



AN ONGOING CE PROGRAM
of the University of Connecticut
School of Pharmacy

EDUCATIONAL OBJECTIVES

GOAL: Pharmacists are in a unique position to engage in and lead community-based tobacco use prevention programs that have the potential to reach high risk and hard to reach populations. This activity will introduce the current status of tobacco use; describe the rationale and role of pharmacy-led delivery of brief tobacco cessation interventions in the community; and discuss effective evidence-based strategies for tobacco cessation.

After participating in this activity, pharmacists and pharmacy technicians will be able to:

- Describe the demographics of tobacco use in the United States
- Discuss reasons why pharmacists are in a great place to address patient engagement in tobacco cessation
- List common resources in the community for tobacco cessation referral
- Describe common evidence-based treatment strategies for tobacco cessation



The University of Connecticut School of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Pharmacists and pharmacy technicians are eligible to participate in this knowledge-based activity and will receive up to 0.2 CEU (2 contact hours) for completing the activity, passing the quiz with a grade of 70% or better, and completing an online evaluation. Statements of credit are available via the CPE Monitor online system and your participation will be recorded with CPE Monitor within 72 hours of submission

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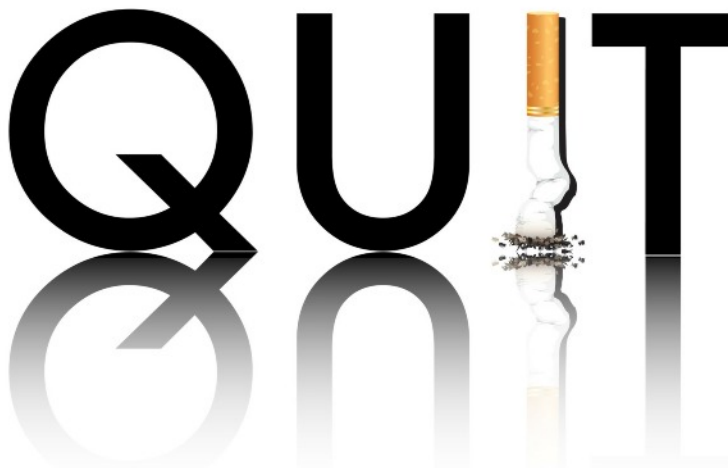
18YC02-JPF33 for pharmacists or

18YC02-XY233 for pharmacy technicians

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The Community Pharmacist: Touchpoint for Tobacco Cessation

ABSTRACT: Tobacco smoke is the number one preventable cause of death in the United States. Community pharmacists' accessibility provides opportunities to expand team-based care into the community to improve population access to preventive services, particularly in hard-to-reach populations. Tobacco cessation is one of the most cost-effective preventive care services and has become an important quality of care metric tied to reimbursement. Strategies for helping smokers quit include behavioral counseling to enhance motivation and to support attempts to quit, and pharmacological intervention to reduce nicotine reinforcement and withdrawal symptoms related to tobacco cessation. In 2015, 68% of adult smokers wanted to stop smoking but only 31% of smokers sought cessation counseling or took any of the seven U.S. FDA-approved medications to boost their chances for success. Combined behavioral and pharmacotherapy interventions increases tobacco cessation by 82%, compared with minimal intervention or usual care. Pharmacists may be the only health professionals to come into contact with many tobacco users prior to or during their quit attempts. Additionally, three nicotine replacement products are available over-the-counter, making them particularly well suited for expanded use in people trying to quit smoking. Pharmacist-led interventions can significantly improve abstinence rates in smokers resulting in quitting success rates similar to other health care professionals. However, many studies have found that pharmacists do not discuss tobacco use routinely with their patients. This activity provides an overview of information and strategies used to support pharmacists' extended role in providing tobacco cessation support in the community.

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INTRODUCTION

Fifty years ago, Americans received the first Surgeon General's report. Today, smoking and secondhand smoke remain the leading causes of preventable disease, disability, and premature death in the United States,¹ despite declines in the prevalence of adult cigarette smoking by more than one half (from 42% in 1965 to 15% by 2015).² This positive trend indicates progress toward achieving the *Healthy People 2020* goal of reducing cigarette smoking's prevalence to 12% or less.³ However, more than 28 million Americans continue to smoke cigarettes (the most commonly used tobacco product) and cigarette smoking continues to be a major contributor to annual healthcare spending.⁴ Disparities in tobacco use continue to persist with slower declines seen across defined groups.² Groups at high risk for smoking include adults who are male; younger (25-44 years of age); American Indian/Alaska Natives; have less education; live below the federal poverty level; live in the Midwest or South; are insured through Medicaid or are uninsured; have a disability/limitation; are lesbian, gay, or bisexual; or have serious psychological distress, mental health conditions, alcohol dependence, or a substance use disorder.^{2,5-7} These disparities underscore the importance of effective population-based interventions to reduce tobacco use in populations with high smoking prevalence.²

Tobacco-control interventions that result in real progress occur at the federal, state, or local levels. Effective interventions include^{2,8,9,10}:

- Implementing the Affordable Care Act (ACA) in 2010. It mandated insurance coverage of evidence-based tobacco interventions that received a grade of A or B from the U.S. Preventative Services Task Force (USPSTF) without barriers or copayments. It also expanded Medicare and Medicaid coverage for cessation treatments
- Increasing tobacco taxation and prices
- Implementing and enforcing comprehensive tobacco-control laws that restrict smoking in public housing and public places, specifically restaurants, bars, and workplaces
- Mounting aggressive media campaigns warning about tobacco's dangers
- Mandating the inclusion of graphic warning labels on all tobacco products
- Increasing access to smoking cessation services through state telephone quitlines, in conjunction with Food and Drug Administration (FDA) regulation of tobacco products

The vast majority of smokers begin smoking during adolescence (87% by age 18).¹ In 2009, the U.S. FDA started regulating the manufacture, distribution, and restricted sale of cigarettes and smokeless tobacco products to minors under the age of 18. However, as cigarette smoking among those under

Pause and Ponder:

Why is tobacco cessation a particularly appropriate role for the community pharmacist?

