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as a once-per-month 380-mg injection. By blocking opioid recep tors, naltrexone decreases activity in the dopamine-rich ventral tegmental reward system and decreases the feeling of pleasure if alcohol is imbibed. A second medication, acamprosate (Campral) (~2 g/d divided into three oral doses), has similar modest effects. Acamprosate inhibits NMDA receptors, decreasing mild symptoms of protracted withdrawal. Several trials of combined naltrexone and acamprosate have reported that the combination is well tolerated, and the efficacy might be superior to either drug alone, although not all studies agree. It is more difficult to establish the asset-to-liability ratio of a third drug, disulfiram, an ALDH inhibitor, used clinically at doses of 250 mg/d, a dose selected to avoid the side effects of the more effective 500 mg/d regimen. This drug produces vomiting and autonomic nervous system instability after drinking as a result of rapidly rising blood levels of acetaldehyde. This reaction to alcohol can be dangerous, especially for patients with heart disease, stroke, diabetes mellitus, or hypertension. The drug itself carries potential risks of temporary depressive or psychotic symptoms, peripheral neuropathy, and liver damage. Disulfiram is best given under super vision by someone (such as a spouse), especially during high-risk drinking situations (such as the Christmas holidays). Regarding other medications, a 16-week, placebo-controlled trial in patients with histories of relatively severe acute withdrawal syn dromes reported good outcomes during the rehabilitation phase with another depressant medication (gabapentin 1200 mg/d), but side effects were considerable; those results have not yet been replicated, and gabapentin can itself be misused. Additional drugs under inves tigation include another opioid antagonist, nalmefene; the nicotinic receptor agonist varenicline; the serotonin antagonist ondansetron; the α-adrenergic agonist prazosin, especially in combination with naltrexone; the GABAB receptor agonist baclofen; the anticonvul sant topiramate; ibudilast in individuals with low-intensity alcohol responses; and possible enhanced outcomes when talk therapies are combined with ketamine or psilocybin sessions. However, it is important to emphasize that currently there are insufficient data to determine the asset-to-liability ratio for these medications in treating alcohol use disorders, and therefore, there is insufficient support for the routine use of these medications in clinical settings. ■ ■GLOBAL CONSIDERATIONS As described above, rates of alcohol use disorders differ across sex, age, ethnicity, and country. There are also differences across countries regarding the definition of a standard drink (e.g., 10–12 g of ethanol in the United States and 8 g in the United Kingdom) and the definition of being legally drunk. The preferred alcoholic beverage also varies across groups, even within countries. That said, regardless of sex, ethnicity, or country, the actual drug in the drink is still ethanol, and the risks for problems, course of alcohol use disorders, and approaches to treatment are similar across the world. ■ ■FURTHER READING Bogenschutz MP et al: Percentage of heavy drinking days following psilocybin-assisted psychotherapy vs placebo in the treatment of adult patients with alcohol use disorder: A randomized clinical trial. JAMA Psychiatry 79:953, 2022. Finn SW et al: Treatment of alcohol

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Nicotine Addiction Nicotine Addiction Ingestion of nicotine in any form (combusted or heated tobacco leaf, oral use, nicotine pouches, or inhaled by vaping nicotine or nicotine salt) can create and sustain addiction if used with sufficient intensity for a sufficient duration. Addicted users of nicotine regulate their nicotine intake by adjusting the frequency and intensity of their tobacco use, both to obtain the desired psychoactive effects and avoid withdrawal. While nicotine does cause some disease processes including complications of pregnancy, the vast majority of the diseases produced by nicotine addiction result from repetitive exposure to the carcinogens and other toxicants in various nicotine containing prod ucts. These exposures produce incremental changes that accumulate to progress toward disease, but it is the addiction to nicotine that causes the long-term, multiple times per day exposures to these agents needed to create sufficient damage to manifest as cancer, heart, and lung disease. Over the last decade, there have been major shifts in product use, with about 40% of the nicotine delivery products being noncombusted and non-tobacco-leaf formulations. This shift has made practitioner advice about nicotine addiction more complicated, in part because many of the noncombusted products offer the potential to deliver nicotine sufficient to satisfy addiction, but with dramatic reductions in most of the toxic constituents found in smoke. Substantial reduction in disease risk can be achieved with the use of nicotine “vaping” products to aid cessation success for combusted cigarette smokers, and their use is likely to provide meaningful disease reduction with long-term complete substitution for combusted cigarette smoking even without breaking nicotine addiction. Nicotine offers little or no benefit for the nonaddicted individual, but regular use of inhaled nicotine can produce a powerful addiction that is difficult to break and expensive to sustain. Any use of nicotine earlier in life predicts a greater use of some nicotine product later in life. For the practitioner, despite the likelihood of much lower disease risks compared to combusted cigarette use, it is hard to justify, or ignore, high-frequency use of noncombusted inhaled nicotine prod ucts in recommendations to patients who have never used combusted tobacco products. THE PROCESS OF NICOTINE

