

BMJ Best Practice

Smoking cessation

Straight to the point of care



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Summary

Healthcare professionals play a central role in motivating and assisting people to stop smoking.

Smoking cessation benefits all people who smoke regardless of age, comorbidities, or current health problems.

The 5 A's is a five-step treatment framework to guide smoking cessation that is used across the world in many treatment settings; abbreviated variants (e.g., Very brief advice) are also available, increasing in usage, and preferentially recommended in some countries and within certain treatment settings.

The combination of behavioural support plus an evidence-based pharmacotherapy for smoking cessation has the best evidence for smoking cessation. Of the available pharmacological options, nicotine replacement therapy (NRT) in combination with varenicline have amassed the greatest volume of data demonstrating safety and efficacy.

The use of e-cigarettes for smoking cessation remains a topic of ongoing debate and research; professional medical bodies in different countries have varying stances on e-cigarettes based on the available evidence and public health considerations.

Definition

Cigarette smoking is the leading cause of preventable disease, disability, and death.^[1] Physicians and other healthcare professionals play a central role in motivating and assisting people who smoke to stop.^[2] Physicians are a credible and trusted source of advice to stop, have opportunities to provide this message to most smokers, and can connect people to behavioural support and pharmacotherapy. These actions are effective at increasing cessation rates.^[3]

According to the Centers for Disease Control and Prevention (CDC), an adult's smoking status at any given point in time may be defined as one of the following:^[4]

- Current smoker: an adult who has smoked 100 cigarettes in his or her lifetime, and who currently smokes cigarettes
- Former smoker: an adult who has smoked 100 cigarettes in his or her lifetime, but who has quit smoking at the time of the interview.

The goal of smoking cessation is to assist the person in changing their behaviour to help them achieve abstinence from smoking or other tobacco use. Sustained or prolonged abstinence from cigarette smoking and other tobacco use may be defined in a number of ways; the most rigorous definition typically used within clinical trials involves avoidance of all tobacco use from the stop day until the time the assessment is made. This definition occasionally allows for lapses.^[5]

Note that this topic covers smoking cessation rather than nicotine eradication; cessation of nicotine e-cigarettes (vaping) is not specifically covered. Nicotine e-cigarette cessation has its own separate and emerging evidence base. A key clinical priority for healthcare professionals who are supporting a person who wishes to stop using nicotine e-cigarettes is to ensure that they do not start (or return to) using combustible tobacco products (i.e., conventional smoking) as an alternative.

Epidemiology

Globally, the prevalence of current use of smoking tobacco among individuals aged 15 years and older is 32.7% among males and 6.6% among females.[6] The regions with the highest prevalence of current smokers in men are east Asia (49.5%), Southeast Asia (48.2%), eastern Europe (44.7%), and Oceania (41.3%) and in women are central Europe (25.9%), Southern Latin America (23.3%), and western Europe (22.7%).[6]

In 2021, approximately 35.6 million US adults (14.5% of the population) smoked tobacco products (including cigarettes, cigars, and pipes).[4] The prevalence of cigarette smoking is the lowest prevalence since data became available, but it remains unacceptably high.[4] The pattern in cigarette use among adults who smoke daily has also shifted, with adults generally smoking fewer cigarettes per day in 2021 than in 2005.[4] The prevalence of any current tobacco product use is higher among men (24.1%) than among women (13.6%).[4]

The global prevalence of smoking during pregnancy is estimated to be 1.7%.[7] The highest prevalence of smoking during pregnancy is in Europe (8.1%).[7] In the US, 7.2% of women who gave birth in 2016 smoked cigarettes during pregnancy.[8] Prevalence of smoking during pregnancy was highest for women aged 20-24 years.[8]

Tobacco smoking usually begins in adolescence or early adulthood (typically before the age of 24 years).[9] Globally, prevalence of tobacco smoking among adolescents remains high, with prevalence of smoking among 13- to 15-year-olds found to be 19.33% on average, according to one large global study.[10] Higher-income countries have been found to have the highest prevalence of adolescent smoking globally, compared with lower-income countries.[10] However, in the US, a decline in cigarette smoking has been seen in young people under the age of 24 years since the late 1990s (from 29.1% to 5.4%).[11] Similar declines in the prevalence of smoking in adolescents have been seen in the UK across a similar time period.[12] Adolescents living in deprived parts of the UK have an approximately twofold higher risk of smoking compared with those living in the least deprived parts of the country.[12]

It is estimated that more than 8 million smoking-attributed deaths occur globally each year.[13] This includes almost 500,000 people in the US who die from smoking-related illnesses.[14] Most smoking-attributed deaths are due to cancer (34%), cardiovascular diseases (32%), or respiratory disease (21%), with nearly 90% of lung cancers and 80% of chronic obstructive pulmonary disease deaths caused directly by smoking.[14] Globally, the health outcomes with the largest number of deaths attributable to smoking tobacco use are ischaemic heart disease; chronic obstructive pulmonary disease; tracheal, bronchus, and lung cancer; and stroke.[6] [15]

Even light or mild smoking can carry significant morbidity. One study showed that a large proportion of the risk of coronary heart disease and stroke comes from smoking only a few cigarettes. This has important consequences for smokers who believe that light smoking carries little or no harm. It was shown that smoking one cigarette per day carries around 40% to 50% of the excess risk for developing coronary heart disease and stroke of smoking 20 cigarettes per day, and smoking 5 cigarettes per day has around 55% to 65% of the excess risk. No safe level of smoking exists for cardiovascular disease.[16]

Smoking reduces the median survival of smokers on average by 10 years, and beyond the age of 40 each additional year of smoking reduces life expectancy by 3 months.[17] By stopping cigarette smoking, a person reduces the risk of lung cancer and other diseases by 20% to 90% and improves survival, even among those who stop after the age of 50 years.[17] Nonetheless, habitual smokers find it extremely difficult to successfully stop smoking. Although 70% of smokers would like to stop, and 40% make at least one stopping

attempt per year, only 3% to 4% of smokers per year are successful in stopping long-term on their own.[18] There is substantial variation across countries in the percentage of smokers who reported making stopping attempts, with the highest in Europe being England, where 46.3% of smokers reported making a stopping attempt in the past 12 months.[19] A decline in the prevalence of stop attempts in England from 44.6% to 33.8% is likely to be associated with a decrease in the population-level prevalence of smokers with a high motivation to stop, and an increase in the mean age of smokers.[20] In a multinational survey of smokers on their most recent stop attempt, many respondents (38.6%) used no aid or assistance in their attempt to stop smoking and in those who did use assistance, nicotine substitution products (nicotine vaping products, nicotine replacement therapy) were the most common methods.[21]

No level of exposure to combustible tobacco smoking is considered safe. In 2017, 1.2 million deaths globally were attributable to second-hand smoke exposure, of which 63,822 occurred among children younger than 10 years old.[22] In the US, it is estimated that of the 20 million Americans who died because of smoking since 1964, 2.5 million were non-smokers who died because of second-hand smoke.[23]

The epidemiology of nicotine e-cigarette use (vaping) is closely interconnected with that of combustible tobacco smoking. In adults in the US and Europe, a rapid increase in nicotine e-cigarette use has been seen since 2010; the vast majority of users are current or former smokers.[24] [25] [26] [27] Nicotine e-cigarette sales and usage have increased substantially in recent years. In the US, during 2020-2022, monthly sales increased by 46.6%: from 15.5 million units in January 2020 to 22.7 million units in December 2022.[28] Population-based studies suggest that, overall, increasing nicotine e-cigarette use among adult smokers is associated with increases in smoking cessation rates.[29] However, among non-smokers, use of nicotine e-cigarettes appears to increase the risk that an individual will initiate combustible cigarette smoking and become a current smoker; the magnitude of this risk is on average around threefold, according to one large meta-analysis.[30] In particular, concerns exist about the health risks associated with dual use of tobacco smoking and e-cigarettes, which exposes users to two sources that are harmful to health.[31] [32] Dual tobacco smoking and nicotine e-cigarette use appears to be the most common pattern of e-cigarette use.[33] In the US, young adults (aged 18-24 and 25-44) are more likely than older adults to be dual users of both nicotine e-cigarettes and combustible cigarettes.[4] Nicotine e-cigarettes have the potential to benefit some adults as a complete substitute for cigarette smoking, although stances from professional medical bodies on this vary internationally.

Usage of nicotine e-cigarettes has increased dramatically in children and adolescents in recent years in countries including the US and UK.[34] [35] Nicotine e-cigarettes are the most commonly used form of nicotine-containing product among high school and middle school students in the US (with 10.1% and 5.4% of students reporting use, respectively).[36] In England, current vaping prevalence in young people was 8.6% in 2022, compared with 4.1% in 2021.[35] A number of studies have found a strong association between e-cigarette use and subsequent smoking initiation among adolescents and young adults, although it is currently unclear whether this relationship is causal.[37] [38] [39] It has been suggested that increasing e-cigarette use among young people may be diverting them away from combustible tobacco smoking, although the evidence is mixed, and it may be that the two trends are in fact independent of each other.[11] Younger e-cigarette users are more likely to have never smoked cigarettes than older nicotine e-cigarette users.[40]

Aetiology

Tobacco smoking usually begins in adolescence or early adulthood (typically before the age of 24 years).[9] Smoking behaviour is influenced by biological, genetic, behavioural, social, and environmental factors. Smoking initiation is more likely in households with current smokers where parental approval is more likely

and there is greater access to cigarettes.[41] Studies of twins and adoptees suggest that there is a modest genetic influence on regular use of cigarettes that probably interacts with environmental factors.[42] Low socioeconomic status is associated with increased smoking rates, with the prevalence among those living below the poverty line in the US at 24.7%, versus 14.8% in those with a high income.[4] Smoking is more prevalent in people with a history of mental health illness or substance use disorder (SUD).[43] Over 53% of people with SUD die of smoking-related causes.[44] The rate of smoking among those with schizophrenia is over 70%.[43] [45] People with HIV/AIDS have high smoking rates (40% to 75%), and the proportion of deaths among people with HIV/AIDS from diseases related to smoking is substantial.[46] Other risk factors for a person deciding to initiate smoking include having peers who smoke, living in a neighbourhood with a high density of tobacco outlets, not participating in team activities, having a high sensation-seeking propensity, and being exposed to smoking in movies.[47]

Adolescents who use nicotine e-cigarettes have been found to be at least 3 times more likely than those who do not to start smoking combustible cigarettes.[48] [49] [50] Cultural and psychological pressures appear to play a role in nicotine use among high school and middle school students, especially for e-cigarettes. In a national youth survey of middle and high school students in the US, the most common reason for first trying them was "a friend used them" (57.8%), and the most cited reason for current use was "I am feeling anxious, stressed, or depressed" (43.4%).[51] Moreover, 75.7% reported exposure to tobacco product advertisements, reflecting the broad reach of marketing and its intended impact in recruiting younger people.[51]

Pathophysiology

Daily cigarette smokers typically keep smoking because they are addicted to nicotine. The binding of nicotine with neuronal nicotinic acetylcholine receptors stimulates the central nervous mesolimbic dopamine system, which is thought to mediate reinforcement and reward.[52] Nicotine is a very addictive substance with both positive reinforcing effects and nicotine withdrawal symptoms during periods of abstinence. Nicotine withdrawal symptoms may include:

- Dysphoric or depressed mood
- Irritability, frustration, anger, and anxiety
- Increased appetite and weight gain.