18 has fallen, the use of new tobacco products, such as non-combustible products, and electronic nicotine delivery systems (ENDS) or e-cigarettes has increased.¹¹

In 2016, the FDA extended its authority to regulate all tobacco products, including e-cigarettes, cigars, hookahs (waterpipes), and pipe tobacco.¹² The federal government introduced the first Tobacco 21 legislation, in an effort to further restrict young people's access to cigarettes and e-cigarettes in 2015. The FDA had strong public support to raise the minimum purchase age of tobacco products to 21 years.¹³ States and localities that adopt this new law may expect to benefit from a 47% reduction in the smoking rate among high school students, along with a decline in area retail tobacco purchases.¹⁴ In 2014, several states implemented or were evaluating state-wide prohibitions to ban tobacco sales in pharmacies lead by a landmark decision made by CVS Caremark to voluntarily withdraw the sale of tobacco products in its stores.¹⁵

SMOKING'S HEALTH CONSEQUENCES

Tobacco products come with inherent risks. Nicotine is addictive. It presents alongside more than 7000 other chemicals (from combusted tobacco products) that are responsible for a wide range of diseases and premature death.¹ Among behavioral risk factors for adverse health outcomes, smoking stands alone in its public health impact. It accounts for nearly 500,000 (or 1 in 5) deaths each year, including nearly 42,000 deaths from secondhand smoke exposure.^{1,5} All-cause mortality is three to five times greater in smokers than in non-smokers.¹⁶ Nearly 80% of smoking-related morbidity and mortality are accounted for by three conditions¹⁷:

- 1) cardiovascular disease (CVD), which is responsible for 40% of all smoking-related deaths
- 2) lung cancer, which accounts for 20% of all smoking-related deaths
- 3) chronic obstructive pulmonary disease (COPD), which accounts for another 20% of all smoking-related deaths

Smoking has also been implicated as a major cause of stroke, peripheral vascular disease, multiple cancers, type 2 diabetes (the risk of developing diabetes is 30% to 40% higher for active smokers than nonsmokers), impaired immune function; age-related macular degeneration; erectile dysfunction; osteoporosis (in postmenopausal women); and in pregnant women, an increased risk of congenital anomalies and perinatal complications.^{1,5} Not surprisingly, smokers' life expectancy is 10 years shorter than nonsmokers'.¹⁸



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Pause and Ponder:

What are the barriers to delivering tobacco cessation support?

Benefits of Quitting

Quitting smoking before age 40 reduces risk of smoking-associated death by about 90%.¹⁸ Even people who quit in their 60s lower their risk of death by 23%.¹⁹ Cancer patients who continue to smoke reduce their risk of dying by 30% to 40% by quitting at the time of diagnosis.²⁰

After 10 years of tobacco cessation, former smokers' risk for lung cancer is reduced by 50%.¹ By 1 year, the risk of coronary heart disease decreases to one half that of a continuing smoker. By 15 years the risk is at the level of never-smokers.¹⁷ After 5 years, stroke risk is reduced to that of a nonsmoker.¹⁷ More immediate benefits after cessation include improved circulation, a drop in blood pressure, and reduced damaging effects on skin, teeth, gums, breath, smell, and taste.¹ Reducing the number of cigarettes smoked per day is much less effective than quitting entirely to avoid smoking-related health consequences and premature death.¹

NICOTINE ADDICTION

Cigarettes and other forms of tobacco are addictive and nicotine causes this addiction.^{21,22} Research suggests that nicotine may be as addictive as heroin, cocaine, or alcohol.¹ Abstinence from nicotine use will lead to withdrawal symptoms which peak within 24 to 48 hours and usually subside within two to four weeks.³ Symptoms include depression, anxiety, irritability, frustration, restlessness, anger, difficulty concentrating, insomnia (but sometimes increased drowsiness), increased appetite, weight gain, and cravings.³ Therefore, people who stop tobacco may require several quit attempts before successfully quitting.³

An inability to maintain abstinence is a key indicator of tobacco dependence. In a clinic-office setting, the most widely used measure of nicotine dependence is the Fagerstrom Test for Nicotine Dependence (FTND) questionnaire.²³ The test (available at <https://cde.drugabuse.gov/instrument/d7c0b0f5-b865-e4de-e040-bb89ad43202b>) consists of six questions, with an overall score of 0 to 10 to gauge the level of nicotine dependence. The single item in the FTND that predicts relapse strongly and consistently is the time to first cigarette (TTFC) after waking.²⁴ TTFC can also be used as a baseline screening tool to target smokers beginning treatment, for instance, to assign a dose of nicotine lozenge therapy.²⁵

Disparities in Tobacco Use

Medicaid enrollees have a cigarette smoking prevalence 27.8%, or more than double that of privately insured Americans (11.1%).² In patients seen at federally qualified health centers (which provide comprehensive health services to economically disadvantaged populations in rural and urban communities), tobacco use is higher than in the general US population.²⁶ The ACA increased the number of insured adults and improved cessation coverage from Medicaid. However, evidence indicates that only approximately 10% of Medicaid smokers receive smoking cessation medications, and use varies widely by state.²⁷ Fewer than half of smokers in Medicaid-managed care plans reported that their physicians offered assistance, such as medications or counseling, to quit.

