VIEWPOINT

Increasing Smoking Cessation in the United States
Expanding the Availability of Over-the-Counter Medications

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The US Centers for Disease Control and Prevention recently reported that cigarette smoking (defined as smoking every day or only on some days) reached a record low in 2017 with a decline to 14% among US adults.[1] Tobacco-associated morbidity has likewise declined steadily in the United States, but remains the leading preventable cause of death for an estimated 480 000 individuals each year.[1] This continued decline in smoking prevalence is an outstanding public health success, but the United States can do better with modest, evidence-driven changes in tobacco treatment practice and policy.

Two-thirds of smokers want to quit, but less than one-third make a quit attempt using evidence-based approaches.[2] Improving treatment options and access are essential for improving quit rates. As the recent CDC report[1] indicated, "barrier-free access to tobacco cessation counseling and approved medications, along with [Food and Drug Administration] FDA regulation of tobacco products, can accelerate progress toward reducing tobacco-related death and disease in the United States."

Improving Tobacco Treatment Rates

Two related practice and policy changes have the potential to significantly increase the use of the most effective treatments to help smokers quit. The first is adoption of recommendations from a new evidence-based practice guideline that varenicline or combination nicotine replacement (eg, patch and lozenge) plus behavioral support be used as the first-line treatment for tobacco addiction for most smokers. The second is consideration of converting varenicline (and possibly other treatments for smoking cessation) from a prescription medication to an over-the-counter (OTC) medication.

First-Line Smoking Cessation Treatments

Every smoker in the United States has access to free behavioral support to assist in quitting via state tobacco quit lines.[1] Many persons use smoking cessation medications approved by the FDA, primarily OTC nicotine replacement therapy (gum, patch, or lozenge). However, 2 meta-analyses of smokers trying to quit[3,4] and a more recent meta-analysis including smokers not ready to quit[5] reported that varenicline was associated with higher quit rates than other single cessation medications, with cessation rates at 6 months of 33.2% compared with 23.4% for the nicotine patch and 24.2% for bupropion.[3]

The EAGLES trial[6] compared varenicline, bupropion, the nicotine patch, and placebo in 8144 smokers with (n = 4116) and without (n = 4028) a history of psychiatric conditions and found rates of abstinence from smoking at 24 weeks that were significantly higher in the varenicline group (21.8%) vs the bupropion (16.2%) and nicotine patch (15.7%) groups. Whether these rates would be maintained at 1 year or longer is not known. The most common adverse events from varenicline included nausea, insomnia, and abnormal dreams. Neuropsychiatric adverse events were comparable across medications, and patients with psychiatric conditions were more likely to report psychiatric adverse events across study medications including placebo.

Meta-analyses also have found that combining 2 different nicotine replacement products (such as the nicotine patch and lozenge) was associated with quit rates similar to varenicline alone.[3,4] Combination therapy requires consistent adherence to both medications to achieve the higher quit rate; however, the adherence rate is less than 2% for combination nicotine replacement therapy.[7]

Given the available evidence, clinicians and health care systems should recognize different tiers of tobacco treatment and ensure that smokers are offered either varenicline or combination nicotine replacement therapy as a first-line treatment option. Combination therapy should be encouraged if there is reason to believe that the smoker will adhere to use of both medications. A smoker may require up to 30 quit attempts before successful smoking cessation is achieved. Therefore, each attempt should involve an individualized approach so that the most effective treatment is offered to afford the best opportunity to achieve sustained abstinence from tobacco.

OTC Medications for Smoking Cessation

Only the nicotine patch, gum, and lozenge are available as OTC medications in the United States, and when these products switched from prescription to OTC, their use increased significantly.[8] Nicotine inhaler and nasal spray, bupropion, and varenicline are available only by prescription. The only published study on the safety and efficacy of a nicotine inhaler as an OTC medication found very low efficacy.[9] The addiction potential of nicotine nasal spray could make it problematic as an OTC product.[3]

The results of the EAGLES study[6] showing that adverse events from bupropion and varenicline are comparable with the OTC nicotine patch suggest that it might be appropriate to switch both treatments from prescription to OTC products. However, some risk of seizure has been identified after use of both bupropion and varenicline. In addition, use of bupropion is contraindicated in persons with an increased seizure risk[3] that could make conversion to an OTC product problematic.

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Converting any smoking cessation medication to an OTC product requires careful consideration of the potential benefits and risks. Early concerns about the safety of bupropion and varenicline (including serious psychiatric adverse effects such as suicidal ideation and depression) resulted in the FDA issuing a boxed warning for varenicline and bupropion in 2009. However, subsequent research has shown that the adverse events associated with varenicline and bupropion that led to the boxed warning were no greater than those associated with the nicotine patch. The boxed warning on varenicline and bupropion was removed in 2016 by the FDA, and the comparable warning was removed in Europe in 2015.

Many medications have been switched from prescription to OTC (eg, antihistamines, contraceptives, acid reducers such as proton pump inhibitors, and analgesics) because the risk of adverse events was small. Postmarketing analyses continue to assess risks from medications that switch from prescription to OTC status, and occasionally such analyses find that access to medications should be reduced (eg, pseudoephedrine). However, medications that have switched to OTC status typically remain available as OTC products.

Switching a medication from prescription to OTC requires that individuals who might use the medication are able to self-diagnose their condition, self-treat their condition, and make decisions regarding whether a medication is appropriate for them based on the labeling. In addition, the medication must be effective if used appropriately. Experience with multiple OTC nicotine replacement products that have been on the market for 2 decades demonstrates that smokers can meet such criteria, and that nicotine replacement therapies can be as safe and effective as OTC medications. Given the comparable safety profile of varenicline relative to the nicotine patch, and that the only contraindication to varenicline use is a history of hyperreactivity to varenicline, it is likely that smokers will be able to make correct decisions about varenicline if that product is made available as an OTC medication.

When prescription medications switch to OTC, medication use increases an average of 30%,[10] thereby eliminating a significant potential barrier to accessing and using the medications, and potentially enabling the achievement of optimal population health benefits. Whether this would be true for varenicline is unclear. When nicotine replacement therapies became available as OTC products, they became available to a far larger number of smokers, many of whom have minimal or no health insurance.

Pharmaceutical company and independent research is needed to determine whether varenicline as an OTC medication can be used optimally and to provide evidence regarding its efficacy and safety. Research funded by the National Institutes of Health is currently under way to assess the safety and efficacy of varenicline as an OTC medication (ClinicalTrials.gov NCT03557294).

Increasing Use of the Most Effective Tobacco Treatments

Increasing population-level smoking cessation requires both increasing the probability of quitting on any single attempt and reducing barriers to accessing the best treatments. The 2 most effective medication options for smoking cessation are varenicline and combination nicotine replacement therapy. Therefore, increasing use of these 2 therapies by designating them as first-line treatments could improve the chances of helping smokers quit, assuming persons diligently adhere to both combination nicotine replacement medications. Increasing access and reach can occur by greater diligence on the part of physicians and other health care professionals to recommend the most effective treatments, and it also may occur if medications deemed sufficiently safe and effective are able to switch from prescription to OTC products.

Given the results of the EAGLES study showing that varenicline resulted in adverse events comparable with both the nicotine patch and bupropion,[6] and that use of bupropion is contraindicated in persons with an increased seizure risk[3] but varenicline is not, varenicline should be considered as an OTC candidate drug. The FDA will need to assess the benefits and risks of switching varenicline or other medications to OTC products. If the potential benefits are determined to outweigh the risks, OTC availability of varenicline or other medications could help more smokers quit and substantially improve population health outcomes.

ARTICLE INFORMATION

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