ADDICTION When nicotine reaches the brain, it reversibly attaches to nicotinic acetylcholine receptors, which are particularly active in brain networks involved in depression, joy, excitement, and happiness. With prolonged

high exposure to nicotine, nicotinic receptors are upregulated on brain cells. For most individuals, daily nicotine use is needed to produce changes in the brain that are the hallmark of addiction. The strength of addiction, and the speed with which it can develop, are influenced by the frequency of use and concentration of arterial levels of nico tine reaching the brain, which can vary widely with use of different products.

As the time since last cigarette becomes longer, nicotine levels in the blood drop, and nicotine detaches from the receptors, leaving them increasingly uncovered. Without high levels of nicotine attaching to these receptors, addicted smokers no longer feel “normal,” creating a compulsive need for the next dose of nicotine. Addicted individuals perceive increasing withdrawal symptoms with increasing duration of abstinence, which can persist for 4–6 weeks. For the practicing clinician, the diagnosis of nicotine addiction is straightforward and is manifest by the patient’s loss of control over their next use of nicotine-containing products. The individual’s need for the next dose of nicotine can be satisfied by the use of multiple products at different times. The loss of control is demonstrated by a history of daily nicotine use coupled with behaviors such as high numbers of uses per day, use shortly after waking in the morning, craving after periods of abstinence, and/or failure of past cessation efforts, among others. PART 13 Neurologic Disorders Several genes have been associated with nicotine addiction. Some reduce the clearance of nicotine, and others have been associated with an increased likelihood of becoming dependent on tobacco and other drugs or a higher incidence of depression. It is likely that genetic sus ceptibility can influence the probability that adolescent experimenta tion with tobacco will lead to addiction as an adult. However, rates of smoking cessation have increased, and rates of nicotine addiction have decreased dramatically since the mid-1950s, suggesting that factors other than genetics are more important influences for tobacco use. In tobacco smoke or vaping aerosol, the fraction of nicotine pres ent in the unprotonated (freebase) form is greater at alkaline pH, and unprotonated nicotine is more easily absorbed into the bloodstream across the oral mucosa. However, high concentrations of unprotonated nicotine are irritating to the airway, reducing the tendency to inhale, limiting the amount of nicotine users will tolerate in the aerosol and slowing the rate of rise in nicotine blood levels. Products delivering nicotine that are highly addictive (cigarettes and aerosols of nicotine salts) are able to deliver high doses of nicotine and rapid rises in arterial blood concentration by producing aerosols that are mildly acidic in the mouth, reducing the irritation that inhibits inhalation. However, as the particles are inhaled into the lung, the pH of the smoke rapidly changes

Per-capita consumption 18+ Male lung cancer death rate Female lung cancer death rate

Per-capita consumption 18+

FIGURE 465-1 Changes in per-capita consumption and lung cancer death rates from 1900 to 2023.

to the more alkaline pH of the blood (~7.4), increasing the fraction of readily absorbable unprotonated nicotine present in the alveoli. The high rate of blood flow through the alveoli rapidly removes the unpro tonated nicotine, increasing conversion of the protonated nicotine or the

