

## Lesson 3: Treatment of Tobacco Use

### Pharmacological Approaches to Tobacco Cessation

Medications play a crucial role in managing withdrawal symptoms and cravings, significantly improving cessation outcomes by addressing the physiological aspects of nicotine addiction.

Nicotine replacement therapy provides controlled amounts of nicotine without the harmful chemicals in tobacco, allowing users to break the behavioral habit of smoking while managing withdrawal symptoms. NRT is available in multiple formulations that differ in speed of delivery and route of administration. The patch delivers a steady amount of nicotine through the skin over 16-24 hours, available over-the-counter in various strengths including 21mg, 14mg, and 7mg for 24-hour patches. Gum provides intermittent nicotine doses through buccal absorption when chewed and "parked" between cheek and gum, available over-the-counter in 2mg and 4mg strengths. Lozenge is similar to gum but doesn't require chewing, dissolving slowly in the mouth, available over-the-counter in 2mg and 4mg strengths. Inhaler consists of a cartridge attached to a mouthpiece, delivering nicotine through inhalation and oral absorption, available by prescription only. Nasal spray delivers nicotine directly through nasal mucosa for rapid absorption, providing the fastest nicotine delivery of all NRT forms, available by prescription only.

Efficacy of NRT has been demonstrated across numerous studies and meta-analyses. All forms of NRT are effective, with quit rates of 16.9% versus 10.5% for placebo, yielding a relative risk of 1.55 (95% CI 1.49-1.61). Combination approaches using multiple forms of NRT, typically a patch for steady baseline nicotine levels plus a faster-acting form like gum or lozenge for breakthrough cravings, increase effectiveness with success rates of 16.9% versus 13.9% for single-form NRT, yielding a relative risk of 1.25 (95% CI 1.15-1.36). Common side effects include local irritation at the site of application or absorption, such as skin irritation with patches, mouth or throat irritation with gum, lozenges, and inhalers, and nasal irritation with spray. Additional side effects may include hiccups, nausea, and sleep disturbances with 24-hour patches. Contraindications are few, with caution advised in patients with recent myocardial infarction, serious arrhythmias, and unstable angina, though even in these patients NRT is generally safer than continued smoking.

Bupropion SR, marketed as Zyban, is a non-nicotine medication that reduces cravings and withdrawal symptoms through effects on brain chemistry. The mechanism involves acting as a dopamine and norepinephrine reuptake inhibitor, increasing levels of these neurotransmitters in the brain, and also antagonizing nicotinic acetylcholine receptors. Dosing typically starts 1-2 weeks before the quit date at 150mg daily for 3 days, then increases to 150mg twice daily for 7-12 weeks, allowing medication levels to build before the quit attempt. Efficacy is well-established, with abstinence rates of 19.0%

versus 11.0% for placebo, yielding a relative risk of 1.64 (95% CI 1.52-1.77). Side effects include insomnia which can often be managed by avoiding evening doses, dry mouth, headache, nausea, anxiety, and constipation. Contraindications include seizure disorders due to bupropion lowering seizure threshold, eating disorders where seizure risk is increased, use of MAO inhibitors within 14 days due to dangerous interactions, and abrupt discontinuation of alcohol or sedatives which increases seizure risk.

Varenicline, marketed as Chantix, is a partial nicotinic receptor agonist specifically developed for smoking cessation and represents the most effective single pharmacotherapy available. The mechanism involves partially stimulating nicotinic receptors to reduce withdrawal symptoms while simultaneously blocking nicotine's rewarding effects if the person smokes. Dosing is titrated over one week to minimize side effects: 0.5mg once daily for days 1-3, then 0.5mg twice daily for days 4-7, then 1mg twice daily for the remainder of treatment, typically 12 weeks. Efficacy is superior to other single agents, with quit rates of 25.6% versus 11.1% for placebo, yielding a relative risk of 2.24 (95% CI 2.06-2.43). Comparative effectiveness studies show varenicline is more effective than NRT in 8 direct comparison studies and more effective than bupropion in 6 direct comparison studies. Side effects include nausea which is the most common and can often be managed by taking medication with food, insomnia, abnormal dreams, headache, and constipation. Safety concerns about neuropsychiatric side effects were raised initially, but the large EAGLES trial found no significant increase in these events compared to NRT or placebo, leading to removal of the black box warning.