The dopaminergic pathway is targeted by existing pharmacotherapies for smoking cessation (nicotine replacement therapy [NRT], varenicline, and bupropion).[1] Nicotine medicines act on nicotinic acetylcholine receptors (nAChRs) to mimic or replace the effects of nicotine from tobacco.[52]

- The principal action of NRT is the relief of withdrawal symptoms when a person stops tobacco use, which reduces motivation to smoke, but other benefits include positive reinforcement, particularly for the arousal and stress-relieving effects.[52] Different modes of delivery of NRT affect the speed of nicotine delivery and the degree of positive reinforcement.[52] Combining different modes of delivery of NRT, such as an NRT patch and rapid-delivery formulations (e.g., nasal spray, gum, lozenge), can increase the chances of successfully stopping smoking.[53]
- Varenicline activates nAChRs and blocks the binding of nicotine from tobacco to the nAChR (although to a lesser extent than nicotine), resulting in reduced withdrawal symptoms and less reward from a lapse to smoking.[1]
- Bupropion (an atypical antidepressant) is a noradrenaline/dopamine reuptake inhibitor that alters nicotine-mediated dopamine responses and can alleviate withdrawal symptoms and reduce the severity of nicotine cravings.[1]

- There is emerging evidence to suggest that genetic variation among smokers may affect smoking cessation success; for example, the minor alleles of four single nucleotide polymorphisms (SNPs) within CHRNA3 or CHRNA5 appear to be risk alleles for cessation failure, and may also indicate a preference for treatment with bupropion over NRT.[54]

Behavioural aspects also contribute to the persistence of smoking and the high relapse rates after cessation.[55] The repetitive nature of smoking reinforces this activity, and there can be learned associations with other pleasurable activities (for example, meals and socialising) and with attempts to regulate mood to cope with stresses.[52] Relapses often occur in social situations or during periods of situational stress.

Case history

Case history #1

A 60-year-old man with spirometry demonstrating airflow obstruction is seen for a follow-up appointment. He continues to smoke 1 pack per day, but he recently attempted to stop and stopped smoking for more than 2 days before relapsing. He expresses a strong interest, but little confidence, in trying to stop again. During the recent attempt to stop he tried nicotine gum, but used it only once or twice daily. Additional past history is significant for hypertension under control and a remote history of a seizure disorder.

Case history #2

An 18-year-old woman with increased anxiety regarding college and social stressors is seen for a first visit with a new primary care provider. She reveals that she initially started using nicotine e-cigarettes (vaping) because a number of friends were using them, and because she enjoyed the candy flavours. Since starting college she has switched to combustible cigarette use. She describes how she and a number of peers share cigarettes with one another, and use smoking for stress and anxiety management.

Other presentations

The experience of smoking and smoking cessation may differ between adolescents and adults. For instance, levels of nicotine dependence in adolescents may not be equal to those of adult smokers.

Approach

Physicians and other healthcare professionals play a central role in motivating and assisting people who smoke to stop.^[2] Physicians are a credible and trusted source of advice to stop, have opportunities to provide this message to most smokers, and can connect people to services offering behavioural support and pharmacotherapy. Ultimately, smoking cessation interventions may be brief or more comprehensive in nature, depending on location and individual patient circumstances.

Two commonly used smoking cessation models are:^[71]

- Very brief advice for smoking, based on an 'Ask, Advise, Assist' structure, which encourages clinicians to ask patients about tobacco use, advise them to stop, and assist them by signposting them to specialist smoking cessation services offering pharmacotherapy and behavioural support.
- A more comprehensive intervention for smoking cessation, which can be provided using the '5 A's' structure: 1) ask about tobacco use; 2) advise to stop through clear, personalised messages; 3) assess willingness to stop; 4) assist in stopping; and 5) arrange follow-up and support.

See Management approach .

Identifying individuals at high risk of smoking-related harm

Published guidance from a number of countries advises prioritising specific groups who are at high risk of tobacco-related harm for intervention, such as people with mental health problems, those with conditions made worse by smoking, those in hospital or who have recently been hospitalised, those preparing for surgery, and pregnant women.^{[63] [72]}

All patients should also be assessed for second-hand smoke exposures, especially individuals who are at significant risk for negative outcomes (e.g., pregnant women, people with known asthma or COPD, people with known cardiac or vascular disease).

Discussing smoking cessation in the context of smoking-related medical disease specific to the individual may be beneficial.

Asking about tobacco and nicotine use

Assess smoking status and usage at every healthcare encounter.^{[2] [71]}

Healthcare professionals should ask all patients whether they smoke tobacco, and record their smoking status.^[72] It is important to ask the person if they ever smoke cigarettes, in order to identify people who smoke intermittently. All healthcare practices and services should have a system for identifying all people who smoke, as well as for documenting current tobacco use.^[72] Smoking status should be readily visible to the physician or healthcare professional at the point of care.^{[73] [74]}

For example, for an outpatient clinic, healthcare workers who obtain vital signs may determine the smoking status of each patient through a set of standard questions. The smoking status should then be clearly indicated on the vital sign record sheet so that it is visible to the healthcare provider. This smoking status identification system should be designed by clinic personnel to fit into the clinic's usual routine of obtaining and recording vital signs so as to minimise disruption of the clinic's workflow.^[73]

In both primary and secondary care, the new patient visit and routine check-ups may be an opportunity to carry out a more detailed assessment of smoking.^[72]

The evidence supporting the effectiveness of a smoking status identification system is substantial, and the use of such a system should be considered the standard of care.[2] The electronic medical record allows for prompts to be embedded within the patient questionnaire. However, responses may be limited by lack of standard terminology and granularity for data collection, shifting cultural attitudes regarding smoking, and potentially frequent changes in an individual's smoking behaviour.[75]

Ask about the type of tobacco product used and duration of use, including water pipe use and other smokeless tobacco products (snuff, ground, or chewing tobacco), as well as e-cigarette use, as use of e-cigarettes also results in nicotine addiction. It is common for people to use both cigarettes and e-cigarettes concurrently. Discuss any stopping attempts and aids to stop smoking that the person has used before, including personally purchased nicotine-containing products.[63]

Assessment of the degree of nicotine dependence predicts the difficulty that a person may have in stopping smoking, and the likely intensity of treatment required. Number of cigarettes per day and time to first cigarette after waking are useful questions to indicate which people may have more problems with nicotine dependence and to guide therapy choices in those who are ready to stop.[76]

Assessing willingness to stop

The following may be used to assess readiness to stop smoking. The person is first asked the following:

- "How important is it for you to try to stop smoking now?"
- "If you decide to stop, how confident are you that you can succeed?"

The person may then be asked to record the answer to the questions on a scale ranging from 0 (not at all) to 10 (extremely), and this can be explored by the clinician and patient together: for example, "Why did you select 4 instead of 0?". This process may help the individual to move up the motivational and confidence scale, and provides an assessment of motivation and self-efficacy.

- The person may be asked to reflect on prior attempts: "What has worked for you in the past? What hasn't?"
- The person may then be asked: "Are you willing to try to stop in the next month?"

Interventions based on the smoker's 'stage of change' (i.e., pre-contemplation, contemplation, preparation, or action) have been popular. However, there is little evidence that these stage-based interventions are more effective than more straightforward strategies of determining whether the person is ready to attempt to stop.[2] [77]

Note that an assessment of willingness to stop is advised as part of a more comprehensive 5 A's approach to smoking cessation, but does not typically form part of a briefer approach to smoking cessation; an alternative to assessing willingness to stop is to offer a proactive offer of treatment to all smokers.

Assess										
How important is it for you to stop smoking now?										
0	1	2	3	4	5	6	7	8	9	10
Not at all									extremely	
If you decide to stop, how confident are you that you can succeed?										
0	1	2	3	4	5	6	7	8	9	10
Not at all									extremely	
Are you willing to try and quit in the next month?										

Questionnaire to assess and improve motivation and self-confidence for stopping

From the collection of Dr Theodore W. Marcy

Additional questions

Comorbidities that may affect treatment choices should also be assessed, including depression, schizophrenia, substance use disorder, current pregnancy or breastfeeding, seizure disorder or lowered seizure threshold, hypertension, unstable cardiac disease or serious arrhythmia, asthma, temporomandibular joint disorders, or dental disorder.[63]

Investigations

Smoking status is obtained by history and self-report. Commonly used assessment tools for establishing the degree of smoking/nicotine dependence may be useful, and include the Heaviness of Smoking Index (HSI) and the Fagerström Test for Nicotine Dependence (FTND).[78] [79] [PhenX Toolkit: protocol - Heaviness of Smoking Index] (<https://www.phenxtoolkit.org/protocols/view/330201>) [National Institute on Drug Abuse: instrument - Fagerstrom Test for Nicotine Dependence (FTND)] (<https://cde.nida.nih.gov/instrument/d7c0b0f5-b865-e4de-e040-bb89ad43202b>) The degree of nicotine dependence predicts the difficulty that an individual will encounter in stopping smoking, and the likely intensity of treatment.

Cotinine and/or carbon monoxide (CO) testing may be useful where additional motivation or proof is required. Cotinine is the primary metabolite of nicotine and is commonly used as a biomarker to detect tobacco exposure, and different levels have been suggested to differentiate between total abstinence, passive tobacco exposure, and active tobacco exposure.[80]

In certain scenarios, it may be important to confirm the smoking status of individuals (e.g., with cotinine testing). It is known that smoking prior to total joint arthroplasty, for example, increases the risk for poor outcomes, including infections, delayed wound healing, and mortality, and there is evidence that when patients know they will be tested, it improves their stopping rates almost twofold, from 15.8% to 28.2%.[81] [82] Some centres require proof of abstinence prior to organ transplant or other high-risk surgeries.