Clinicians were also less likely to screen black and Hispanic smokers than whites for tobacco use and provide interventions, even after controlling for socioeconomic and healthcare factors.^{28,29} Smokers from lower socioeconomic groups are also less likely to stop smoking than more affluent smokers, even when they access smoking cessation services.³⁰

Smoking-related medical costs are responsible for 10% of Medicaid expenditures.⁴ Providing barrier-free access to cessation treatments (such as removing copayments and prior authorization for treatment) and promoting their use, can reduce smoking and smoking-related disease, death, and health care costs.³¹ Medicaid smoking cessation initiatives lower smoking rates, reduce hospital admissions, are cost-effective, and generate a positive return on investment.³²

Why Treat?

Tobacco dependence is increasingly recognized as a chronic, relapsing, and dynamic process that requires repeated interventions and multiple attempts before succeeding.³ Among current U.S. adult cigarette smokers, nearly seven of ten (68%) reported that they wanted to quit completely in 2015. More than half (55%) of smokers made a quit attempt in the preceding year, but only 7% who tried to quit succeeded.³³ Advice from clinicians to quit also increased. Fifty seven percent recommended that patients stop smoking; however, only 31% of smokers sought cessation counseling or took any of the seven U.S. FDA-approved medications to boost their chances for success.

Among smokers who tried to quit, about 7% used counseling, 29% took medication, and 5% used both.³³ It is well established that use of cessation counseling and medication increases quit rates, especially when they are combined.^{3,34,35} Combined behavioral and pharmacotherapy interventions increase cessation by 82%, compared with minimal intervention or usual care.⁹

Tobacco cessation is one of the most cost-effective preventive care services. It has become an important metric for determining quality of care assessments tied to reimbursement mechanisms for many stakeholders.³ The USPSTF has given tobacco screening and delivery of cessation interventions an “A” grade recommendation.⁵ The Joint Commission, which accredits more than 15,000 hospitals and healthcare systems, instituted an accreditation requirement for tobacco cessation performance measures for all admitted patients in 2012.³⁶ The Centers for Medicare and Medicaid (CMS) has implemented quality measures for tobacco cessation counseling and treatment in the hospital setting for patients having diseases or adverse health effects linked to tobacco use as described by the U.S. Surgeon General.³⁷ In 2013, USPSTF recommended annual lung cancer screening using low-dose CT for smokers, ages 55 to 77 with smoking histories exceeding 30 pack-years or former smokers who quit within the last 15 years. (A pack year is defined as twenty cigarettes smoked everyday for one year.) In an effort to maximize the health benefit from screening, CMS mandates that all Medicare beneficiaries undergo screening; for institutions to be reimbursed for this service, patients must also receive smoking cessation assistance.³⁸

To enhance cessation rates, it is critical for clinicians to identify smokers consistently, advise them to quit, and offer evidence-based cessation treatments.³³ Approximately 70% of smokers see physicians annually, and even brief physician advice to quit increases quit rates.³ Treatment delivered by a variety of healthcare providers increases abstinence rates,³ and involvement of multiple professionals has the potential to substantially increase quitting and readiness to quit.³⁹ Therefore, all professionals should provide smoking cessation interventions.³

PHARMACIES: GREAT PLACES TO ENGAGE

The community pharmacist is one of the only healthcare professionals who has regular interactions with large numbers of people “in health” and “in sickness.”^{40,41} This creates opportunities for partnerships with other health professionals to expand team-based care into the community. It also improves population access to health promotion and disease prevention services, particularly in hard-to-reach populations.^{41,42} The Centers for Disease Control (CDC) supports the role of pharmacists as health care extenders.⁴³ Smoking cessation is a particularly appropriate role for community pharmacists because three of the nicotine replacement therapies (NRT; skin patch, gum, lozenge) are available without a prescription. CDC encourages pharmacists to advise on the correct use of these products and to provide behavioral support or counseling.⁴¹ Community

pharmacies are also convenient locations for cessation services. Pharmacists and pharmacy staff are particularly well suited to play a more active role either through direct delivery of services or by providing brief education and referrals for people trying to quit smoking.⁴¹ Trained community pharmacy personnel may affect smoking cessation rates positively.⁴¹

Pharmacies are retooling to become an integral part of the health care system and moving into the treatment arena with the advent of retail health clinics.¹⁵ Community pharmacy personnel, therefore, have the potential to close gaps of care. They are particularly well positioned to assist patients in tobacco cessation using a community-wide approach. It includes increasing tobacco screening, delivering brief interventions for tobacco cessation, and referral to local resources for quitting or to state tobacco quitlines. Resources include a national network at 1-800-QUIT-NOW for free telephone support service and intensive specialist-delivered interventions.^{42,44,45}