nicotine salt to release the unprotonated form and allowing most of the nicotine in the aerosol to be absorbed into the bloodstream. The resulting rapid rise in arterial blood nicotine levels reaching the brain makes cigarettes and nicotine salt vaping devices more addictive, and more able to satisfy addiction, compared with other forms of nicotine delivery. TRENDS IN NICOTINE PRODUCT USE Manufactured cigarettes have been the dominant form of nicotine exposure over the last 100 years. Figure 465-1 presents the rise and decline in U.S. per-capita consumption (total cigarettes sold divided by the U.S. population over age 18) since 1900, together with the rise and subsequent fall of the male and female lung cancer death rates resulting from that consumption. The figure demonstrates the enormous success of tobacco control efforts in changing a human risk behavior, with current adult cigarette smoking prevalence now approaching 10%. Among high school seniors, any cigarette use in the last 30 days has declined from 31% in 2000 to 2.9% in 2023, with only 0.7% smoking daily. As these post-2000 high school students aged into their 20s, their smoking initiation rates did not increase substantially, and only 5% of 18- to 24-year-old adults currently smoke. Unfortunately, smoking prevalence rates among those over age 40, the population more likely to develop disease, have declined more slowly. In addition, the population continuing to smoke has shifted heavily toward socially disadvantaged groups, indicating that the need for health care–based smoking inter ventions remains a priority. A vast array of devices to deliver nicotine without smoke have been introduced over the last decade. These include devices, many sold without U.S. Food and Drug Administration (FDA) approval, that aerosolize nicotine solution or nicotine salts, or deliver nicotine as strips or flavored nicotine pouches for oral use. With the exception of vaping, very limited data are available on patterns of use for most of these products in the United States. For vaping among adolescents, any use in the last 30 days peaked at about 25% in high school seniors in 2019 and declined to about 17% in 2023 with daily use at about 5.8% in 2023. The dramatic fall in combusted cigarette use over the past 2 decades among adolescents resulted from changes in the regulation of cigarette advertising and

Lung cancer death rate per 100,000

Year

the increasing social stigma associated with cigarette smoking. The introduction of vaping products as substitute sources of nicotine had little effect on the reduction in adolescent cigarette smoking, and the availability of vaping products has not increased adolescent smoking prevalence. For adults, about 5% report using e-cigarettes some days or every day, with 11% of the 18–24 group reporting at least some days. Rea sons for using e-cigarettes may include the following: for recreation, to sustain addiction, or to attempt to quit cigarette smoking. A substantial proportion of those using e-cigarettes for cessation report use of both e-cigarettes and combusted cigarettes interchangeably, called dual use. In contrast to the United States, tobacco consumption in many other countries remains high, particularly among lesser developed countries. Worldwide tobacco consumption recently declined slightly for the first time after a persistent rise over the recent decades. Changes in cost and relative rates of taxation for different tobacco products has resulted in an increase in smoking of cigars and “roll your own” cigarettes, but past recommendations about lower risk with use of cigars and pipe tobacco no longer apply. Most cigars are now manufac tured in much the same way as cigarettes with small changes in weight to qualify for lower tax rates, and most pipe tobacco is now used for “roll your own” cigarettes also because of lower tax rates. As a result, smok ing these products currently has risks similar to smoking manufactured cigarettes.

Practitioners should ask about their use and should not rec ommend them as lower-risk forms of satisfying nicotine addiction. DISEASE MANIFESTATIONS OF CIGARETTE SMOKING Approximately 40% of cigarette smokers will die prematurely due to cigarette smoking unless they are able to quit. The major diseases caused by cigarette smoking are listed in Table 465-1. The ratio of smoking-related disease rates in smokers compared to never smokers (relative risk) increases with advancing age for most cancers and for chronic obstructive pulmonary disease (COPD). Relative risk declines with advancing age for cardiovascular diseases due to the increas ing contribution of other risk factors to cardiovascular disease as age advances. Nevertheless, even for cardiovascular disease, the absolute difference in mortality rate between smokers and never smokers, called excess death rate, continues to increase with advancing age, as one would expect from a process of cumulative injury. ■ ■CARDIOVASCULAR DISEASES Cigarette smokers are more likely than nonsmokers to develop both large-vessel atherosclerosis and small-vessel disease. Approximately 90% of peripheral vascular disease in the nondiabetic population can be attributed to cigarette smoking, as can ~50% of aortic aneurysms. In contrast, 24% of coronary artery disease and ~11% of ischemic and hemorrhagic strokes are attributed to cigarette smoking. There is a multiplicative interaction between cigarette smoking and other cardiac risk factors such that the increment in risk produced by smok ing among individuals with hypertension or elevated serum lipids is substantially greater than the increment in risk produced by smoking for individuals without these risk factors. In addition to its role in promoting atherosclerosis, cigarette smok ing also increases the likelihood of myocardial infarction and sudden cardiac death by promoting platelet aggregation and vascular occlu sion. Reversal of these effects on coagulation may explain the rapid benefit of smoking cessation for a new coronary event demonstrable among those who have survived a first myocardial infarction. This effect may also explain the substantially higher rates of graft occlusion among continuing smokers following vascular bypass surgery for cardiac or peripheral vascular disease. Cessation of cigarette smoking reduces the risk of a second coronary event within 6–12 months. Rates of first myocardial infarction and death from coronary heart disease decline within 2–4 years following cessation among those with no prior cardiovascular history. After 15 years of abstinence, the risk of stroke, a new myocardial infarction, and death from coronary heart disease in former smokers is similar to that for those who have never smoked.