CO monitoring involves measurement of exhaled breath to give an indication of levels of CO in the blood, given that CO is a marker of recent smoking. CO monitoring is recommended in some countries (e.g., the UK) as a motivational tool to facilitate smoking cessation.[63] According to UK guidance, CO measurement is recommended at each contact during smoking cessation in order to gauge progress and help motivate people to stop smoking. Guidance from the National Institute for Health and Care Excellence (NICE) in the UK states that a CO level of 10 parts per million (ppm) or less suggests that the person is a non-smoker.[63] However, note that clinical experience indicates that any value above 5 ppm usually suggests exposure to tobacco smoking, either from personal use or from second-hand exposure; further questioning may therefore be warranted for results within this range.[83] CO monitoring is recommended routinely for all pregnant women at antenatal appointments in the UK.[63] In pregnancy, a reading of 4 ppm or above is an indication to offer referral for stop-smoking support according to UK guidance.[63]

Providing feedback to smokers about the physical effects of smoking by physiological measurements (e.g., exhaled CO, lung function, genetic risk factors for cancer) may increase motivation to stop, but there is a theoretical risk that this may cause increased anxiety that may impede stopping efforts.[84] In one Cochrane review, while there was no statistically significant evidence that including risk assessments such as genetic markers for cancer, effect on lung age, and other biomedical markers affected smoking cessation, it did not suggest there was harm in this.[84] The authors of the study instead concluded that when applying a sensitivity analysis that removed those studies at high risk of bias, a benefit was detected.[84]

History and exam

Key diagnostic factors

number of cigarettes per day (common)

- A simple question that can indicate which people may have more problems with nicotine dependence and guide intensity of nicotine replacement therapy.[76] For those smoking <10 cigarettes/day, an as-needed form of nicotine replacement (gum, lozenge, inhaler, nasal spray) may be preferred rather than using continuous therapies such as the nicotine patch or bupropion.[2]

time to first cigarette (TTFC) (common)

- A simple question that can indicate which patients may have more problems with nicotine dependence and guide intensity of nicotine replacement therapy (NRT).[76] If the TTFC is ≤ 30 minutes, higher doses of NRT may be recommended.

use of alternative tobacco and nicotine delivery products (common)

- Although not directly relevant to assisting people with cessation of combustible tobacco smoking, asking about use of alternative tobacco and nicotine delivery products may provide further context about tobacco/nicotine use and dependence. E-cigarettes do not contain tobacco and instead use a liquid made from chemicals that can have different flavours and different amounts of nicotine.[57] [58] [85] [86] Other products include heat-not-burn tobacco devices (e.g., e-hookah), waterpipe ('hookah') use, and smokeless tobacco products (e.g., snuff, ground, or chewing tobacco). Asking about frequency and volume of use, and the time to first use at the start of the day, is useful.

history of substance use disorder (SUD) (common)

- Suggests a high risk of tobacco-related harm.[63] Requires coordinated treatment. Over 53% of people with SUD die of tobacco-related causes.[44] People with SUD should be screened for tobacco use and those who use tobacco supported in interventions to help them stop.[87]

pregnancy or breastfeeding (uncommon)

- Suggests a high risk of tobacco-related harm.[63] Smoking in pregnancy represents a special circumstance with additional considerations. While smoking during pregnancy is a well-established risk factor for adverse pregnancy outcomes including preterm deliveries, low birth weight, and preterm-related deaths, it is still prevalent to varying degrees globally.[7]

Other diagnostic factors

history of depression (uncommon)

- Suggests a high risk of tobacco-related harm.[63] A history of depression is associated with a higher rate of smoking.[88] People with depression may require coordinated treatment and caution in some treatment options otherwise offered in smoking cessation.

history of schizophrenia (uncommon)

- Suggests a high risk of tobacco-related harm.[63] People with schizophrenia demonstrate greater rates of smoking than the general population, leading to higher morbidity and mortality from smoking-related illnesses.[45]

seizure disorder (uncommon)

- Any seizure history, head injury, or other lowered seizure threshold should be noted, and caution exercised in selecting pharmacological agents in smoking cessation.

hypertension (uncommon)

- Special considerations may apply when choosing smoking cessation treatments in the context of hypertension.

unstable cardiac disease (uncommon)

- Special considerations may apply when choosing smoking cessation treatments in the context of unstable cardiac disease. The relative lack of evidence regarding safety and efficacy of nicotine replacement therapy (NRT) in acute coronary syndrome (ACS) and the theoretical concern for nicotine's vasoconstrictive properties mean that NRT use may be limited during hospitalisation for patients with ACS and life-threatening arrhythmias. The American College of Cardiology notes, however, that given the robust safety profile and efficacy of NRT in the general population, and the clear dangers of smoking, NRT is recommended as first-line therapy in hospitalised patients with ACS.[89]
- There is evidence that varenicline, bupropion, and NRT do not increase the risk of cardiovascular events in the general population of smokers.[90]

ventricular arrhythmia (uncommon)

- Special considerations may apply when choosing smoking cessation treatments in the context of ventricular arrhythmia.

asthma (uncommon)

- Suggests a high risk of tobacco-related harm.[63] Limits use of nicotine replacement delivery by inhaler.

chronic obstructive pulmonary disease (COPD) (uncommon)

- Suggests a high risk of tobacco-related harm.[63] COPD is exacerbated (and typically caused) by smoking.[63]

temporomandibular joint or dental disorder (uncommon)

- May limit appropriateness of nicotine replacement gum.

Risk factors

Strong

age <24 years

- Smoking usually begins in adolescence or early adulthood (typically before the age of 24 years).[9] Although older teens are more likely to smoke than younger teens, the earlier a person starts smoking or using any addictive substance, the more likely they are to develop an addiction. Males are also more likely to take up smoking in adolescence than females.[56]

low socioeconomic status

- Low socioeconomic status is associated with increased smoking rates, with the prevalence among those living below the poverty line in the US at 24.7%, versus 14.8% in those with a high income.[4]

history of mental illness or substance use disorder

- Smoking is more prevalent in people with a history of mental health illness or substance use disorder (SUD).[43] Over 53% of people with SUD die of smoking-related causes.[44] The rate of smoking among those with schizophrenia is over 70%.[43] [45]

history of HIV/AIDS

- People with HIV/AIDS have high smoking rates (40% to 75%), and the proportion of deaths among people with HIV/AIDS from diseases related to smoking use is substantial.[46]

use of alternative tobacco and nicotine delivery products

- E-cigarettes (vapes) do not contain tobacco and instead use a liquid made from chemicals that can have different flavours and different amounts of nicotine.[57] [58] A number of studies have found a strong association between e-cigarette use and subsequent smoking initiation among adolescents and young adults, although it is currently unclear whether this relationship is causal.[37] [38] [39]
- Use of smokeless tobacco products (snuff, ground, or chewing tobacco) may be a risk factor for later development of cigarette smoking, and may increase the risk for nicotine addiction, periodontal disease, and cancer.[58]

Weak

genetics

- Studies of twins and adoptees suggest that there is a modest genetic influence on regular use of cigarettes that probably interacts with environmental factors.[42]

Investigations

1st test to order

Test	Result
<p>self-report of smoking status</p> <ul style="list-style-type: none"> • Assessing a patient's smoking history should be done at every visit to a healthcare professional.[2] [71] Use of a smoking status identification system questionnaire should be standard; however, it may be limited by lack of standard terminology and granularity for data collection, shifting cultural attitudes regarding tobacco use, and potentially frequent changes in individuals' smoking behaviour.[75] Overall, self-reported data are shown to be reliable, but some misreporting of smoking status may occur and is subject to recall bias.[91] [92] 	<p>if former or current smoker: details of duration of time smoked, type and amount of tobacco product used, and number of stopping attempts</p>
<p>Fagerström Test For Nicotine Dependence (FTND)</p> <ul style="list-style-type: none"> • A 6-item self-report tool assessing the intensity of physical addiction to nicotine. It assesses the quantity of cigarette consumption, the compulsion to use, and dependence.[79] 	<p>test is scored from 0-10: score 8+ = high dependence; score 5-7 = moderate dependence; score 3-4 = low to moderate dependence; score 0-2 = low dependence</p>
<p>Heaviness of Smoking Index (HSI)</p> <ul style="list-style-type: none"> • A 2-item self-report tool derived from the Fagerström Test for Nicotine Dependence, with questions on time to first cigarette and number of cigarettes smoked per day.[78] 	<p>test is scored from 1-6, with higher scores indicating higher degrees of nicotine dependence</p>

Other tests to consider

Test	Result
<p>carbon monoxide (CO) monitoring</p> <ul style="list-style-type: none"> CO monitoring involves measurement of exhaled breath to give an indication of levels of CO in the blood, given that CO is a marker of recent smoking. CO monitoring is recommended in some locations (e.g., the UK) at each contact during smoking cessation as a motivational tool.[63] CO monitoring is also recommended routinely for all pregnant women at antenatal appointments in the UK.[63] A CO level of 10 parts per million (ppm) or less suggests that the person is a non-smoker.[63] However, note that clinical experience indicates that any value above 5 ppm usually suggests exposure to tobacco smoking, either from personal use or from second-hand exposure, and so further questioning may be warranted for results within this range.[83] In pregnancy, a reading of 4 ppm or above is an indication to offer referral for stop-smoking support according to UK guidance.[63] 	<p>CO level above 5 ppm suggests likely exposure to smoke</p>
<p>cotinine level</p> <ul style="list-style-type: none"> Cotinine levels may be obtained from blood or saliva in scenarios where tobacco abstinence is required (e.g., prior to knee replacement or organ transplant in some centres). Provides a more accurate measurement of exposure to smoking than CO monitoring, indicative of exposure over the past few days, rather than hours.[63] Different levels have been suggested to differentiate between total abstinence, passive tobacco exposure, and active tobacco exposure; however, the optimal cut-offs for classification vary with population characteristics or regions and over time.[80] [92] 	<p>negative in tobacco or nicotine product abstinence</p>

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Substance use disorder	<ul style="list-style-type: none"> Concomitant dependence on other addictive substances. 	<ul style="list-style-type: none"> Urine toxicology screening tests for drugs of abuse and therapeutic drugs may identify substance.[93]

Criteria

Tobacco withdrawal DSM-5-TR criteria[94]

There are 7 symptoms of nicotine withdrawal described in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) for individuals who have had daily use of tobacco for at least several weeks. If 4 or more of the following symptoms appear within 24 hours after cessation or reduction in the amount of tobacco used, cannot be attributed to another medical condition, and cause significant clinical distress or impairment in social, occupational, or other important areas of functioning, the patient meets DSM-5-TR criteria of tobacco withdrawal.