The pharmacist’s role in counseling patients for tobacco cessation is not new.^{41,46-54} Pharmacist-led interventions can significantly impact abstinence rates in smokers,^{41,47,50,53,55-57} and are cost-effective.^{1,32,58-61} Having community pharmacists provide tobacco cessation interventions resulted in quitting success rates similar to other health care professionals, which ranged from 9.9% to 26%.⁵⁶ Pharmacists trained in tobacco cessation support are more likely to deliver it, spend more time on it, and adhere to evidence-based standards than those who receive no training.⁴⁹

Delivering a Brief Intervention

Frameworks such as the 5 A’s (Ask, Advise, Assess, Assist, Arrange), from the U.S. Public Health Service *Clinical Practice Guideline*, provide a feasible framework to deliver a brief tobacco cessation intervention.^{3,5} However, community pharmacists do not routinely integrate tobacco cessation screening and counseling activities into their daily pharmacy workflow.⁴⁶ Common perceived barriers include time limitations, lack of knowledge and skills, lack of training in effective counseling techniques, perception that behavioral counseling is beyond their role, lack of space, difficulty in identifying smokers at point of care, low patient demand, lack of opportunity to network with other primary care professionals, and lack of financial incentives for counseling smokers.^{41,46,48,49,62}

An alternative approach to the 5As involves an abbreviated three step process—“Ask, Advise, and Refer” (AAR). AAR offers a feasible means for busy practice settings to deliver brief tobacco interventions and addresses time barrier issues.³ It requires less than five minutes and allows pharmacy technicians to help.⁴² This three stage approach has been shown to be an effective model for community pharmacies to “ask about tobacco use,” and “advise tobacco users to quit.” They “refer tobacco users” who want to quit to an intensive, specialist-delivered intervention (e.g. state telephone quitlines or local resources).^{44,45,62-67} Pharmacy

technicians can participate in the Ask, prepare enrollment forms, and fax referrals to state quitlines.⁴²

Keys to maintaining vigorous tobacco-cessation programs in pharmacies include strong staff training, incorporation of tobacco screening and brief intervention into pharmacy work-flow, documentation of process and clinical outcomes, and continuous feedback from staff and patients.⁶⁸ Safeway was the first community pharmacy chain to incorporate an organization-wide initiative to implement brief smoking cessation interventions. It uses AAR as a routine component of patient care and promotes referrals to state quitlines in partnership with state public health departments.⁶⁹ Another large pharmacy chain, CVS, claims its pharmacists have counseled more than 260,000 patients and filled nearly 600,000 NRT prescriptions since banning sale of tobacco products in 2014.⁷⁰

Members of the public who are counseled by a trained pharmacist about smoking cessation are more likely to value the intervention, to find it helpful, and to consider pharmacist intervention appropriate.⁴⁹ Despite this, pharmacy-based quit programs are not widely used. Evidence suggests the public may be unaware of the extended services provided by pharmacists; some may lack confidence in the pharmacist's non-dispensing role and have concerns about privacy in pharmacy outlets.⁴⁹

Pharmacists believe that endorsement of an extended role by national directives and/or a professional body will help them to better deliver tobacco cessation support to the public. Integrating an academic detailer or "facilitator" who would help deliver tobacco cessation counseling can be helpful. Introduction of new pharmacy roles, especially the certified pharmacy technician, can help with ever increasing dispensing workloads.⁴⁹

COMMON EVIDENCE-BASED TREATMENT STRATEGIES

Evidence-based effective treatments (individual, group, and telephone cessation counseling) and seven FDA-approved medications help tobacco users quit.³ Counseling and medication are effective when used alone for treating tobacco dependence. The combination of counseling and medication is more effective than either alone,³³ typically producing long-term abstinence rates of 25% to 30% after any single quit attempt.⁷¹

Non-Pharmacologic Treatment

Brief clinical approaches for patients willing and unwilling to quit are described in the 2008 practice guidelines. Strategies include brief clinical interventions using the 5A or AAR approaches.³ Even brief low-intensity counseling, including those lasting only three minutes or fewer, increase long-term quit rates. A strong dose-response relationship exists between the intensity of counseling and cessation rates (that is, more or longer sessions improve cessation rates).^{3,5} Direct comparisons between intensive and minimal advice suggest that more intensive advice

Table 1. Components of Behavioral Counseling³

Training smokers in problem solving skills (i.e. 1. recognizing danger situations e.g. being around smokers, cues, and urges; 2. developing coping skills e.g. anticipate and avoid triggers, developing cognitive strategies to reduce negative moods and stress, and 3. altering routines)

Providing basic information (e.g. health consequences of continued smoking, benefits of quitting, nicotine withdrawal symptoms)

Providing social support (i.e. helping smokers identify strategies to build social networks [identifying a buddy] can sustain motivation to quit or sustain a tobacco-free life).

offered a significant advantage.⁹ Behavioral therapy alone increases quit rates by 1.5 to 2.1.³ **Table 1** describes effective components of behavioral counseling.