TABLE 465-1 Relative Risks for Current Smokers of Cigarettes AGE 35–44 45–64 65–74 ≥75 Males Lung cancer 14.33 19.03 28.29 22.51 Coronary heart disease 3.88 2.99 2.76 1.98 Cerebrovascular disease 2.17 1.48 1.23 1.12 Other vascular diseases 7.25 4.93 Chronic obstructive pulmonary disease (COPD) 29.69 23.01 All causes 2.55 2.97 3.02 2.40 Females Lung cancer 13.30 18.95 23.65 23.08 Other tobacco-related cancers 1.28 2.08 2.06 1.93 Coronary heart disease 4.98 3.25 3.29 2.25 CHAPTER 465 Cerebrovascular disease 2.27 1.70 1.24 1.10 Other vascular diseases 6.81 5.77 COPD 38.89 20.96 All causes 1.79 2.63 2.87 2.47 Relative Risks for Selected Other Cancers Nicotine Addiction Other cancers Male Female Larynx 14.6

Lip, oral cavity, pharynx 10.9 5.1 Esophagus 6.8 7.8 Bladder 3.3 2.2 Kidney 2.7 1.3 Pancreas 2.3 2.3 Stomach

1.4 Liver 1.7 1.7 Colorectal 1.2 1.2 Cervix 1.6 Acute myeloid leukemia 1.4 1.4 ■ ■CANCER Tobacco smoking causes cancer of the lung; lip; oral cavity; naso-, oro-, and hypopharynx; nasal cavity and paranasal sinuses; larynx; esophagus; stomach; pancreas; liver (hepatocellular); colon and rec tum; kidney (body and pelvis); ureter; urinary bladder; uterine

cervix; and acute myeloid leukemia. There does not appear to be a causal link between cigarette smoking and cancer of the endometrium, and there is a lower risk of uterine cancer among postmenopausal women who smoke. The risks of cancer increase linearly with the increasing num ber of cigarettes smoked per day and logarithmically with increasing duration of smoking. Additionally, there are synergistic interactions between cigarette smoking and alcohol use for cancer of the oral cavity and esophagus. Several occupational exposures synergistically increase lung cancer risk among cigarette smokers, most notably occupational asbestos and radon exposure. Cessation of cigarette smoking reduces the risk of developing cancer relative to continuing smoking after about 4 years of abstinence, but even 20 years after cessation, there is a persistent three- to fourfold increased risk of developing lung cancer compared to those who have never smoked. ■ ■RESPIRATORY DISEASE Cigarette smoking is responsible for 80% of COPD. Within 1–2 years of beginning to smoke regularly, many young smokers will develop inflammatory changes in their small airways, although lung function measures of these changes do not predict subsequent development of chronic airflow obstruction. Chronic mucous hyperplasia of the larger airways results in a chronic productive cough in as many as 80% of smokers >60 years of age. Chronic inflammation and narrowing of the

small airways, and/or enzymatic digestion of alveolar walls resulting in pulmonary emphysema, reduce expiratory airflow sufficiently to produce clinical symptoms of respiratory limitation in ~15–25% of smokers.