1. Irritability, frustration, or anger

2. Anxiety
3. Difficulty concentrating
4. Increased appetite
5. Restlessness
6. Depressed mood
7. Insomnia.

Screening

UK guidance from the National Institute for Health and Care Excellence (NICE) advises that health professionals ask people at every opportunity if they smoke, and if they smoke, deliver very brief advice (VBA) and refer to their local smoking cessation service.^[63] The US Preventive Services Task Force (USPSTF) recommends that clinicians ask all adults about tobacco use at each visit, advise them to stop using tobacco, provide behavioural interventions to all adults who use tobacco, and provide US Food and Drug Administration (FDA)-approved pharmacotherapy for cessation to non-pregnant adults who use tobacco.^[71] The American Academy of Pediatrics (AAP) recommends that all teenagers be screened for tobacco and nicotine use in primary care, and that those who want to stop smoking are offered referral for a behavioural intervention, with consideration given to offering nicotine replacement therapy (NRT) for those with moderate or severe tobacco dependence.^[60]

Smoking status should be readily visible to the physician or healthcare professional at the point of care.^[73]^[74]

A prompt in the electronic health record to mention smoking cessation may be beneficial, in addition to decision support tools and links to resources. These tools may increase the rate of physician cessation interventions, the proportion of smokers receiving behavioural support, and stopping rates.^[95]

Screening for smoking with CO monitoring is recommended routinely for all pregnant women at antenatal appointments in some locations, including the UK.^[63]

Approach

All people who are current smokers should be advised of the benefits of smoking cessation regardless of age, comorbidities, or current health problems. Clinicians should offer a menu of cessation resources (pharmacotherapy and behavioural support) to those who are ready to stop. Overall, the combination of behavioural support plus an evidence-based pharmacotherapy for smoking cessation has the best evidence for smoking cessation.[2] [96] [97] [98]

Service models and common approaches to smoking cessation vary according to location of practice. Two commonly used smoking cessation models are:[71]

- Very brief advice for smoking, based on an 'Ask, Advise, Assist' structure, which encourages clinicians to ask patients about tobacco use, advise them to stop, and assist them by signposting them to specialist smoking cessation services offering pharmacotherapy and behavioural support.
- A more comprehensive intervention for smoking cessation, which can be provided using the '5 A's' structure: 1) ask about tobacco use; 2) advise to stop through clear, personalised messages; 3) assess willingness to stop; 4) assist in stopping; and 5) arrange follow-up and support.

Evidence directly comparing different smoking cessation models is limited. It suggests that both brief and comprehensive models can be effective, but that their effectiveness may vary depending on the individual, and according to the clinical setting.[1] According to one Cochrane review, assuming an unassisted stopping rate of 2% to 3%, a very brief advice intervention can increase stopping by a further 1% to 3%.[99] Although this effect is low at an individual level, a brief intervention has the potential to reach many people who smoke. These actions are therefore likely to be economical and effective in increasing cessation rates at a population level.[3] Although more intensive interventions may result in slightly better outcomes overall, they may be less practical in some clinical contexts.[71] [72] [99][100] Clinicians may choose to prioritise comprehensive interventions for those with greater nicotine dependence, or previous unsuccessful stopping attempts.

In locations such as the UK and New Zealand, a very brief intervention (also known as 'very brief advice') for smoking cessation is usually recommended at the initial point of patient contact.[63] [72][101] People who wish to stop smoking are then referred to specialist local smoking cessation services following this.[63]

The more comprehensive 5 A's approach is adopted in full or as a modified form in many international smoking cessation guidelines, and is frequently used within the US.[2] [71] [102] Some professional organisations in the US recommend using a briefer initial approach to smoking cessation, the rationale being that an abbreviated version incorporating more members of the wider care team is likely to be more feasible to deliver in real-world clinical settings.[71] [89]

A variant of the 5 A's approach that is endorsed by the American College of Cardiology is to omit the step of offering readiness to stop, and instead to proactively offer smoking cessation treatment to every smoker, with people having the option to refuse treatment.[89] This approach echoes a typical chronic condition management strategy, where the expectation is that patients will be offered treatment. There is some randomised controlled trial (RCT) evidence to suggest that this more proactive approach to the 5 A's increases rates of smoking cessation compared with usual care in some patient groups.[103] [104] [105] [106]

Very brief advice for smoking cessation

A brief advice intervention for smoking cessation may be given in as little as 30 seconds, and involves:[63]

- Asking about current and past smoking behaviour
- Advising on the risks of smoking and the benefits of stopping smoking by providing verbal and written information
- Advising on the options for stopping smoking, including behavioural support and evidence-based medication for smoking cessation
- Referring the person to a specialist service (e.g., local smoking cessation service, tobacco dependence specialist, and/or telephone quitline), if they wish to stop smoking.

Physicians may be more effective in promoting attempts to stop smoking if they offer assistance to all smokers rather than only those who are motivated to stop smoking.[107] If the offer of a brief advice intervention for smoking is declined, it may still be offered at future consultations, as brief advice interventions are designed to be given repeatedly without antagonising the individual.[63] It is not uncommon for life events and changes in circumstances to precipitate stopping attempts even by people who appear to be entrenched smokers.[108]

The 5 A's

The 5 A's steps are as follows:

- 1) Ask about a patient's smoking status.
- 2) Advise those who smoke to stop.
- 3) Assess their readiness to stop.
- 4) Assist smokers in their stopping attempts.
- 5) Arrange for follow-up on these attempts.

Because it may be challenging for one person to implement all of the 5 A's within a single clinical encounter, healthcare professionals and clinic staff may work together as a team to address different parts of the list.

Ask

Step 1 of the 5 A's is to ask all patients about tobacco usage.

Tobacco usage should be assessed at every healthcare encounter.[2] [71] Use of a smoking status identification system questionnaire should be standard. See Diagnostic approach .

Advise

Step 2 of the 5 A's is to advise smoking cessation.

There is robust evidence to suggest that brief advice (less than 5 minutes' duration) from a clinician to stop smoking at each clinical encounter increases smoking abstinence rates.[71] [99]

Those who are actively smoking every day or most days should be advised to stop.[2] An open, reflective, patient-centred discussion may begin with asking permission to discuss smoking. The physician can then identify the patient's personal goals that would be furthered by stopping. If not ready to stop, the patient can be invited to discuss again at the following visit.

Discussing smoking cessation in the context of smoking-related medical disease specific to the individual patient is recommended by clinicians. For people with smoking-related disease, it may be appropriate to offer more intensive clinical advice.^[71]

The use of physiological measurements such as cotinine and carbon monoxide (CO) testing may be considered as an additional motivational tool in specific clinical scenarios. See Investigations .

Assess

Step 3 of the 5 A's is to assess readiness to stop.

The following questions may be used to assess readiness to stop smoking:^[2]

- How important is it for you to try to stop smoking now?
- If you decide to stop, how confident are you that you can succeed?
- What has worked for you in the past? What hasn't?
- Are you willing to try to stop in the next month?

An alternative to assessing readiness to stop is to use a proactive approach and offer treatment to all smokers.

Assist

Step 4 of the 5 A's is to assist smokers who are ready to stop.

Overall, the combination of behavioural support plus an evidence-based medication for smoking cessation has the best evidence for smoking cessation (see below).^{[2] [96]}

The following are some simple recommendations that healthcare providers can offer to help people build a stopping plan, in addition to referral to a behavioural support programme and offering pharmacotherapy:^{[63] [109]}

1. Identify your reasons for smoking
2. Set a stop date and commit to it
3. Let family members, friends, and colleagues know you are stopping
4. Remove reminders of smoking
5. Identify your smoking triggers (e.g., stress, seeing others smoking, becoming intoxicated) and develop coping strategies
6. Explore ways to manage cravings, e.g., distraction strategies, talking to a friend or family members
7. Explore ways to avoid relapse, e.g., by avoiding situations in which you would usually smoke
8. Have places you can turn to for immediate help.

Education about the likely timing of withdrawal symptoms and strategies for management (using medication and/or behavioural techniques) is also important.

Arrange follow-up

Step 5 of the 5 A's is to arrange follow-up.

The risk of relapse is highest in the 2 weeks following cessation. Physicians should arrange follow-up for a smoker attempting to stop within 1 week of the planned stopping date. Setting up follow-up with a behavioural support service (quitline or in-person one-to-one or group behavioural support) is both feasible and encouraged if available.^{[110] [111]}

The motivational intervention should be repeated every time an unmotivated patient visits the clinic setting. Tobacco users who have been unsuccessful in previous stopping attempts should be told that most people make repeated stopping attempts before they are successful.

Behavioural support

Behavioural support encompasses multimodal approaches that can require significant time and expertise. It has consistently shown benefit for smoking cessation, compared with receiving minimal support, or receiving pharmacotherapy alone.[111] [112] There is evidence from one Cochrane review that increasing the amount of behavioural support available increases the chance of success by about 10% to 20%.[98] Another Cochrane review determined that group-based interventions in adults appear to be more promising than self-help and other less intensive interventions. There was not enough evidence to evaluate whether groups are more effective than intensive individual behavioural support.[110] There is moderate-certainty evidence that the provision of adjunctive counselling by a health professional other than the physician (e.g., nurse, smoking cessation specialist, smoking quitline) increases smoking cessation rates in primary care.[113]

Internet-based interventions are available that increase the likelihood of cessation and help patients avoid relapse.[114] [115] Text messaging interventions have been shown to have a beneficial impact on 6-month cessation outcomes.[116] [117] Financial-incentive programmes have been shown to improve tobacco cessation rates in both low- and high-income groups.[118] [119][120] Reward-based programmes are more commonly accepted than deposit-based programmes and have led to higher smoking cessation rates.[121]

In some locations (e.g., the UK), behavioural support is typically offered via weekly sessions delivered by a specialist service for a minimum of 4 weeks.[63] [72] In the US, behavioural support is often given simply via brief clinician counselling in the clinic; in this context, supplementation via telephone quitline, internet or text message support, or more intensive behavioural support may increase efficacy, given evidence suggesting that more intensive interventions are more effective than less intensive interventions.[110] [113]

First-line pharmacotherapy

Two types of medicine have amassed the greatest volume of data demonstrating safety and efficacy for smoking cessation: nicotine replacement therapy (NRT) with a combination of short-acting and long-acting NRT (e.g., patches, gum, lozenges, and nasal spray), and varenicline.[122] [123][124] [125] Both NRT and varenicline have US Food and Drug Administration (FDA) approval for smoking cessation. In the UK, they are recommended by the National Institute for Health and Care Excellence (NICE).[63] Both are considered first-line treatments and produce significantly higher stop rates for 6 months or more than does placebo alone.[63] [76]

Nicotine replacement therapy (NRT)

- All NRT is safer than smoking a cigarette. NRT with patches, gum, lozenges, oral inhaler, or nasal spray more than doubles the success rate of a stopping attempt compared with placebo.[124] NRTs attenuate withdrawal symptoms, and can provide a coping strategy for the behavioural aspects of withdrawal, such as oral (gum, lozenge) and hand-to-mouth (inhaler) stimulation.
- There is strong evidence that adding a short-acting 'on-demand' form of NRT (e.g., gum, lozenge) to a long-acting nicotine patch increases success rates, and so this strategy is preferred over monotherapy where possible.[53] [63] [122][124] [126] Evidence from one Cochrane review

suggests that lower-dose nicotine patches and gum may be less effective than higher-dose products.[53]

- The choice of nicotine delivery method is guided by patient preferences, prior experience, and availability. In most countries, the patch, gum, and lozenges are available without a prescription. The nasal spray generally requires a prescription. An inhaler and nicotine mouth spray may be available in some countries, but they are not currently available in the US.[76]
- Ensure that the person has NRT ready to start the day before the stopping date.[63]