Pharmacotherapy

All pharmacotherapy aids for tobacco cessation relieve nicotine withdrawal symptoms. Clinical guidelines consider seven first-line agents for tobacco cessation that reliably increase abstinence rates relative to placebo control. These agents include nicotine replacement therapy (NRT; skin patch, gum, lozenge, inhaler, nasal spray), bupropion, and varenicline.^{3,5} Healthcare providers should encourage all smokers—with the exception of women who are pregnant or breast-feeding, adolescents, and those with medical contraindications—to use pharmacotherapy. Clinicians should recommend behavioral therapy alone to patients who cannot use pharmacotherapy.³

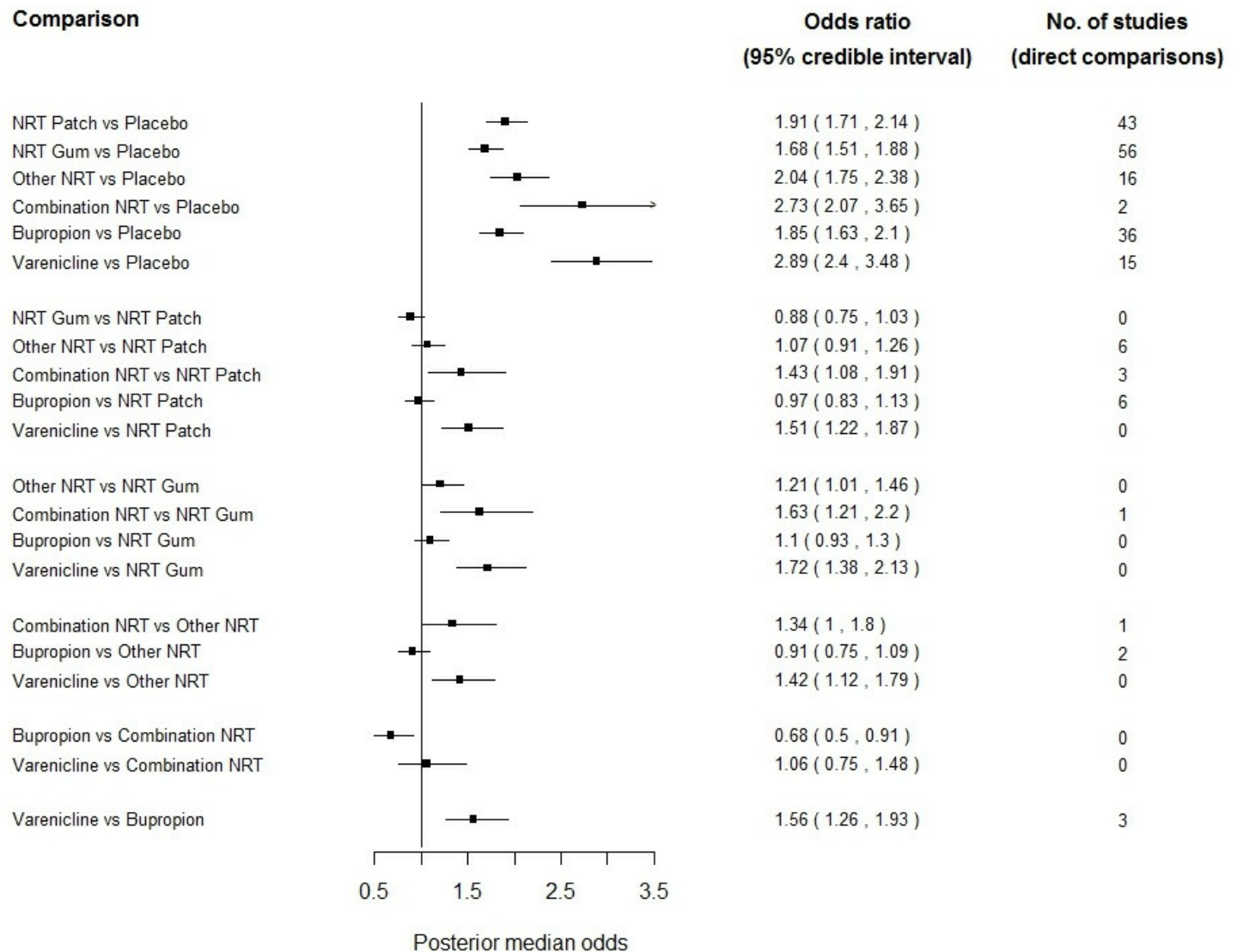
In an updated comparative review that included 267 studies (involving 101,804 participants),⁷² all three treatments (NRT, bupropion, varenicline), were associated with higher rates of tobacco cessation compared with placebo. Direct comparisons between NRT and bupropion showed no difference in efficacy. Varenicline was shown to be superior to any single type of NRT (OR, 1.57 [CI, 1.29-1.91]) and to bupropion (OR, 1.59 [CI, 1.29-1.96]). However, it was not more effective than combination NRT.⁷² Combining two types of NRT (discussed below) was found superior to a single form.^{9,72} In summary, varenicline (27.6%) and combination NRT (31.5%) were most effective for achieving tobacco cessation. None of the therapies were associated with an increased rate of serious adverse events (see **Figure 1**).⁷³

Product-specific information are provided in **Table 2 (Pages 9-10)**

Nicotine Replacement Therapies

NRT reduces withdrawal symptom severity and cravings. It also reduces the reinforcing effects of nicotine delivered via tobacco while providing an alternative source of nicotine.⁷⁴ Currently, five NRT products are sold in the U.S.: three nonprescription products (skin patch, gum, and lozenge) and two prescription-only products (oral inhaler and nasal spray).⁷⁵ Different forms of NRT are equally effective and increase quit rates by 50% to 70% at six months.^{72,74}

Figure 1. Effectiveness of Various Pharmacotherapies for Smoking Abstinence of 6 Months or More



SOURCE: Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis (Review). Cochrane Database of Systematic Reviews. 2013;5.No.:CD009329. DOI:10.1002/14651858.CD009329.pub2. Reprinted with Permission.