Changes in the small airways of young smokers will reverse after 1–2 years of abstinence. There is also a small increase in measures of expiratory airflow following smoking cessation among many individu als who have already developed chronic airflow obstruction, but the major change following cessation is a slowing of the rate of decline in lung function with advancing age rather than a return of lung function toward normal. ■ ■PREGNANCY Cigarette smoking is associated with several maternal complications of pregnancy: premature rupture of membranes, abruptio placentae, and placenta previa. There is also a small increase in the risk of spontane ous abortion among smokers. Infants of smoking mothers are more likely to experience preterm delivery, have a higher perinatal mortality rate, be small for their gestational age, and have higher rates of infant respiratory distress syndrome. They are more likely to die of sudden infant death syndrome and appear to have a developmental lag for at least the first several years of life. Since it is likely that some of these pregnancy-related risks are caused or enhanced by nicotine, vaping and oral use of nicotine remain a concern in pregnancy except as a strategy to abstain from cigarette smoking. PART 13 Neurologic Disorders ■ ■OTHER CONDITIONS Smoking delays healing of peptic ulcers and increases the risk of devel oping periodontal disease, diabetes, active tuberculosis, rheumatoid arthritis, osteoporosis, senile cataracts, and neovascular and atrophic forms of macular degeneration. It results in premature menopause, wrinkling of the skin, gallstones, cholecystitis in women, and male impotence. Patients who continue to smoke during treatment for can cer with chemotherapy or radiation have poorer outcomes and reduced survival. ■ ■ENVIRONMENTAL TOBACCO SMOKE Long-term exposure to environmental tobacco smoke increases the risk of lung cancer and coronary artery disease among nonsmokers. It also increases the incidence of respiratory infections, chronic otitis media, and asthma in children, and it causes exacerbation of asthma in children. LOWER TAR AND NICOTINE CIGARETTES Filtered cigarettes with lower machine-measured yields of tar and nico tine commonly use ventilation holes in the filters and other engineer ing designs to artificially lower the machine measurements. Smokers compensate for the

lowered nicotine delivery resulting from these design changes by changing the manner in which they puff on the ciga rette or the number of cigarettes smoked per day to restore their level of nicotine intake to that needed to satisfy their addiction. As a result, actual tar and nicotine deliveries to smokers are not reduced with use of these products, negating any reduction in disease risks from switch ing to these products. The amount of carcinogenic tobacco-specific nitrosamines in the tobacco used in cigarettes has increased over time, and cigarette design changes that reduce machine-measured tar and nicotine also lead to deeper inhalation of the smoke in the lung, presenting increased amounts of the more carcinogenic smoke to the alveolar portions of the lung. These changes increase the risk of adenocarcinoma of the lung above that produced by smoking older nonfiltered cigarettes. The changes in cigarette design and composition of cigarettes over the past six decades are the cause of the increase in rates of adenocarcinoma of the lung observed over the past half century, and the increased adeno carcinoma rate has increased total lung cancer rates, as there has not been a decline in the risk of other cell types with the changes in ciga rette design. An increased risk for COPD may also be present. There has been no increase in risk of all lung cancer or adenocarcinoma of the lung over the same period among never smokers.

PHARMACOLOGIC INTERACTIONS Cigarette smoking may interact with a variety of other drugs. Cigarette smoking induces the cytochrome P450 system, which may alter the metabolic clearance of drugs such as warfarin. This may result in inad equate serum levels in smokers as outpatients when the dosage is estab lished in the hospital under nonsmoking conditions. Correspondingly, serum levels may rise when smokers are hospitalized and not allowed to smoke. Smokers may also have higher first-pass clearance for drugs such as lidocaine, and the stimulant effects of nicotine may reduce the effect of benzodiazepines or beta blockers. OTHER FORMS OF TOBACCO USE Other major forms of tobacco use are loose moist snuff or packets deposited between the cheek and gum and chewing tobacco. Oral tobacco use leads to gum disease and can result in oral and pancreatic cancer. There are dramatically higher risks evident for products used in Africa or Asia as, including for heart disease, compared to those used in the United States and Europe. NICOTINE AEROSOLS A continually expanding array of devices and oral formulations that deliver nicotine in quantities capable of creating and sustaining addic tion are available. Many of these devices deliver levels of nicotine comparable to a cigarette, and different concentrations of nicotine are often offered. Nicotine salt aerosols use mild acids to facilitate inhala tion of the aerosol and can deliver very high amounts of nicotine even with novice users, potentially enhancing their addictiveness compared to devices that deliver solutions of nicotine. Nicotine intake is higher for users of devices delivering nicotine salts, and they report a greater frequency of symptoms of dependence with abstinence. Biomarker evidence on exposure to smoke toxicants demonstrates markedly lower exposures among those using e-cigarettes exclusively compared to cigarette smokers, suggesting that they have less disease risk with use. However, both biomarker and behavioral evidence dem onstrate the capacity for these devices to create and sustain addiction. The long-term rates with which adults addicted to nicotine vaping quit nicotine completely or migrate to or relapse back to combusted prod uct use as they age remain to be determined. There is convincing randomized controlled cessation trial evi dence that the use of e-cigarettes that deliver sufficient nicotine are as effective as other nicotine-replacement or varenicline medications in achieving sustained abstinence from cigarettes, but a meaningful proportion of those who achieve abstinence still use e-cigarettes at 12-month follow-up, suggesting continued nicotine addiction. Rates of longer-term relapse back to smoking among individuals with persistent nicotine addiction remain to be