Varenicline

- Varenicline attenuates withdrawal symptoms and blocks the reinforcing effects of nicotine. It has been shown to increase the chances of successful long-term smoking cessation by 2-3 times compared with placebo.[127] More people stop successfully with varenicline than with bupropion or with a single form of NRT. Varenicline may be as effective as or more effective than dual-form NRT.[127] [128] Guidance from the American Thoracic Society (ATS) and a statement from the American College of Cardiology both recommend varenicline over bupropion or NRT.[89] [129] Varenicline combined with behavioural support increases abstinence more than other pharmacotherapy with behavioural support combinations.[130]
- Early reports of possible links of varenicline to cardiovascular and psychiatric events have not been confirmed by current research.[90] [128] [131] There is evidence from one Cochrane review that people taking varenicline may be at increased risk of adverse cardiac events, but at decreased risk of neuropsychiatric adverse events, although the evidence was equivocal and compatible with both benefit and harm.[127]
- Varenicline is relatively slow-acting, and so should be started 1-2 weeks in advance of the stopping date.[63]

Second-line pharmacotherapy

Bupropion

- Has received FDA approval for smoking cessation, and is recommended in the UK by NICE as one potential option for smoking cessation, although NICE notes that this is 'off-label' use of bupropion, and that it is less effective than other types of smoking cessation pharmacotherapy including combination NRT and varenicline.[63]
- Demonstrated to increase smoking cessation rates; it is as effective as single NRT, and has been shown to increase the chances of long-term abstinence by approximately 50% to 80% compared with placebo.[122] [123]
- Less effective than varenicline.[122] [123]
- Use of bupropion increases the risk of psychiatric adverse events, and is less well tolerated than placebo.[123]
- Significant contraindications include seizures, eating disorders, and use of monoamine oxidase inhibitors.
- Bupropion is relatively slow-acting, and so should be started 1-2 weeks in advance of the stopping date.[63]

Nortriptyline[2] [132]

- Has not received FDA approval for smoking cessation, and is not recommended by NICE in the UK.[63]
- Second-line therapy for smoking cessation due to higher rates of adverse events; these include arrhythmias and changes in contractility and blood flow.

- Nortriptyline has demonstrated low-moderate efficacy for smoking cessation.[123] [125]
- One Cochrane review found evidence that nortriptyline aided smoking cessation when compared with placebo, but also some evidence that it was inferior to bupropion; findings were sparse and inconsistent as to whether nortriptyline had a particular benefit for people with current or previous depression. Data on harms and tolerability were limited.[123]
- Begin 12-28 days before the stopping date, and continue for 12 weeks then taper.

Combination pharmacotherapy

Most tobacco cessation monotherapies and combination therapies are more effective than placebo at helping participants to achieve sustained abstinence.[133] Combining drugs with different mechanisms of action may increase stopping rates more than single agents.[76] One network meta-analysis showed a high probability that the combination of varenicline and NRT is more likely to achieve sustained abstinence than NRT or bupropion as monotherapies.[133] However, one RCT showed no significant difference in abstinence among those treated with combined varenicline plus nicotine patch therapy versus varenicline monotherapy.[134] Combining varenicline with NRT has been associated with higher rates of adverse effects (e.g., nausea, headaches).[2]

Evidence to support the use of combination therapy with bupropion and NRT is not strong and its use is somewhat controversial. The US Public Health Service guidelines recommend combination of the nicotine patch with bupropion, although this combination is not recommended in other countries.[2]

Nicotine electronic cigarettes (e-cigarettes or vapes)

Nicotine electronic cigarettes (also known as e-cigarettes or vaping) vaporise nicotine fluid formulation with a feel that approximates regular smoking. In some locations, such as the UK, nicotine e-cigarettes may be considered in specific circumstances as an alternative option to conventional NRT in adults.

Efficacy of nicotine e-cigarettes

There is a mounting body of evidence demonstrating that nicotine e-cigarettes are an effective method of nicotine delivery and can be used as NRT.[63] [135][136]

In one Cochrane review, smoking cessation rates were higher in people randomised to nicotine e-cigarettes than in those randomised to NRT.[137] Another Cochrane review found high-certainty evidence that e-cigarettes are equal in efficacy to varenicline for smoking cessation, and slightly more effective than combination NRT.[125]

Safety of nicotine e-cigarettes

A report on the public health consequences of e-cigarettes by the National Academies of Sciences, Engineering, and Medicine found that exposure to nicotine from e-cigarettes is highly variable and depends on product characteristics (including device and e-liquid characteristics), as well as how the device is operated.[138] It also found that, in addition to nicotine, most e-cigarette products contain and emit numerous potentially toxic substances. However, the report found conclusive evidence that completely substituting combustible tobacco cigarettes for e-cigarettes reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes. Early molecular and clinical evidence suggests various acute physiological effects on the circulatory system from nicotine e-cigarettes (e.g., increases in heart rate and blood pressure, endothelial dysfunction, and platelet aggregation), which may pose harms to users, especially those with pre-existing cardiovascular disease.[139]

Dual use of nicotine e-cigarettes and combustible tobacco smoking has been highlighted as a particular cause for concern, and there is some evidence to suggest that it may increase the risk of respiratory and cardiovascular disease compared with conventional tobacco smoking.[32] [140] [141] [142]

Current evidence on safety suggests that the incidence of death or serious adverse events is low across RCTs undertaken to date.[135] However, arguments that e-cigarettes have not caused extensive disease in the past decade are premature, and it is currently unknown what diseases may develop following longer-term use.[57] [138]

An assessment of the published data on emissions from cigarettes and e-cigarettes calculated the lifetime cancer risks.[143] It concluded that the cancer potencies of e-cigarette emissions were largely under 0.5% of the risk of smoking tobacco cigarettes.[143] [144]

An outbreak of severe lung injury associated with vaping was reported in 2019 in the US. Although this was related to tetrahydrocannabinol (THC)-containing e-cigarettes that contained vitamin E acetate and not to commercial nicotine e-cigarettes, further contamination cannot be ruled out.[76] [86]

Nicotine e-cigarettes: variation in recommendations worldwide

Unlike conventional NRT, nicotine e-cigarettes are not licensed medicines, and their regulation and quality control varies across different countries and regions. Their use for smoking cessation is a topic of ongoing debate and research. While they are generally considered to be less harmful than combustible cigarettes, their use as tobacco cessation aids is controversial due to limited evidence on current devices, and uncertainty about safety of long-term use.[137]

Professional medical bodies in different countries have different stances on e-cigarettes based on the available evidence and public health considerations.[1] [63] [71] [145] The US Preventive Services Task Force (USPSTF) and the 2020 Surgeon General's report note insufficient evidence to evaluate the balance of benefits and risks of nicotine e-cigarettes for smoking cessation, and that clinicians should direct smokers to FDA-approved smoking cessation medicines instead.[1] [71] Use of e-cigarettes for smoking cessation is not typically recommended by guidelines or professional medical bodies in Europe (excluding the UK).[146] [147]

In the UK, recommendations are generally more supportive; NICE and the Royal College of Physicians (RCP) support the use of nicotine electronic cigarettes as a smoking cessation tool in adults in certain circumstances, when licensed treatments are not sufficient.[63] [148] [149] Although NICE does not specifically recommend nicotine e-cigarettes and emphasises that they cannot be offered on prescription, it does recommend ways in which health professionals may increase their accessibility.[63] Ultimately, the aim should be to stop all forms of nicotine (including nicotine e-cigarettes), but this should not be done at the expense of relapsing to smoking.[150]

There is universal agreement among professional medical bodies worldwide that use of e-cigarettes should be discouraged in people who have never smoked, and that they should not be used for smoking cessation in children and adolescents, owing to safety risks in this age group, and a lack of evidence supporting their efficacy compared with behavioural support and NRT.

Harm reduction

For people who are unwilling or not ready to stop smoking, harm reduction may be considered.[63] [129]

Approaches to harm reduction vary and include:[63]

- Cutting down before stopping smoking, with or without pharmacotherapy (varenicline or NRT)
- Smoking reduction, with or without pharmacotherapy (varenicline or NRT)
- Temporary abstinence from smoking, with or without pharmacotherapy (varenicline or NRT).

Shared decision making is key to selecting the most suitable approach for the individual.

Many people ask if stopping abruptly is harder than tapering smoking, also known as the reduction-to-quit method. This approach provides NRT to support a reduction in cigarette consumption as a first step towards abstinence. Some trials of 'NRT-assisted reduction to stop' (or cut down to stop) demonstrate that long-term abstinence rates among smokers provided with NRT for this purpose are double those among smokers given placebo, and that adverse events are not increased despite receiving nicotine from both the NRT and cigarettes.[151] [152] [153] Forms of NRT that have been studied include the use of nicotine gum or inhaler for up to 18 months and the use of nicotine patches for 6 weeks before a stopping date.[151] [152] [153] Many of these studies include behavioural support.

For patients who are not willing to stop in the next month but are willing to reduce cigarette consumption and stop in 3 months, varenicline therapy for 24 weeks has been shown to significantly increase smoking cessation rates.[154] However, neither reduction-to-quit nor abrupt stopping interventions result in superior long-term stopping rates when compared with one another.[155]

Smoking cessation management in specific patient groups

Pregnant/breastfeeding women

- Smoking in pregnancy represents a special circumstance with additional considerations. Smoking during pregnancy is a well-established risk factor for adverse pregnancy outcomes including preterm deliveries, low birth weight, and preterm-related deaths, and it is prevalent to varying degrees globally.[7] [156] All pregnant women who smoke should be advised on the adverse effects of smoking on their fetus (low birth weight, preterm birth) and offered access to smoking cessation interventions.[157]
- The USPSTF recommends that clinicians ask all pregnant persons about tobacco use, advise them to stop using tobacco, and provide behavioural interventions of cessation to pregnant persons who use tobacco.[71]
- In this population, behavioural and psychological interventions are considered first-line treatments in some locations, including the US.[71] [157]
- One Cochrane review determined that NRT used for smoking cessation in pregnancy may increase smoking cessation rates in late pregnancy; however, the evidence is of low certainty and there was no conclusive evidence on either positive or negative effects on birth outcomes.[158] There is insufficient evidence on either the effectiveness or the safety of bupropion or varenicline for smoking cessation in pregnancy.[158]
- While not expressly recommending against using medicines, the USPSTF concluded that the current evidence was insufficient to assess the balance of benefits and harms of pharmacological interventions, including NRT, bupropion, and varenicline for tobacco cessation in pregnant or breastfeeding women.[71] The American College of Obstetrics and Gynecology recommends using NRT only after a detailed discussion with the patient of the known risks of continued smoking, the possible risks of NRT, and need for close supervision.[159]
- In the UK, NICE recommends that NRT be considered alongside behavioural support in pregnant women who use tobacco, as most smoking-related health problems are caused by other components in tobacco smoke, not by the nicotine.[63] Use of NRT instead of smoking reduces

their nicotine exposure.[160] NICE advises against using other pharmacotherapy options for smoking cessation, such as varenicline or bupropion, during pregnancy and breastfeeding.[63]