The patch has a slow onset, but produces steady nicotine levels for 16 or 24 hours (depending on the specific product). It offers prolonged withdrawal relief without requiring frequent administration, is easy to use, and promotes the best adherence.⁷⁵ However, once applied, it is difficult to titrate the dose to control “breakthrough cravings” or withdrawal symptoms.

The other four NRT formulations (nicotine gum, lozenge, inhaler, and nasal spray) have more rapid onsets and shorter durations of action. Subsequently, patients need repeated administration on a fixed schedule that is tapered appropriately to maintain stable nicotine blood levels if used alone. Their major advantage is ad-libitum (meaning as desired or at the patient’s discretion) dosing to cope with situationally-induced breakthrough cravings or withdrawal symptoms when used together with a long-acting medication (such as nicotine patches, bupropion, or varenicline).⁷⁵ Evidence indicates that combining

the patch with the shorter-acting NRT products is safe and more effective than any single NRT, and as effective as varenicline.⁷²

Patients typically start NRT products on the first day of quitting smoking (quit day) for 8 to 12 weeks (or up to 6 months for inhaler and nasal spray).³ Current evidence is limited or conflicting for using pre-quit NRT (i.e. use for several weeks prior to tobacco cessation),^{76,77} extended duration NRT,⁷⁸ higher dose,⁷⁹ or relapse prevention,⁸⁰ and in cessation induction among smokers who are not yet ready to quit.^{81,82}

PAUSE AND PONDER:

How do patients and the public perceive pharmacist-based tobacco cessation support and other non-dispensing pharmacist roles?

NON-NICOTINE MEDICATIONS

The FDA has approved two non-nicotine medications for tobacco cessation, bupropion SR and varenicline.

Bupropion SR

The FDA initially approved bupropion as an atypical antidepressant. Later, the FDA approved a 150-mg sustained-release (SR) tablet for tobacco cessation to be taken in two daily doses at least eight hours apart. Bupropion is equally effective in smokers with and without histories of depression.⁸³ Dosing for one week before quitting is recommended to achieve steady-state blood levels and patients should set a target quit date within the first two weeks of treatment.³ Bupropion's mode of action is not completely understood, but it is likely that blocking neuronal dopamine reuptake reduces the severity of nicotine cravings and withdrawal symptoms.³ Its most common adverse effects are insomnia (30% to 40% of patients) and dry mouth (approximately 10%).⁸³ Bupropion increases seizure risk in 0.1% of smokers and is therefore contraindicated in smokers with seizure or eating disorder histories (see [Table 2](#) for contraindications).³ As an aid to smoking cessation treatment, it is typically prescribed for seven to 12 weeks, and FDA approved for long-term maintenance of smoking cessation for up to six months.³

Varenicline

Varenicline has dual effects. It is a partial agonist at the alpha-4-beta-2 ($\alpha 4\beta 2$) nicotinic receptor subtype in the brain that mediates nicotine dependence.^{84,85} As a partial agonist, it relieves nicotine withdrawal symptoms while blocking the reinforcement of smoking by preventing nicotine from binding to the $\alpha 4\beta 2$ receptor (antagonist action). Varenicline at standard dose increases the odds of long-term abstinence between two- and three-fold compared with pharmacologically unassisted quit attempts.⁸⁶ Patients typically start varenicline one week before quitting and continue for a total of 12 weeks.^{84,85}

Alternatively, newer dosing strategies employ more flexible schedules to allow a longer pre-treatment period up to 35 days before the quit date and a more gradual quit approach (for individuals unwilling or unable to quit within the next month but willing to reduce smoking and make a quit attempt at three months). Alternative schedules significantly improved the rates of achieving higher continuous abstinence compared to placebo of 31% vs. 8% (week 1 after target quit date through the end of treatment) and 24% vs. 6% (from weeks 15 through 52), respectively.^{87,88}

Furthermore, varenicline maintenance therapy for up to six months yielded 44% continuous abstinence compared with 37% for placebo. Maintenance therapy is FDA-approved for extended treatment, with safety established for up to one year.⁸⁹

Based on the evidence so far, varenicline delivers one extra successful quitter for every 11 people treated, compared with

Update: Neuropsychiatric Adverse Effects

In 2009, the FDA reviewed case reports for all smoking cessation drugs and reported that varenicline and bupropion, but not NRT, were “associated with reports of changes in behavior such as hostility, agitation, depressed mood, and suicidal thoughts or actions.” It mandated a *Boxed Warning* on product labeling.⁹⁰ However, researchers collected subsequent data from a large comparative trial of the three first-line smoking cessation drugs in more than 8000 adult smokers with and without psychiatric disorder. The data did not support an increase in adverse neuropsychiatric events.⁹¹ The FDA removed the *Boxed Warning* for both drugs at the end of 2016.⁹²

smokers trying to quit without varenicline.⁸⁶ The most common dose-dependent adverse effect is nausea, occurring in 30% of users. Nausea can be mitigated by taking varenicline with food and adequate water or reducing the dose.⁸⁴⁻⁸⁶ Additional information is provided in [Table 2](#).