examined. An additional concern is that evidence on e-cigarette use in the United States shows that approximately one-half of adult e-cigarette users continue to also smoke conventional cigarettes, negating the ben efits of reduced toxicant exposure and successful abstinence. Refillable or reloadable e-cigarette devices can be used to aerosolize a variety of liquids other than those provided by the manufacturer. Disposable “pods” and liquids for these devices can be purchased from the manufacturer but are also available from other sources that may use poor-quality manufacturing practices and control of contaminants. They may also contain marijuana oils, other drugs, and flavors not evaluated for potential lung injury with inhalation. CESSATION The process of stopping smoking is commonly a cyclical one, with the smoker sometimes making multiple attempts to quit, and failing, before finally being successful. Approximately 70–80% of smokers would like to quit smoking. More than one-half of current cigarette smokers attempted to quit in the last year, but only 6% quit for

6 months, and only 3% remain abstinent for 2 years. Clinician-based smoking interventions should repeatedly encourage smokers to try to quit and to use different forms of cessation assistance with each new cessation attempt.

Advice from a clinician to quit smoking, particularly at the time of an acute illness, is a powerful trigger for cessation attempts, with up to half of patients who are advised to quit making a cessation effort. CLINICIAN INTERVENTIONS (TABLE 465-2) The shift in the nicotine market to products containing nicotine but not tobacco, and particularly to aerosolized nicotine salt products, has complicated provider diagnosis and treatment recommendations. Two considerations should guide this process. First, assessment of nicotine addiction should include the cumulative number of episodes of use for all nicotine products used regularly when considering the intensity of nicotine ingestion. This is important particularly when there is varia tion in the type of product used from day to day. Inquiries about cigar and roll your own use, as well as vaping and oral nicotine products, are necessary. It is the frequency of any nicotine dosing, not the product source, that creates and sustains addiction. Second, it is the other toxicants carried along with the nicotine that cause the majority of the disease risk, so eliminating the smoke intake can have benefits even in the presence of continued addiction to nicotine. All patients should be asked the total daily frequency with which they use any nicotine product, how long they have used at least one nicotine product regularly, their past experience with quitting, and whether they are currently interested in quitting. The goal is to identify whether the individual has a pattern of use that demonstrates a compulsive need for the next dose of nicotine. The number of episodes of smoking or vaping per day, how they are spaced during the day, as well as use of nicotine smoking within 30 min of waking are helpful measures of the intensity of nicotine addiction. Even those who are not interested in quitting should be encouraged and motivated to quit by providing a clear, strong, and personalized message by the clinician that smoking cigarettes is an important health concern and that vaping can be addicting. Those uninterested indi viduals should be told that assistance is available if they become inter ested in quitting in the future. Many of those not currently expressing an interest in quitting may nevertheless make an attempt to quit in the subsequent year. TABLE 465-2 Clinical Practice Guidelines Physician Actions Ask: Systematically identify all tobacco and nicotine use at every visit Advise: Strongly urge all smokers to quit Identify smokers willing to quit Assist the patient in quitting Arrange follow-up contact Effective Pharmacologic Interventionsa First-line therapies Nicotine gum (1.5) Nicotine patch (1.9) Nicotine nasal inhaler (2.3) Nicotine oral inhaler (2.1) Nicotine lozenge (2 mg: 2.0, 4 mg: 2.8) Bupropion (2.0) Varenicline