Second-line medications provide additional options when first-line treatments fail or are contraindicated. Nortriptyline, a tricyclic antidepressant, has been shown to approximately double cessation rates compared to placebo, though it has more side effects than first-line medications. Clonidine, an alpha-2 adrenergic agonist, reduces withdrawal symptoms but has significant side effects including dry mouth, drowsiness, and dizziness that limit its use. Cytisine is a partial nicotinic receptor agonist similar to varenicline, widely used in Eastern Europe but not FDA-approved in the US, showing efficacy similar to NRT at lower cost.

## **Non-Pharmacological Treatments for Tobacco Cessation**

Behavioral and psychosocial interventions form the foundation of effective tobacco cessation treatment, addressing the psychological, behavioral, and social aspects of addiction.

Counseling approaches in various formats demonstrate effectiveness in supporting cessation. Individual counseling through one-on-one sessions with a trained specialist significantly increases quit rates compared to minimal intervention, with relative risk of 1.48 (95% CI 1.34-1.64). Group counseling provides peer support and shared problem-solving, with quit rates approximately double those of self-help approaches,

yielding relative risk of 1.88 (95% CI 1.52-2.33). Telephone counseling through proactive quitline services increases cessation rates by 25-38% compared to minimal intervention, providing accessible support regardless of location. Brief clinical interventions demonstrate that even short 3-5 minute advice from physicians increases quit rates by 76% compared to no intervention, with relative risk of 1.76 (95% CI 1.58-1.96), making this one of the most time-efficient interventions in medicine.

Cognitive-behavioral therapy addresses the thoughts, feelings, and behaviors associated with tobacco use through structured interventions. Components include self-monitoring to increase awareness of smoking patterns and triggers, identifying triggers that prompt smoking urges, developing coping skills to manage cravings and high-risk situations, managing negative emotions that may lead to smoking, and preventing relapse through planning and skill development. Efficacy has been demonstrated through meta-analyses showing that CBT approaches significantly increase cessation rates and are more effective when combined with pharmacotherapy, addressing both biological and psychological aspects of addiction. Delivery formats can include individual sessions, group programs, or self-help materials, with similar effectiveness when properly implemented, allowing flexibility to match patient preferences and available resources.

Motivational approaches help patients resolve ambivalence and strengthen commitment to quitting. Motivational interviewing is a client-centered counseling style that explores and resolves ambivalence about behavior change through empathic listening, developing discrepancy between current behavior and personal values, rolling with resistance rather than confronting it, and supporting self-efficacy. Stage-based interventions are tailored to patients' readiness to quit based on the Transtheoretical Model of Change, recognizing that different strategies are appropriate for people at different stages of readiness. Efficacy is most pronounced for patients who are not initially ready to quit or who have low motivation, helping move them toward readiness for a quit attempt.

Technology-based interventions leverage digital platforms to extend the reach of cessation support beyond traditional in-person or telephone counseling. Web-based programs provide interactive websites offering tailored content based on user characteristics, self-monitoring tools for tracking progress, and community support through forums or social features. Mobile applications offer smartphone apps providing on-demand support when cravings strike, tracking of progress and patterns, and personalized feedback based on user data. Text messaging programs like SmokefreeTXT provide regular messages of tips, motivation, and support, maintaining connection between counseling sessions. Efficacy of mobile phone-based interventions has been demonstrated, with quit rates of 9.5% versus 5.6% for controls, yielding relative risk of 1.54 (95% CI 1.19-2.00).

Specialized approaches for specific populations recognize that different groups have

unique needs and challenges. For pregnant women, behavioral counseling increases cessation rates from 12.2% to 16.4% for controls, yielding relative risk of 1.35 (95% CI 1.23-1.48), and improves birth outcomes including reduced low birth weight and preterm birth. For adolescents, school-based programs and interventions addressing social influences show promise, though evidence remains limited due to challenges in conducting research with this population. For patients with mental health conditions, integrated treatment addressing both tobacco use and mental health symptoms is most effective, recognizing the high comorbidity and interconnections between these conditions.

### **Social Influences on Tobacco Use and Cessation: Networks, Norms, and Support**

Tobacco use is profoundly influenced by social networks, with smoking behavior clustering within social groups and spreading through social ties in predictable patterns. The Framingham Heart Study demonstrated that smoking cessation spreads through social networks, with individuals being 36% more likely to quit if a spouse quits, 34% more likely if a friend quits, and 25% more likely if a sibling quits. Conversely, having friends or family members who smoke significantly reduces the likelihood of successful cessation, with each additional smoking contact in a person's social network decreasing their odds of quitting by approximately 10%. Social norms around smoking within one's peer group create powerful influences on both initiation and cessation, with individuals often underestimating the extent to which their social environment shapes their tobacco use.

