Despite the strong efficacy of pharmacologic smoking cessation aids demonstrated in clinical trials, a recent nationally representative cohort study found no evidence of their effectiveness in the general population of smokers, who rarely combine these medications with behavioral counseling. The study, from the University of California at San Diego (UCSD) School of Medicine in La Jolla, California, appears in the Journal of the National Cancer Institute (2018;110:581-587).

The US Public Health Service clinical practice guideline “Treating Tobacco Use and Dependence” recommends that smokers use a pharmaceutical aid to quit smoking. However, in a study appearing in Tobacco Control in 2016, no more than 30% of US smokers who quit long term attributed their success to using 1 or more of these aids (2016;25:464-469).

In addition, several observational studies have suggested that the effectiveness of pharmaceutical cessation aids used in community settings is less convincing than the efficacy of these medications under more optimized conditions in randomized clinical trials (in which they are administered and used in a more standardized manner and usually are combined with behavioral counseling). Interpretation of the available observational evidence is challenging because the use of cessation medicine is not random. Instead, smokers’ choices regarding cessation methods often are correlated with characteristics that influence their success in remaining tobacco free. The researchers at UCSD used propensity score matching, a statistical method that can overcome this limitation more completely than the ordinary multivariable methods used in previous studies of this topic.

In this new study, the researchers found that the majority of smokers who used the pharmacological tools to quit resumed smoking within 30 days. “While clinical practice guidelines have outlined pharmacological treatments that have proven efficacy in randomized trials, our study raises doubts that these medications are having their intended [long-term] effect in the [general] population,” says study author John P. Pierce, PhD, Sam M. Walton Professor for Cancer Research in the department of family medicine and public health at UCSD. Dr. Pierce says that less than 2% of smokers who use a pharmaceutical aid also underwent behavioral counseling, as recommended by current guidelines.

To evaluate whether pharmaceutical aids helped with smoking cessation

KEY POINTS
• Pharmacological smoking cessation aids alone do not help the majority of smokers quit permanently.
• Women were more likely to try smoking cessation aids.
• A larger percentage of men said they remained abstinent for at least 30 days at follow-up.
• Less than 2% of smokers who use a pharmaceutical aid also underwent behavioral counseling.
• To quit for good, tobacco users should use pharmacotherapy and counseling.
in the “real world” outside of clinical trials, the researchers used the National Cancer Institute’s Tobacco Use Supplement to the Current Population Survey. Using 2 cohorts surveyed nearly a decade apart, in 2002 through 2003 and 2010 through 2011, they gauged the effectiveness of medications to aid quitting among adult smokers who attempted to quit prior to 1 year of follow-up.

The researchers used a multivariable logistic model to calculate propensity scores for the use of pharmacological cessation aids for each of the 2129 study participants. The propensity score model included 12 confounders: age, sex, race/ethnicity, education, smoking intensity, nicotine dependence, previous quit history, a combination of interest in quitting and self-efficacy to quit, smoke-free homes, survey year, and prior cessation aid use. Dr. Pierce and his colleagues then compared the cessation success of pharmacologic aid users and nonusers who were matched according to similar propensity scores, to achieve a balanced comparison of cessation success with and without pharmaceutical aids.

The Tobacco Use Supplement to the Current Population Survey used standard national tobacco questions. For example, to identify ever-established smokers, they asked “Have you smoked at least 100 cigarettes in your entire life?” To identify current and former smokers, subjects were asked “Do you now smoke cigarettes every day, some days, or not at all?”

To gauge previous quitting history, subjects were asked “Have you ever tried to quit smoking completely?” and “During the past 12 months, have you stopped smoking for 1 day or longer because you were trying to quit smoking?”

In the study, users were asked whether they had used any of the following: nicotine patch, gum, lozenge, nasal spray, or an inhaler or varenicline (Chantix), bupropion (Zyban or Wellbutrin), or a different pill. Varenicline was commercially available only for the 2010 through 2011 surveys. Electronic cigarettes were not included.