(3.1) Other Effective Interventionsa Physician or other medical personnel counseling (10 min) (1.84) Intensive group smoking cessation programs (at least 4–7 sessions of 20- to 30-min duration lasting at least 2 and preferably 8 weeks) (1.3) Intensive individual counseling (1.7) Systemwide cessation tracking and assistance (5) Telephone counseling (1.6) Exclusive E-cigarette use (3.0) aNumerical value following the intervention is the multiple for cessation success compared to no intervention.

For those interested in quitting, a quit date should be negotiated, usually not the day of the visit but within the next few weeks. A followup contact by office staff around the time of the quit date should be provided. There is a relationship between the amount of assistance a patient is willing to accept and the success of the cessation attempt.

Building smoking cessation as a priority into health care delivery systems by including systemwide tracking of smoking status, prompt ing of practitioners to ask about smoking and interest in cessation, system-based outreach to smokers to offer cessation assistance and programs between visits, and tracking of cessation outcomes can dramatically enhance sustained abstinence, with 12-month abstinence rates as high as 25%. There are a variety of cessation products listed in Table 465-2, including over-the-counter nicotine patches, gum, and lozenges, as well as nicotine nasal and oral inhalers available by prescription. These products can be used for up to 3–6 months, and some products are formulated to allow a gradual step-down in dosage with increasing duration of smoking abstinence. Antidepressants such as bupropion (300 mg in divided doses for up to 6 months) have also been shown to be effective, as has varenicline, a partial agonist for the nicotinic ace tylcholine receptor (initial dose 0.5 mg daily increasing to 1 mg twice daily at day 8; treatment duration up to 6 months). Combined use of nicotine-replacement therapy (NRT) and antidepressants, as well as the use of gum or lozenges for acute cravings in patients using patches, can increase cessation outcomes. CHAPTER 465 Nicotine Addiction Pretreatment with antidepressants or varenicline is recommended for 1–2 weeks prior to the quit date. Pretreatment with nicotine patches for 2 weeks prior to a cessation date is also useful. Longer duration of nicotine replacement as a maintenance therapy for those who are unsuccessful in quitting with a shorter duration of use is a useful strategy. NRT is provided in different dosages, with higher doses being recommended for more intense smokers. Antidepressants are more effective among smokers with a history of depression symptoms. Current recommendations are to offer pharmacologic treatment, usually with nicotine patches or varenicline, to all who will accept it, and to provide counseling and other support as a part of the cessation attempt. Cessation advice alone by clinicians or their staff is likely to increase success compared with no intervention, but a more compre hensive approach with advice, pharmacologic assistance, and counsel ing can increase cessation success nearly threefold. Data from multiple studies show that switching from cigarettes to exclusive use of e-cigarettes, particularly those with nicotine salts that deliver high doses of nicotine, is as or more effective in achieving smok ing abstinence compared to FDA-approved medications, and it may be more acceptable for some patients. It should be recommended only with a strong caution to avoid dual use. Dual use with combusted cigarettes is unlikely to lead to smoking cessation or long-term risk reduction. Current recommendations suggest that FDA-approved cessation methods be tried initially, with aerosolized nicotine salt products rec ommended to those who fail initial attempts to quit, are quitting on their own, or are reluctant to use FDA-approved medications. PREVENTION Prevention of smoking initiation must begin early, preferably in the elementary school years. Practitioners who treat adolescents should be sensitive to the prevalence of this problem even in the preteen popula tion. Practitioners should ask all

adolescents whether they have experi mented with nicotine or currently use nicotine products, reinforce the fact that most adolescents and adults do not smoke or use nicotine, and explain that all forms of nicotine intake can be both addictive and potentially harmful. ■ ■FURTHER READING Christen SE et al: Pharmacokinetics and pharmacodynamics of inhaled nicotine salt and free-base using an e-cigarette: A random ized crossover study. Nicotine Tob Res 10:ntae074, 2024. Eisenberg MJ et al: Effect of e-cigarettes plus counseling vs counsel ing alone on smoking cessation: A randomized clinical trial. JAMA 324:1844, 2020.

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