Combination Pharmacotherapy

Combination pharmacotherapy may increase abstinence. The guidelines endorse combination pharmacotherapy for treating tobacco dependence in patients who fail monotherapy; have breakthrough cravings; are highly dependent smokers; or in managing nicotine withdrawal symptoms.^{3,5,93} Using two or more forms of NRT has the strongest evidence base and includes the use of a long-acting nicotine patch plus ad lib short-acting NRT (gum, lozenge, or nasal spray) to deal with acute cravings and withdrawal symptoms.^{3,94} Bupropion plus NRT is an FDA-approved combination commonly used in practice. However, there is inconclusive evidence that this combination increases long-term abstinence rates (lasting six or more months) compared with NRT alone.^{3,83} Data are limited concerning other pharmacotherapy combinations; studies have examined varenicline and bupropion in combination⁹⁵ and varenicline and NRT in combination.⁹⁶



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ENDS: Unapproved as a Smoking Cessation Aid

The FDA has not approved any specific electronic nicotine delivery systems as cessation interventions.⁹ Limited data demonstrates efficacy on cessation rates at 6 months or more among smokers intending to quit, and the evidence regarding these devices' safety for smoking cessation is inconclusive.^{5,9} Health-care providers should not recommend ENDS as aids to tobacco cessation.

CONCLUSION

Community pharmacies are convenient locations for cessation services. Pharmacists and pharmacy staff are particularly well suited to play a more active role as information sources and support providers for people trying to quit smoking. Extending pharmacy-based tobacco cessation services in the community as a public health initiative could reach vulnerable populations at high risk for tobacco use. Trained, credentialed pharmacy personnel are more likely to deliver tobacco cessation support to members of the public.

Common Resources for Tobacco Cessation

Pharmacists: Help Your Patients to Quit Smoking

<https://www.cdc.gov/tobacco/campaign/tips/partners/health/pharmacist/index.html>

Direct smokers to **state tobacco quit lines**

Available through a national network at
1-800-QUIT-NOW (1-800-784-8669)
[CDC.gov/tips](https://www.cdc.gov/tips)

Tobacco Use Counseling

Fact sheets and resources; AHRQ website: www.ahrq.gov



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Table 2. Comparison of First-line Medications for Tobacco Cessation

Formulation	Availability	Specific Instructions	Dosing Guidelines	Dosing	Duration	Common Adverse Effects	Specific Comments
*Nicotine Patch (Nicoderm CQ, generic) (24-h release)	OTC	Note: Apply anywhere on the body that is dry, clean, and hairless.	Based on cigarettes smoked per day: >10 cigs/day: 10-week plan Start with Step 1 (21mg) x 6 wk <10 cigs/day: 8-week plan, Start with Step 2 (14mg) x 6 wk	Step 1 - 21 mg daily x 6 wk Step 2 - 14mg daily x 2 wk Step 3 - 7mg daily x 2 wk	8-10 weeks	local skin reactions (erythema, pruritus, burning) at site of application; rotate sites sleep disturbances (insomnia, abnormal or vivid dreams)	Rotate sites to avoid skin reactions. For sleep disturbances, remove patch at bedtime and reapply in the morning
*Nicotine gum (Nicorette)	OTC	Note: Gum should be chewed slowly until a "tingling" sensation emerges, then parked between cheek and gum to facilitate nicotine absorption. Resume chewing when tingle fades. Each piece should be "chewed" and "parked" intermittently for approximately 30 minutes. Note: Lozenge should NOT be chewed and swallowed. It should be moved from one side of the mouth to the other until completely dissolved.	2 mg, 4 mg Starting dose based on time to first cigarette after waking <30 min: 4 mg >30 min: 2 mg	Wk 1-6: 1 piece every 1-2 h Wk 7-9: 1 piece every 2-4 h Wk 10-12: 1 piece every 4-8 h 9 pieces/d (Max 24)	12 weeks	mouth and throat soreness, jaw fatigue, hiccups, dyspepsia, and undesirable taste	No food or beverages 15 minutes before or during use. Contraindicated in TMJ disorder.
*Nicotine lozenge, mini-lozenge	OTC	Note: Lozenge should NOT be chewed and swallowed. It should be moved from one side of the mouth to the other until completely dissolved.	2 mg, 4 mg Starting dose based on time to first cigarette after waking <30 min: 4 mg >30 min: 2 mg	Wk 1-6: 1 lozenge every 1-2 h Wk 7-9: 1 lozenge every 2-4 h Wk 10-12: 1 lozenge every 4-8 h 9 pieces/d (Max 20) in the first 6 weeks; ≤ 5 pieces in 6 hours.	12 weeks	Nausea, hiccups, cough, heartburn, flatulence, insomnia	No food or beverages 15 minutes before or during use. Contraindicated in TMJ disorder.
*Nicotine Inhaler (NicoInhaler)	Rx	Mouthpiece and plastic cartridge. The cartridge is inserted into the mouthpiece prior to use. Note: Best effects with continuous puffing for 20 minutes; puff in short breaths as if lighting a pipe; do NOT inhale into lungs (like a cigarette).	10 mg cartridge delivers 4mg inhaled nicotine vapor <30 min: 4 mg >30 min: 2 mg	6-16 cartridges/day individualize dosing. patients may self-titrate to the level of nicotine they require Gradual reduction after 6 weeks	3 to 6 months	Mouth and/or throat irritation, cough, dyspepsia	No food or beverages 15 minutes before or during use. Use with caution in patients with severe bronchospastic airway disease
*Nicotine Nasal Spray (NicoInhaler NS)	Rx	Metered spray Note: tilt head back slightly; insert tip of bottle into nostril; breathe through mouth; spray once in each nostril. Do not sniff, swallow, or inhale through the nose as the spray is being administered. If nose runs, gently sniff to keep spray in nose and wait 2 or 3 minutes before blowing nose.	10ml spray bottle contains 100mg nicotine (10mg/ml) or 200 sprays One dose (1 mg of nicotine) = 2 sprays, one in each nostril: each spray delivers 0.5 mg nicotine in 50 microliter aqueous nicotine solution to the nasal mucosa.	1-2 doses/hour (8-40 doses/day) For best results, initially use at least 8 doses/day. (Max: 5 doses/hour or 40 doses/day)	3 to 6 months	Nasal and/or throat irritation (hot, peppery, or burning sensation), rhinorrhea, tearing, sneezing, cough (transient and lessens after 3 weeks)	Not recommended in patients with chronic nasal disorders (e.g. allergic rhinitis, nasal polyps, and sinusitis) AND in severe reactive airway disease. Higher potential for abuse and dependency due to its greater speed of onset and greater capacity for self-titration of dose compared to other NRT products
Bupropion SR (Zyban) [†]	Rx	Begin therapy 1 week prior to quit date.	150 mg sustained-release tablet	150 mg PO q day x 3, then 150 mg PO bid (interval of at least 8 hours).	7-12 weeks Up to 6 months	Insomnia; Dry mouth Seizures	Contraindicated in people with a history of seizures, eating disorders, & use of an MAO inhibitor within past 14 days Boxed warning removed (2016) for neuropsychiatric adverse events and suicide; downgraded to a warning. Dose adjustment required with renal and hepatic impairment.