Adolescents aged <18 years

- Data on efficacy of cessation treatments in adolescents are limited.[62] [161] This is due, in part, to challenges in conducting studies in this population. In addition, the experience of smoking and smoking cessation may differ between this age group and adults. For instance, levels of nicotine dependence may not be equal to those of adult smokers.
- One Cochrane review found evidence to suggest that behavioural support delivered via a group setting is effective in increasing smoking cessation among adolescents.[161]
- The US Preventive Services Task Force (USPSTF) concludes that the current evidence is insufficient to assess the balance of benefits and harms of primary-care feasible interventions for smoking cessation in children and adolescents younger than 18 years.[62] The American Academy of Pediatrics (AAP) recommends that for adolescents who smoke and who wish to stop using tobacco, clinicians offer referral for a behavioural intervention for smoking cessation. They recommend that smoking cessation pharmacotherapy (NRT) may be considered for adolescents who are moderately to severely dependent on tobacco.[60] UK guidance from NICE recommends that clinicians consider NRT for children and adolescents aged 12 years and over who are smoking and dependent on tobacco, in conjunction with behavioural support.[63]
- E-cigarettes are not recommended for smoking cessation in children and adolescents.[60]
- In one Cochrane review, there was no clear evidence for the effectiveness of pharmacological (NRT, bupropion) interventions in young people.[161] However, a review of studies of pharmacotherapy for smoking cessation in adolescents concluded that if an adolescent shows signs of dependence, a nicotine patch may be prescribed in addition to a behavioural intervention.[162] One trial suggested that a combination of NRT and cognitive behavioural therapy is associated with significantly higher abstinence rates in adolescent smokers at 6 months.[163] In one meta-analysis, bupropion was found to improve sustained smoking abstinence, but a pooled analysis of pharmacotherapy overall showed increased abstinence rates for only 4 weeks of follow-up.[164] Data for varenicline suggested safety and early abstinence, but no sustained effect.[165]
- Clinicians should consult local prescribing recommendations and guidance, but note that in some locations (e.g., the UK), commonly used pharmacotherapies for smoking cessation, such as varenicline and bupropion, should not be prescribed to those aged under 18 years.[63]

Active smokers admitted to hospital

- Hospital admissions present a window of opportunity to initiate cessation interventions in active smokers for several reasons:
 1. If admitted for a smoking-related illness, active smokers may have increased motivation to stop.
 2. As most hospitals are smoke-free, smokers have enforced abstinence from smoking.
 3. Some hospitals have trained specialist clinicians to assist with smoking cessation.
 4. Those eligible to receive pharmacotherapy can be instructed on its use and can experience pharmacotherapy while being observed.
- For people diagnosed with many types of cancer including lung cancer, post-diagnosis smoking cessation is associated with increased survival rates.[166] [167] An argument can be made for routine integration of smoking cessation services within oncology care.[168]
- There is high-certainty evidence to suggest that behavioural support by a trained cessation specialist initiated during the admission to hospital and continued for more than 1 month after

discharge is effective in increasing stopping rates in hospitalised patients, regardless of the admitting diagnosis.[169] Behavioural support provided only in hospital, without post-discharge support, may have a modest impact on stopping rates, but the evidence is less certain.[169] Therefore, active smokers should be connected with outpatient behavioural support resources at discharge, where possible.[170] When patients receive behavioural support in hospital, high-certainty evidence indicates that providing both behavioural support and pharmacotherapy after discharge increases stopping rates compared with no post-discharge intervention.[169]

- Evidence suggests an improvement in stopping rates when NRT is used in patients admitted to hospital.[169] NRT may also help relieve withdrawal symptoms during the enforced abstinence from smoking. A retrospective review of observational studies demonstrated that perioperative NRT is not associated with adverse outcomes after surgery.[171] An RCT comparing the relative cardiovascular safety risk of varenicline, bupropion, and NRT showed no evidence that the use of any of these smoking cessation pharmacotherapies increased the risk of serious cardiovascular adverse events.[90]
- One effective programme for inpatient smoking cessation is the Ottawa Model for Smoking Cessation, which improves long-term stopping rates by 11%, and involves identification of smoking status for all admitted patients, brief advice, personalised bedside smoking cessation, behavioural support, timely pharmacotherapy, and follow-up after discharge.[172] [University of Ottawa Heart Institute: Ottawa model for smoking cessation] (<https://ottawamodel.ottawaheart.ca>)
- The relative lack of evidence regarding safety and efficacy of NRT in acute coronary syndrome (ACS) and the theoretical concern for nicotine's vasoconstrictive properties mean that NRT use may be limited during hospitalisation for patients with ACS and life-threatening arrhythmias. The American College of Cardiology notes, however, that given the robust safety profile and efficacy of NRT in the general population, and the clear dangers of smoking, NRT is recommended as first-line therapy in hospitalised patients with ACS.[89]
- There is moderate-certainty evidence to suggest that starting varenicline in hospitalised patients helps more patients to stop smoking than placebo or no medication. There is less evidence of benefit for bupropion in this setting.[169]

Perioperative patients

- Patients who smoke who require surgery represent a special opportunity for smoking cessation. The perioperative risks of smoking have been well established, and include infection, ACS, neurological complications, prolonged length of stay, and death, among others.[173] [174] Although optimal timing for smoking cessation prior to surgery has been suggested to be as long as 4 weeks, even short durations of abstinence may be helpful.[175]
- Among patients scheduled for elective non-cardiac surgery, varenicline combined with a 10- to 15-minute behavioural support session, educational material, and referral to a quitline was found to increase long-term abstinence by 62% compared with brief behavioural support and self-referral to a quitline alone.[176] Both bupropion and varenicline are relatively slow-acting, and so should be started at least 1-2 weeks in advance of the scheduled surgery. If cessation does not occur preoperatively, NRT used in the immediate postoperative period can mitigate the nicotine withdrawal symptoms, due to its rapid onset of action.[177]
- Intensive multicomponent interventions appear to be more effective than brief interventions in achieving abstinence and reducing post-surgical complications.[178] Concomitant preoperative intensive behavioural support has been shown to improve outcomes in perioperative patients, usually in conjunction with NRT, according to one Cochrane review.[179] Brief interventions of 90 minutes or less have been associated with a small reduction in smoking by the time of surgery.[179]

- There is some evidence to suggest that preoperative smoking cessation interventions result in longer-term smoking cessation after 1 year, compared with usual care (25% vs. 8%).^[180]

Active smokers presenting to the accident and emergency department

- In some locations such as the US, people without insurance coverage may present to the emergency department rather than to primary care, reducing opportunities for primary care-based smoking cessation interventions. One study showed that an intensive 6-week intervention (including motivational interview by a trained research assistant, a supply of nicotine transdermal patches and gum started in the emergency department, a referral to a smoker's quitline, a booster call, and a brochure) improved tobacco abstinence rates in low-income patients presenting to the accident and emergency department.^[181]

People with co-existing mental health conditions

- People with mental health conditions are several times more likely to smoke than the general population, and smoking is believed to be the single largest contributor to the 7-25 year reduced life expectancy within this group.^[182] However, people with mental health conditions are less likely to be offered smoking cessation treatment compared with the general population without mental illness.^[183]
- Concerns are sometimes noted that smoking cessation could exacerbate symptoms of psychiatric illness. In fact, the evidence suggests that smoking cessation results in improved physical and mental health within a few months, among those with and without a pre-existing mental health condition.^{[182] [184] [185]} However, owing to a theoretical risk that nicotine withdrawal may negatively impact mood in the short term, it is advisable to monitor mental health during smoking cessation in people with pre-existing mental illness.
- Smoking increases metabolism of many psychotropic medications, and a dose reduction may be required immediately on smoking cessation in order to prevent toxicity. Careful monitoring of psychiatric medications is therefore required. Examples include a number of commonly used antidepressants, antipsychotics, and benzodiazepines, as well as carbamazepine. If smoking is resumed, original doses may need to be reinstated.^[182]
- In those with current depression, use of the antidepressants bupropion or nortriptyline may be considered, as they also have efficacy in improving cessation rates, although data to support this approach are limited, and as a general guide, first-line treatments for smoking cessation should be considered preferentially. Nortriptyline and bupropion are second-line therapies for smoking cessation because of higher rates of adverse events.^{[2] [132]}
- Treatment with bupropion and contingent reinforcement (e.g., with money) has been shown to be helpful for smoking cessation in people with schizophrenia. There is no evidence to suggest that NRT, bupropion, or varenicline lead to worsening of psychiatric symptoms; these agents are effective and are not associated with changes in psychiatric symptoms.^{[186] [187]}

Substance use disorder

- Over 53% of people with substance use disorder die of tobacco-related causes.^[44]
- People with a history of substance use should be encouraged to pursue smoking cessation as they undergo treatment for other drug dependencies.^{[87] [188] [189]}
- Given the challenges with this group of patients, all should receive behavioural support, ideally with therapists with training in both tobacco and substance use disorder.
- Some medications prescribed for substance use disorders (e.g., methadone) may be affected by smoking cessation; in people with opioid use disorder requiring treatment with methadone, careful monitoring for opioid toxicity is required, with consideration of dose reduction.^[190]

- People with active alcohol or substance use disorder may have a reduced threshold for seizures, increasing the risk of this complication from treatment with bupropion.
- There is no evidence to suggest that receiving treatment for smoking increases use of other substances.[191]
- In one systematic review, varenicline had a significant effect on short-term smoking cessation when used in people with alcohol dependence, but the number of studies was small.[192] Of interest, in studies of varenicline for the treatment of alcohol dependence, a concomitant reduction of both smoking and alcohol use was seen.[193]
- There is also evidence for NRT, behavioural support, and bupropion for smoking cessation, as well as for combination treatment, in this patient group.[194] [195]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Acute		(summary)
hospitalised active smokers		
1st	brief or comprehensive intervention for smoking cessation	
plus	behavioural support	
adjunct	nicotine replacement therapy (NRT) and/or varenicline	

Ongoing		(summary)
active smokers ready to stop: adults (not pregnant/breastfeeding)		
1st	brief or comprehensive intervention for smoking cessation	
plus	behavioural support	
adjunct	nicotine replacement therapy (NRT) and/or varenicline	
2nd	brief or comprehensive intervention for smoking cessation	
plus	behavioural support	
adjunct	bupropion or nortriptyline	
active smokers ready to stop: pregnant/breastfeeding women or adolescents		
1st	brief or comprehensive intervention for smoking cessation	
plus	behavioural support	
adjunct	nicotine replacement therapy (NRT)	
active smokers not ready to stop		
1st	brief intervention for smoking cessation	
plus	motivational messages	
adjunct	harm-reduction measures	