Partner and family support significantly predicts cessation success, making involvement of loved ones an important component of comprehensive tobacco treatment. Spouses and partners can provide encouragement, help manage withdrawal symptoms, participate in distraction activities during cravings, and reinforce the decision to quit. However, when partners or household members continue to smoke, cessation becomes significantly more challenging due to environmental cues, easy access to cigarettes, and social modeling of smoking behavior. Addressing household smoking through concurrent cessation attempts or establishing smoke-free home policies supports individual quit attempts while providing health benefits for all household members. Healthcare providers should assess patients' social smoking context, including household members' tobacco use, friends' smoking patterns, and social situations that trigger smoking.

Social support interventions enhance cessation outcomes through multiple mechanisms. Peer support programs connect individuals attempting to quit with others

who have successfully quit or are in the process of quitting, providing role modeling, practical advice, and emotional support. Group cessation programs offer structured support combined with education and skill-building, with the shared experience creating accountability and reducing isolation. Online communities and text messaging support programs extend social support beyond geographic boundaries, providing 24/7 access to encouragement and advice. Healthcare providers should help patients identify supportive relationships that can facilitate cessation while developing strategies to navigate social situations that involve smoking. For patients whose social networks are heavily composed of smokers, building new social connections with non-smokers may be an important component of sustained cessation. When relationship dynamics significantly complicate cessation efforts, such as when a partner actively undermines quit attempts, addressing these relationship issues may be necessary for successful tobacco treatment.

## **Integrated Treatment Approaches**

Combining pharmacological and behavioral interventions provides the most effective approach to tobacco cessation, addressing multiple aspects of addiction simultaneously.

Combination therapy benefits are well-established through research demonstrating that integrated approaches yield superior outcomes compared to single-modality treatment. Combined behavioral counseling and pharmacotherapy shows higher abstinence rates than usual care, with success rates of 15.2% versus 8.6%, yielding relative risk of 1.83 (95% CI 1.68-1.98). Adding behavioral support to pharmacotherapy increases success rates by approximately 15%, from 17% to 20%, yielding relative risk of 1.15 (95% CI 1.08-1.22). The synergistic effect occurs because medications address physical dependence and withdrawal symptoms while behavioral strategies address psychological and behavioral aspects including triggers, coping skills, and motivation.

Implementation models provide frameworks for integrating cessation interventions into healthcare settings. The 5A's model involves Ask about tobacco use, Advise to quit, Assess readiness, Assist with quitting, and Arrange follow-up, providing a comprehensive framework for systematic intervention. The 2A's and R model offers a streamlined approach focusing on Asking, Advising, and Referring to specialized resources, appropriate for very brief encounters. The AAC model emphasizes Ask, Advise, and Connect patients directly to quitline services through electronic referral, facilitating access to intensive support. All models emphasize the importance of systematic screening and intervention for all patients rather than selective intervention based on provider assumptions.

Stepped care approaches match treatment intensity to patient needs and response,

beginning with less intensive interventions and intensifying as needed. Initial treatment typically begins with less intensive interventions for lighter smokers or those with lower dependence, such as brief advice plus single medication. Treatment is intensified for those who fail initial approaches or who have high dependence, comorbidities, or multiple failed quit attempts, potentially including adding medications, combining medications, extending treatment duration, or increasing counseling frequency and intensity. This approach ensures that patients receive appropriate intensity of treatment while using resources efficiently.

Relapse prevention strategies maintain long-term abstinence after initial cessation. Extended use of pharmacotherapy beyond the standard 8-12 weeks reduces relapse risk for patients with high dependence or history of rapid relapse. Continued behavioral support, particularly during high-risk periods such as holidays, stressful life events, or social situations involving alcohol, enhances long-term success. Skills training for identifying and managing high-risk situations prevents lapses from becoming relapses by preparing patients with specific coping strategies.

### **Special Considerations in Tobacco Cessation Treatment**

Certain clinical scenarios and patient populations require tailored approaches that address their unique circumstances and needs.

Pregnant and breastfeeding women require careful consideration to balance cessation benefits against potential treatment risks. Behavioral interventions are first-line treatment, showing both increased cessation rates and improved perinatal outcomes including reduced low birth weight, preterm birth, and pregnancy complications. NRT use is controversial during pregnancy, with mixed evidence on effectiveness and limited data on safety, creating uncertainty about risk-benefit balance. The USPSTF concludes that evidence is insufficient to assess the balance of benefits and harms of NRT during pregnancy. Decision-making should consider the severity of tobacco dependence, with heavier smokers potentially benefiting more from NRT despite uncertain risks, and engage in shared decision-making that respects patient autonomy while providing full information about known and unknown risks.