Table 2. Comparison of First-line Medications for Tobacco Cessation

Formulation	Availability	Specific Instructions	Dosing Guidelines	Dosing	Duration	Common Adverse Effects	Specific Comments
Varenicline (Chantix) [†]	Rx	<p>Begin therapy 1 week prior to quit date.</p> <p>Or Alternatively: <i>Flexible Quit Approach:</i> begin dosing and then quit smoking between days 8 and 35 of treatment</p> <p><i>Gradual/Quit Approach:</i> gradually reduce smoking by 50% from baseline by first 4 weeks, by an additional 50% in next 4 weeks, and continue reducing with the goal of quitting by week 12 or sooner. Continue for an additional 12 weeks for a total of 24 weeks of treatment.</p>	<p>-0.5 mg, 1.0 mg tablet</p> <p>-Continuing Month Pak: 1 mg</p> <p>-Starting Month Pak: 0.5 mg x 11 and 1 mg x 42</p>	<p>Days 1 to 3: 0.5 mg once daily</p> <p>Days 4 to 7: 0.5 mg twice daily</p> <p>Weeks 2-12: 1 mg twice daily</p>	12 weeks Up to 6 months	<p>Nausea, insomnia, abnormal/vivid dreams, constipation, flatulence, and vomiting (usually transient)</p>	<p>-CrCl < 30 mL/min: initiate: 0.5mg daily; titrate to 0.5mg twice daily</p> <p>-ESRD receiving hemodialysis: maximum dose of 0.5mg daily.</p> <p>-Doses should be administered after meals with a full glass of water.</p> <p>New or worsening seizures: caution in people with a history of seizures, alcohol use, or other factors that can lower the seizure threshold.</p> <p>New warning: of somnambulism (2016)</p> <p>Boxed warning removed (2016) for neuropsychiatric adverse events and suicide; downgraded to a warning.</p>

*All forms nicotine replacement products (NRT) include the following contraindications and precautions: 1) recent (<2 weeks) myocardial infarction; 2) serious underlying arrhythmias; 3) serious or worsening angina pectoris; 4) pregnancy category D, avoid in pregnant and breastfeeding women; 5) < 16 years of age.

† Contraindicated in adolescents < 18 years of age; cautious use in pregnant and breastfeeding women; however, pregnant smokers should be encouraged to attempt cessation using educational and behavioral interventions before pharmacological approaches are used.

References: www.chantix.com; Zyban Package Insert accessed June 13, 2017: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Zyban/pdf/ZYBAN-PI-MG.PDF; Nicoderm CQ Patch: accessed June 13, 2017 at https://www.nicodermcq.com/products.html?rotation=7170000009402807&barrier=58700000401391859&kw=6026530627&qoqgle=e_&ocid=CL6c4p_Lu9OCFZ2Kswodp0kNaQ&ndsrc=3aw.ds; Nicorette gum and lozenge. Accessed June 13, 2017 at www.nicorette.com; Nicotrol Inhaler accessed June 13, 2017 at www.nicotrol.com; Nicotrol NS Spray package insert accessed June 13, 2017 at http://www.pfizer.com/files/products/uspi_nicotrol.pdf

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