The 2010 survey included 2 other questions. The first asked how soon after awakening the subject smoked their first cigarette. The subject was classified as “more nicotine dependent” if they took their first puffs within 30 minutes after waking. The second variable was a combination of interest in quitting and self-efficacy for quitting.

Results
More women than men reported that they tried a pharmaceutical aid during their most recent attempt at quitting (36% vs 31.2%). Use of a pharmaceutical aid was more frequent among respondents who were aged older than 35 years (age 18-34 years: 25.2%; age 35-54 years: 37.1%; and age 55 years and older: 36.4% \(P < .001\)).

In addition, the use of pharmaceutical aids was found to be higher among adults who smoked more cigarettes at baseline (<10 cigarettes per day [CPD]: 27.1%; 10-19 CPD: 33.3%; and 20 or more CPD: 41.2% \(P < .001\)), those who intended to quit in the 6 months after their baseline survey (37.1% vs 29.9% for no intent; \(P = .001\)), and among those who previously had tried to quit smoking prior to their baseline survey (36.1% vs 24.3% for no quitting attempts; \(P < .001\)). The researchers also found that a larger percentage of the cohort for the 2010 through 2011 survey was abstinent for 30 days or more at follow-up compared with the 2002 through 2003 survey cohort (21.0% vs 14.8%; \(P < .001\)). The most important result noted was that none of the 3 pharmacological aids evaluated—varenicline, bupropion, or nicotine replacement therapy (NRT)—significantly increased the probability of 30 or more days of smoking abstinence at the time of the second survey.

Implications for Practice
Richard D. Hurt, MD, emeritus medical director of the Nicotine Dependence Center of the Mayo Clinic in Rochester, Minnesota, is not surprised by the study results. “This is a second report that shows, at a population level, that pharmacotherapy for tobacco users is not effective,” he says.

However, Dr. Hurt adds that this study did not consider how much pharmacotherapy actually was used and for how long, or how many pharmacological aids were used. “In the hands of tobacco treatment specialists, combinations of long-acting pharmacotherapy with short-acting agents for withdrawal symptom control is the rule now. Monotherapy is uncommon.”
Dr. Hurt also noted that the study lumped nicotine products together, which could affect the results. “There is only one long-acting NRT—patches—and the others are short acting. The point is that all NRT is not alike. Further, the absolute numbers of subjects reporting using bupropion or varenicline were small, 186 and 118, respectively. The authors make a lot of the overall sample being over 2000, but the number of users of these 2 medications is relatively small.”

“Of course,” says Dr. Pierce, “randomized trials show that a drug can work (efficacy) but they are not generalizable to the population because of how they recruit smokers and the eligibility criteria to be randomized. Observational studies such as ours are critical postmarket surveillance of the effectiveness of the treatment.” Dr. Pierce adds that in both of the nationally representative longitudinal studies, smokers who reported using a pharmaceutical aid were no more successful at quitting than those who did not. “Thus, the way that pharmaceutical aids are used in the general population does not result in the level of successful quitting obtained in their efficacy randomized trials,” he says. “One key difference is the level of support that smokers receive in a randomized trial which smokers do not receive in the general population. It is very disappointing that the use of pharmaceutical aids to help smokers quit was not associated with increased successful quitting.”

Dr. Hurt is concerned that the study could lead some physicians and patients to be pessimistic concerning pharmacotherapy for tobacco users and result in it not being recommended for individual patients. “This would be unfortunate because evidence-based medicine is derived from randomized clinical trials, not population-based assessments.” He recommends that clinicians use the US Public Health Service clinical practice guideline “Treating Tobacco Use and Dependence.” He adds, “though the population level of effectiveness is not proven, individual patients who are tobacco users should be offered pharmacotherapy and counseling.”

Dr. Pierce also hopes that clinicians do not consider his study as a reason to stop trying to encourage smokers to quit. Rather, he noted, “To be more successful, it would seem to be important to try to get smokers this additional counseling support.”

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