Patients with psychiatric comorbidities require specialized approaches due to high smoking prevalence and unique challenges in this population. Contrary to previous concerns, quitting smoking generally improves mental health outcomes rather than exacerbating symptoms, with studies showing improved mood and reduced anxiety after successful cessation. Standard cessation medications appear safe and effective in most psychiatric populations, based on the EAGLES trial which included patients with mental health conditions. More intensive and longer-duration treatment may be needed, often integrated with mental health care to address both conditions simultaneously. Addressing misconceptions about smoking's "benefits" for mental health is crucial, as many patients and providers incorrectly believe that smoking helps manage psychiatric

symptoms when evidence suggests it actually worsens mental health over time.

Patients with medical comorbidities benefit substantially from cessation but may require treatment modifications. For cardiovascular disease, NRT is safe even in patients with stable coronary disease, with benefits of quitting far outweighing any potential risks from NRT. For COPD and asthma, combination therapy is particularly effective, though providers should consider potential medication interactions with respiratory medications. For cancer, cessation improves treatment outcomes and quality of life, though coordination with cancer treatment is important to avoid interactions. For substance use disorders, concurrent treatment can improve outcomes for both conditions, though monitoring for potential interactions between cessation medications and addiction treatment medications is important.

Light and non-daily smokers represent a growing population requiring adapted approaches. Standard dependence measures like the FTND may not accurately assess dependence in this group, as these tools were developed for daily smokers. Pharmacotherapy benefits are less clear for light smokers, though NRT used situationally when cravings occur may help some individuals. Behavioral interventions addressing psychological and social aspects of smoking are particularly important for this group, as their smoking is often more situation-dependent than driven by physical dependence.

Electronic cigarette users constitute an emerging population with unique cessation needs. Limited evidence exists on effective cessation strategies for exclusive e-cigarette users, as most research has focused on combustible cigarette smoking. The role of e-cigarettes in cessation from conventional cigarettes remains controversial, with some evidence suggesting they may help some smokers quit but concerns about their long-term health effects. The USPSTF concludes that evidence is insufficient to recommend e-cigarettes for smoking cessation. Continued e-cigarette use after smoking cessation, occurring in 38-80% of users in studies, raises concerns about sustained nicotine dependence and potential health effects of long-term vaping.

## **Treatment Monitoring and Follow-up**

Ongoing support and monitoring significantly improve long-term cessation outcomes by providing accountability, problem-solving, and encouragement.

Follow-up schedule should include regular contact that enhances success rates and allows for treatment adjustment. First follow-up should occur within the first week after the quit date, when relapse risk is highest and early intervention can prevent return to smoking. Subsequent contacts should be scheduled based on individual needs and relapse risk, with more vulnerable patients requiring more frequent contact. More intensive follow-up involving more frequent and longer duration contact is associated with higher success rates, though even brief contacts provide benefit.

Monitoring parameters guide ongoing treatment through comprehensive assessment. Abstinence status should be assessed through self-reported smoking status, ideally with biochemical verification when feasible using carbon monoxide breath testing or cotinine testing. Withdrawal symptoms should be evaluated for severity and duration to guide pharmacotherapy adjustments, with persistent severe symptoms suggesting need for medication adjustment. Medication adherence and side effects require assessment to ensure proper use and manage adverse effects that might lead to discontinuation. Coping strategies should be evaluated for effectiveness, adjusting behavioral techniques as needed. Weight, mood, and stress levels require monitoring to address common challenges to maintaining abstinence.

Managing lapses and relapses requires responding constructively to smoking resumption. Distinguish between lapses involving temporary slips with smoking of one or a few cigarettes and complete relapses involving return to regular smoking, as the response differs. Frame lapses as learning opportunities rather than failures, exploring what triggered the lapse and what can be learned to prevent future occurrences. Intensify treatment after lapses by adjusting medications, increasing counseling frequency, or adding new interventions to prevent progression to full relapse. For full relapses, assess reasons for relapse, address barriers that contributed to relapse, and develop a new quit plan when the patient is ready, recognizing that most successful quitters make multiple attempts.

Pharmacotherapy adjustments modify medication regimens based on response and side effects. Consider extending duration for patients with significant withdrawal or strong cravings beyond the standard treatment period. For inadequate response to single NRT, add a second form such as combining patch with gum or lozenge, or switch to varenicline which is more effective than NRT. Manage side effects through dose adjustments, timing changes such as taking medications with food to reduce nausea, or medication switches if side effects are intolerable. For patients who relapse on pharmacotherapy, consider a different medication or combination approach for subsequent attempts, as response varies among individuals.

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