms of action, cessation medications reduce physical withdrawal in the early phases of quitting. Further, through desensitization of nicotinic receptors, cessation medications counter the immediate, reinforcing effects of nicotine absorbed if the individual does smoke, to prevent relapse.

Rapidity of absorption is an important determinant of a drug's addictiveness. Cigarette smoking is the most rapid method of nicotine delivery, whereas nicotine replacement therapy (NRT) provides lower and slower increasing plasma nicotine concentrations, without exposure to toxic combustion products. A network meta-analysis of 267 clinical trials with 101 804 participants found the odds ratio for any form of NRT vs placebo was 1.84(95%CI, 1.71-1.99), with no difference by form of NRT and comparable with bupropion.[2] Combining slow-release NRT (the patch) with rapid-release forms (nicotine gum, lozenge, inhaler, or nasal spray) increases the effectiveness of NRT and is comparable with treatment with varenicline.[2] Nicotine replacement therapy is considered safe, including in combination form or if used while smoking.[2] Among the different forms of NRT, adherence is greatest with the patch.

Long-term quit rates with cessation medications are approximately 20%. To boost the efficacy of existing medications, extended use has been considered, similar to insulin treatment for diabetes or methadone maintenance for opioid addiction. Generally, the FDA has approved cessation medications for short-term use (8-12 weeks). A small number of previous studies have examined tobacco cessation treatment for 6 months or longer, and the study by Schnoll et al[3] in *JAMA Internal Medicine* adds to the literature.

In an effort to better understand the long-term effectiveness for nicotine patch treatment, patients were randomized into 3 groups: smokers were treated with standard (8-week), extended (24-week), or maintenance (52-week) nicotine patch. All groups received 12 sessions of supportive cessation counseling. At 8 weeks, less than a third of the sample was abstinent. By 52 weeks, abstinence rates, defined as no smoking in the past 7 days, were similar for the 3 groups: 22% for standard treatment, 26% for extended, and 20% for maintenance. Aminority of participants reported wearing the patch at least 6 days per week: 38% in standard, 47% in extended, and 32% in maintenance. Continuous abstinence was 8.3% for standard, 9.8% for extended, and 9.1% for maintenance.

The authors concluded that study findings supported the safety of long-term use of nicotine patch treatment but not the efficacy beyond 24 weeks of treatment. Based on the study's final end point, however, even the 24-week treatment was not more effective than the standard 8-week course of NRT. The rate of serious adverse events, confirmed by site physicians, was 4.7%. The study was underpowered to detect between-group differences for safety end points and lacked a placebo-controlled comparison.

The lack of benefit for maintenance NRT reported by Schnoll et al[3] is consistent with prior research. A randomized trial with older smokers found 52 weeks of maintenance nicotine gum did not increase abstinence when added to a 12-week treatment of nicotine gum, bupropion, and group counseling. Nicotine gum use averaged 85 of 365 days provided (23%). In contrast, 52-week individual counseling with a focus on relapse prevention significantly increased abstinence, to more than 50% at 2-year follow-up.[4] A parallel study found 52 weeks of bupropion, individual counseling, or both increased abstinence over the 12-week treatment, with highest quit rates in the condition combining bupropion and counseling (48% abstinent at 2 years).[5] Bupropion use averaged 20 weeks.

More akin to clinical practice, studies have evaluated extended cessation treatment only in early responders. Studies of bupropion and varenicline started with a 12-week open-label phase and then at the end of standard treatment randomized abstainers to continued active drug or placebo. In a study of 52-week bupropion therapy, abstinence was increased at 1 year but not sustained at the 2-year follow-up.[6] Varenicline dosed for 6 months yielded 44% continuous abstinence vs 37% for placebo and is approved by the FDA for extended treatment.[7] In a sample of smokers with schizophrenia, Evins et al[8] tested varenicline therapy for 52 weeks and reported 30% sustained abstinence at 76 weeks compared with 11% for those randomized to receive placebo during the maintenance phase.

The Affordable Care Act recommends coverage of at least 2 tobacco-cessation attempts per year, to include 4 tobacco-cessation counseling sessions, each at least 10 minutes, and any FDA-approved cessation medications for a 12-week treatment regimen when prescribed by a physician. For nicotine patch, the findings of Schnoll et al[3] do not support extended or maintenance treatment. Worth testing, however, is combination NRT continued among initial treatment responders with a placebo-controlled comparison. Limiting extended use to those who initially show benefit likely will improve adherence. In addition, with an emphasis on personalized medicine, it will be important to examine patients for whom extended cessation pharmacotherapy is warranted, such as smokers with schizophrenia or other co-occurring

disorders.[8] Variation in the speed at which individuals metabolize nicotine has demonstrated evidence for cessation medication matching[9] and is worth exploring as an indicator of smokers most in need of continuing care. Furthermore, extended cessation counseling has shown relapse prevention effects,[4,5] and technologies to disseminate the treatment more broadly should be tested.

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REFERENCES

1. World Lung Foundation. The Tobacco Atlas. 5th ed.. American Cancer Society; Atlanta, GA: 2015.
2. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation. Cochrane Database Syst Rev. 2013; 5:CD009329.
3. Schnoll RA, Goelz PM, Veluz-Wilkins A, et al. Long-term nicotine replacement therapy. JAMA Intern Med. 2015; 175(4):504–511. [PubMed: 25705872]
4. Hall SM, Humfleet GL, Muñoz RF, Reus VI, Robbins JA, Prochaska JJ. Extended treatment of older cigarette smokers. Addiction. 2009; 104(6):1043–1052. [PubMed: 19392908]
5. Hall SM, Humfleet GL, Muñoz RF, Reus VI, Prochaska JJ, Robbins JA. Using extended cognitive behavioral treatment and medication to treat dependent smokers. Am J Public Health. 2011; 101(12):2349–2356. [PubMed: 21653904]
6. Hays JT, Hurt RD, Rigotti NA, et al. Sustained-release bupropion for pharmacologic relapse prevention after smoking cessation. Ann Intern Med. 2001; 135(6):423–433. [PubMed: 11560455]
7. Tonstad S, Tønnesen P, Hajek P, et al. Effect of maintenance therapy with varenicline on smoking cessation. JAMA. 2006; 296(1):64–71. [PubMed: 16820548]
8. Evins AE, Cather C, Pratt SA, et al. Maintenance treatment with varenicline for smoking cessation in patients with schizophrenia and bipolar disorder. JAMA. 2014; 311(2):145–154. [PubMed: 24399553]
9. Lerman C, Schnoll RA, Hawk LW Jr, et al. Use of the nicotine metabolite ratio as a genetically informed biomarker of response to nicotine patch or varenicline for smoking cessation. Lancet Respir Med. 2015; 3(2):131–138. [PubMed: 25588294]