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Acute

hospitalised active smokers

- 1st** **brief or comprehensive intervention for smoking cessation**
- » Hospital admissions present a window of opportunity to initiate cessation interventions in active smokers for several reasons: if admitted for a smoking-related illness, active smokers may have increased motivation to stop; as most hospitals are smoke-free, smokers have enforced abstinence from smoking; some hospitals have trained specialist clinicians to assist with smoking cessation; those eligible to receive pharmacotherapy can be instructed on its use and can experience it while being observed.
 - » The initial approach to smoking cessation varies according to location of practice. Two commonly used models are: i) very brief advice for smoking, based on an 'Ask, Advise, Assist' structure, which encourages clinicians to ask patients about tobacco use, advise them to stop, and assist them by signposting them to specialist smoking cessation services offering pharmacotherapy and behavioural support; ii) a more comprehensive intervention for smoking cessation, which can be provided using the '5 A's' structure: 1) ask about tobacco use; 2) advise to stop through clear, personalised messages; 3) assess willingness to stop; 4) assist in stopping; and 5) arrange follow-up and support.^[71]
 - » Both brief and comprehensive smoking cessation models may be used within an inpatient hospital setting. Evidence directly comparing smoking cessation models is limited. It suggests that both brief and comprehensive models can be effective, but that effectiveness may vary depending on the individual and on the clinical setting.^[1] Clinicians may choose to prioritise for comprehensive interventions those with greater nicotine dependence, or previous unsuccessful stopping attempts.
 - » When patients receive behavioural support in hospital, high-certainty evidence indicates that providing both behavioural support and pharmacotherapy after discharge increases

Acute

stopping rates compared with no post-discharge intervention.[169]

» One effective programme for inpatient smoking cessation is the Ottawa Model for Smoking Cessation, which improves long-term stopping rates by 11%, and involves identification of smoking status for all admitted patients, brief advice, personalised bedside smoking cessation, behavioural support, timely pharmacotherapy, and follow-up after discharge.[172] [University of Ottawa Heart Institute: Ottawa model for smoking cessation] (<https://ottawamodel.ottawaheart.ca>)

plus behavioural support

Treatment recommended for ALL patients in selected patient group

» There is high-certainty evidence to suggest that behavioural support by a trained cessation specialist initiated during the admission to hospital and continued for more than 1 month after discharge is effective in increasing stopping rates regardless of the admitting diagnosis.[169]

Behavioural support provided only in hospital, without post-discharge support, may have a modest impact on stopping rates, but the evidence is less certain.[169] Therefore, active smokers should be connected with outpatient behavioural support resources at discharge, where possible.[170]

» Cochrane reviews determined that group-based interventions appear to be more promising than individual-based interventions. [110] [161]

adjunct nicotine replacement therapy (NRT) and/or varenicline

Treatment recommended for SOME patients in selected patient group

Primary options

» **nicotine transdermal**: 21 mg once daily for 6 weeks initially, followed by 14 mg once daily for 2 weeks, followed by 7 mg once daily for 2 weeks

Can start patient on 14 mg/day if smoke <10 cigarettes/day. Other strengths may be available.

-or-

» **nicotine lozenge**: 2-4 mg lozenge every 1-2 hours for 6 weeks, then taper gradually over 6 weeks, maximum 5 lozenges/6 hours or 20 lozenges/day

Acute

-or-

» **nicotine gum**: 2-4 mg gum every 1-2 hours for 6 weeks, then taper gradually over 6 weeks, maximum 24 gum pieces/day

-or-

» **nicotine nasal**: 0.5 mg (1 spray) in each nostril once or twice an hour initially, adjust dose according to response, maximum 10 sprays/hour or 80 sprays/day

--AND/OR--

» **varenicline**: 0.5 mg orally once daily for 3 days initially, followed by 0.5 mg twice daily for 4 days, followed by 1 mg twice daily for 12-24 weeks

» Evidence supports an improvement in stopping rates when NRT is added to behavioural support in patients admitted to hospital.[169] NRT may also help relieve withdrawal symptoms during the enforced abstinence from smoking. One retrospective review of observational studies demonstrated that perioperative NRT is not associated with adverse outcomes after surgery.[171]

» NRT has been considered safe in hospitalised patients including in patients admitted for acute coronary syndrome, and is recommended for use by the American College of Cardiology.[89] We suggest individualising therapy depending on patient variables.

» In the US, non-pharmacological options are considered first line for pregnant or breastfeeding women, and adolescents.[2] [62] [71] Consult a specialist for guidance on selection of treatment in pregnant/breastfeeding women and adolescents.

» There is moderate-certainty evidence to suggest that starting varenicline in hospitalised patients helps more patients to stop smoking than placebo or no medication.[169] There is insufficient evidence on the effectiveness or safety of varenicline for smoking cessation in pregnancy.[158]

» Most tobacco cessation monotherapies and combination therapies are more effective than placebo at helping participants to achieve sustained abstinence.[133] Combining drugs with different mechanisms of action may increase stopping rates more than single agents.[76] One network meta-analysis showed a high probability that the combination of varenicline and NRT is more likely to achieve sustained abstinence than NRT or bupropion as

Acute

monotherapies.[133] However, one randomised controlled trial showed no significant difference in abstinence among those treated with combined varenicline plus nicotine patch therapy versus varenicline monotherapy.[134] Combining varenicline with NRT agents has been associated with higher rates of adverse effects (e.g., nausea, headaches).[2]

» The choice of nicotine delivery method is guided by patient preferences, prior experience, and availability. In most countries, the patch, gum, and lozenges are available without a prescription. The nasal spray generally requires a prescription. An inhaler and nicotine mouth spray may be available in some countries, but they are not currently available in the US.[76] Product literature should be consulted for further guidance on dosage of specific brands of NRT products.

Ongoing

active smokers ready to stop: adults
(not pregnant/breastfeeding)

1st brief or comprehensive intervention for smoking cessation

» The initial approach to smoking cessation varies according to location of practice. Two commonly used models are: i) very brief advice for smoking, based on an 'Ask, Advise, Assist' structure, which encourages clinicians to ask patients about tobacco use, advise them to stop, and assist them by signposting them to specialist smoking cessation services offering pharmacotherapy and behavioural support; ii) a more comprehensive intervention for smoking cessation, which can be provided using the '5 A's' structure: 1) ask about tobacco use; 2) advise to stop through clear, personalised messages; 3) assess willingness to stop; 4) assist in stopping; and 5) arrange follow-up and support.[71]

» Evidence directly comparing smoking cessation models is limited. It suggests that both brief and comprehensive models can be effective, but that effectiveness may vary depending on the individual and on the clinical setting.[1] Clinicians may choose to prioritise for comprehensive interventions those with greater nicotine dependence, or previous unsuccessful stopping attempts.

» Following the initial clinical contact, clinicians should offer a menu of cessation resources (medicines and behavioural support) to those who are ready to stop. Overall, the combination of behavioural support plus an evidence-based medication for smoking cessation has the best evidence for smoking cessation.[2] [96] Some people may choose to attempt smoking cessation with behavioural support alone.

plus behavioural support

Treatment recommended for ALL patients in selected patient group

» Behavioural support has consistently shown benefit for smoking cessation, compared with receiving minimal support, or receiving pharmacotherapy alone.[111] [112] Cochrane review evidence suggests that increasing the amount of behavioural support available increases the chance of success by about 10% to 20%.[98] Another Cochrane review determined that group-based interventions in adults appear to be more promising than self-

Ongoing

help and other less intensive interventions. There was not enough evidence to evaluate whether groups are more effective than intensive individual behavioural support.[110] There is moderate-certainty evidence that the provision of adjunctive behavioural support by a health professional other than the physician (e.g., nurse, smoking cessation specialist, smoking quitline) increases smoking cessation rates in primary care.[113]

» Internet-based interventions are available that increase the likelihood of cessation and help patients avoid relapse.[114] [115] Text messaging interventions have been shown to have a beneficial impact on 6-month cessation outcomes.[116] [117] Financial-incentive programmes have been shown to improve tobacco cessation rates in both low- and high-income groups.[118] [119][120]

» Reward-based programmes are more commonly accepted than deposit-based programmes and have led to higher smoking cessation rates.[121]

adjunct **nicotine replacement therapy (NRT) and/or varenicline**

Treatment recommended for SOME patients in selected patient group

Primary options

» **nicotine transdermal**: 21 mg once daily for 6 weeks initially, followed by 14 mg once daily for 2 weeks, followed by 7 mg once daily for 2 weeks

Can start patient on 14 mg/day if smoke <10 cigarettes/day. Other strengths may be available.

-or-

» **nicotine lozenge**: 2-4 mg lozenge every 1-2 hours for 6 weeks, then taper gradually over 6 weeks, maximum 5 lozenges/6 hours or 20 lozenges/day

-or-

» **nicotine gum**: 2-4 mg gum every 1-2 hours for 6 weeks, then taper gradually over 6 weeks, maximum 24 gum pieces/day

-or-

» **nicotine nasal**: 0.5 mg (1 spray) in each nostril once or twice an hour initially, adjust dose according to response, maximum 10 sprays/hour or 80 sprays/day

--AND/OR--

Ongoing

» **varenicline**: 0.5 mg orally once daily for 3 days initially, followed by 0.5 mg twice daily for 4 days, followed by 1 mg twice daily for 12-24 weeks

» Two types of medicine have amassed the greatest volume of data demonstrating safety and efficacy for smoking cessation: NRT with a combination of short-acting and long-acting NRT (patches, gum, lozenges, and nasal spray), and varenicline.^{[122] [123] [124] [125]} Both are considered first-line treatments and produce significantly higher stop rates for 6 months or more than does placebo alone.^{[63] [76]}

» NRTs attenuate withdrawal symptoms and can provide a coping strategy for the behavioural aspects of withdrawal, such as oral (gum, lozenge) and hand-to-mouth (inhaler) stimulation. There is strong evidence that adding a short-acting 'on-demand' form of NRT (e.g., gum, lozenge) to a long-acting nicotine patch increases success rates, and so this strategy is preferred over monotherapy where possible.^{[53] [63] [122] [124] [126]} Evidence from one Cochrane review suggests that lower-dose nicotine patches and gum may be less effective than higher-dose products.^[53]

» The choice of nicotine delivery method is guided by patient preferences, prior experience, and availability. In most countries, the patch, gum, and lozenges are available without a prescription. The nasal spray generally requires a prescription. An inhaler and nicotine mouth spray may be available in some countries, but they are not currently available in the US.^[76]

Product literature should be consulted for further guidance on dosage of specific brands of NRT products. NRT should be started at the same time as the planned stop date.

» Varenicline attenuates withdrawal symptoms and blocks the reinforcing effects of nicotine. It has been shown to increase the chances of successful long-term smoking cessation by 2-3 times compared with placebo.^[127]

More people stop successfully with varenicline than with bupropion or with a single form of NRT. Varenicline may be as effective as or more effective than dual-form NRT.^{[127] [128]}

Guidance from the American Thoracic Society (ATS) and a statement from the American College of Cardiology both recommend varenicline over bupropion or NRT.^{[89] [129]}

Varenicline combined with behavioural support increases abstinence more than other pharmacotherapy with behavioural support

Ongoing

combinations.[130] Early reports of possible links of varenicline to cardiovascular and psychiatric events have not been confirmed by current research.[90] [128] [131] There is evidence from one Cochrane review that people taking varenicline may be at increased risk of adverse cardiac events, but at decreased risk of neuropsychiatric adverse events, although the evidence was equivocal and compatible with both benefit and harm.[127] Physicians should consider warning patients of the potential for these effects and advising them to seek medical help if the patient (or their family or carer) observes any mood or behavioural changes.[196] Varenicline is relatively slow-acting, and so should be started 1-2 weeks in advance of the stopping date.[63] To prevent nausea, varenicline can be taken after meals with a full glass of water, dosage can be increased slowly, or dose can be reduced.

» Most tobacco cessation monotherapies and combination therapies are more effective than placebo at helping participants to achieve sustained abstinence.[133] Combining drugs with different mechanisms of action may increase stopping rates more than single agents.[76] One network meta-analysis showed a high probability that the combination of varenicline and NRT is more likely to achieve sustained abstinence than NRT or bupropion as monotherapies.[133] However, one randomised controlled trial showed no significant difference in abstinence among those treated with combined varenicline plus nicotine patch therapy versus varenicline monotherapy.[134] Combining varenicline with NRT agents has been associated with higher rates of adverse effects (e.g., nausea, headaches).[2]

» In some locations, nicotine e-cigarettes may be considered in certain circumstances as an alternative to conventional NRT. Unlike conventional NRT, nicotine e-cigarettes are not licensed medicines, and their regulation and quality control varies across different countries and regions. Their use for smoking cessation is a topic of ongoing debate and research. There is a mounting body of evidence demonstrating that nicotine e-cigarettes are an effective method of nicotine delivery and can be used as NRT.[63] [125] [135][136][137] While they are generally considered to be less harmful than combustible cigarettes, their use as tobacco cessation aids remains controversial due to limited evidence on current devices, and

Ongoing

uncertainty about possible health risks of long-term use.[137] Many countries (including the US) currently take a precautionary approach, and recommend against the use of e-cigarettes for smoking cessation.[1] [71] [72] In the UK, recommendations on nicotine e-cigarette use for smoking cessation are more supportive. A number of UK professional bodies including the National Institute for Health and Care Excellence (NICE) and the Royal College of Physicians (RCP) support the use of nicotine e-cigarettes as a smoking cessation tool in adults in certain circumstances: for example, when licensed treatments are not sufficient.[63] [148][149]

2nd **brief or comprehensive intervention for smoking cessation**

» The initial approach to smoking cessation varies according to location of practice. Two commonly used models are: i) very brief advice for smoking, based on an 'Ask, Advise, Assist' structure, which encourages clinicians to ask patients about tobacco use, advise them to stop, and assist them by signposting them to specialist smoking cessation services offering pharmacotherapy and behavioural support; ii) a more comprehensive intervention for smoking cessation, which can be provided using the '5 A's' structure: 1) ask about tobacco use; 2) advise to stop through clear, personalised messages; 3) assess willingness to stop; 4) assist in stopping; and 5) arrange follow-up and support.[71]

» Evidence directly comparing smoking cessation models is limited. It suggests that both brief and comprehensive models can be effective, but that effectiveness may vary depending on the individual and on the clinical setting.[1] Clinicians may choose to prioritise for comprehensive interventions those with greater nicotine dependence, or previous unsuccessful stopping attempts.

» Following the initial clinical contact, clinicians should offer a menu of cessation resources (medicines and behavioural support) to those who are ready to stop. Overall, the combination of behavioural support plus an evidence-based medication for smoking cessation has the best evidence for smoking cessation.[2] [96] Some people may choose to attempt smoking cessation with behavioural support alone.

plus **behavioural support**

Treatment recommended for ALL patients in selected patient group

Ongoing

» Behavioural support has consistently shown benefit for smoking cessation, compared with receiving minimal support, or receiving pharmacotherapy alone.^{[111] [112]} Cochrane review evidence suggests that increasing the amount of behavioural support available increases the chance of success by about 10% to 20%.^[98] Another Cochrane review determined that group-based interventions in adults appear to be more promising than self-help and other less intensive interventions. There was not enough evidence to evaluate whether groups are more effective than intensive individual behavioural support.^[110] There is moderate-certainty evidence that the provision of adjunctive behavioural support by a health professional other than the physician (e.g., nurse, smoking cessation specialist, smoking quitline) increases smoking cessation rates in primary care.^[113]

» Internet-based interventions are available that increase the likelihood of cessation and help patients avoid relapse.^{[114] [115]} Text messaging interventions have been shown to have a beneficial impact on 6-month cessation outcomes.^{[116] [117]} Financial-incentive programmes have been shown to improve tobacco cessation rates in both low- and high-income groups.^{[118] [119][120]}

» Reward-based programmes are more commonly accepted than deposit-based programmes and have led to higher smoking cessation rates.^[121]

adjunct bupropion or nortriptyline

Treatment recommended for SOME patients in selected patient group

Primary options

» **bupropion**: 150 mg orally (extended-release) once daily for 3 days initially, followed by 150 mg twice daily for 7-12 weeks

Secondary options

» **nortriptyline**: 25 mg orally once daily at bedtime for 3 days initially, followed by 50 mg once daily at bedtime for 4 days, then 75 mg once daily at bedtime thereafter for at least 12 weeks, adjust dose according to response, maximum 125 mg/day

» Bupropion has received US Food and Drug Administration (FDA) approval for smoking cessation, and is recommended in the UK by

Ongoing

the National Institute for Clinical Excellence (NICE) as one option for smoking cessation, although NICE notes that it is less effective than combination nicotine replacement therapy (NRT) and varenicline.^[63] Demonstrated to increase smoking cessation rates; it is as effective as single NRT, and has been shown to increase the chances of long-term abstinence by approximately 50% to 80% compared with placebo.^{[122] [123]} It is less effective than varenicline.^{[122] [123]} Use of bupropion increases the risk of psychiatric adverse events, and is less well tolerated than placebo.^[123]

Significant contraindications include seizures, eating disorders, and use of monoamine oxidase inhibitors. People with active alcohol or substance use disorder may have a reduced threshold for seizures, increasing the risk of this complication from treatment with bupropion. Bupropion is relatively slow-acting, and so should be started 1-2 weeks in advance of the stopping date.^[63]

» Nortriptyline has not received FDA approval for smoking cessation, and is not recommended by NICE in the UK.^[63] Nortriptyline has demonstrated low-moderate efficacy for smoking cessation.^{[123] [125]} One Cochrane review found evidence that nortriptyline aided smoking cessation when compared with placebo, but also some evidence that it was inferior to bupropion; findings were sparse and inconsistent as to whether nortriptyline had a particular benefit for people with current or previous depression. Data on harms and tolerability were limited.^[123] Considered a second-line therapy for smoking cessation due to higher rates of adverse events; these include arrhythmias and changes in contractility and blood flow. Treatment is started 12-28 days before stopping date and continued for 12 weeks, then tapered gradually.

» Either bupropion or nortriptyline may be considered in people with current depression, given that they are both antidepressants, although data to support this approach are limited, and as a general guide, first-line treatments for smoking cessation should be considered preferentially.^[123]

» Evidence to support the use of combination therapy with bupropion and NRT is not strong and its use is somewhat controversial. The US Public Health Service guidelines recommend combination of the nicotine patch with bupropion, although this combination is not recommended

Ongoing

in other countries.[2] Combination treatment with nortriptyline and NRT is not supported by the available evidence base.

**active smokers ready to stop:
pregnant/breastfeeding women or
adolescents**

1st brief or comprehensive intervention for smoking cessation

» Smoking in pregnancy and smoking in adolescents represent special circumstances with additional considerations.

» As in the general adult population, the initial approach to smoking cessation varies according to location of practice. Two commonly used models are: i) very brief advice for smoking, based on an 'Ask, Advise, Assist' structure, which encourages clinicians to ask patients about tobacco use, advise them to stop, and assist them by signposting them to specialist smoking cessation services offering pharmacotherapy and behavioural support; ii) a more comprehensive intervention for smoking cessation, which can be provided using the '5 A's' structure: 1) ask about tobacco use; 2) advise to stop through clear, personalised messages; 3) assess willingness to stop; 4) assist in stopping; and 5) arrange follow-up and support.[71]

» Smoking during pregnancy is a well-established risk factor for adverse pregnancy outcomes including preterm deliveries, low birth weight, and preterm-related deaths, and it is still prevalent to varying degrees globally.[7] [156] All pregnant women who smoke should be advised on the adverse effects of smoking on their fetus (low birth weight, preterm birth) and offered access to smoking cessation interventions.[157] Likewise, all adolescents who smoke should be advised to stop smoking, and offered evidence-based interventions.[63] Data on efficacy of cessation treatments in adolescents are limited.[62] [161] This is due, in part, to challenges in conducting studies in this population. In addition, the experience of smoking and smoking cessation may differ between this age group and adults. For instance, levels of nicotine dependence may not be equal to those of adult smokers.

plus behavioural support

Treatment recommended for ALL patients in selected patient group

Ongoing

» In pregnancy, behavioural and psychological interventions are considered first-line treatments in some locations, including the US.[71] [157]

» The American Academy of Pediatrics (AAP) recommends that for adolescents who smoke and who wish to stop using tobacco, clinicians offer referral for a behavioural intervention for smoking cessation.[60]

» In the UK, the National Institute for Health and Care Excellence (NICE) recommends behavioural support as one of a range of treatment options (both pharmacological and non-pharmacological) for smoking cessation in pregnant women and adolescents.[63]

» Behavioural support interventions to prevent tobacco use in children and adolescents are effective, but the data on efficacy of cessation treatments in adolescents are limited.[62] [161] One Cochrane review found evidence to suggest that behavioural support delivered via a group setting is effective in increasing smoking cessation among adolescents.[161]

adjunct nicotine replacement therapy (NRT)

Treatment recommended for SOME patients in selected patient group

» Recommendations on pharmacological treatment for smoking cessation in pregnancy and in adolescents differ according to country of practice, and clinicians should be familiar with local guidance.

» In pregnancy, behavioural and psychological interventions are considered first-line treatments in the US.[71] [157] While not expressly recommending against using medicines, the US Preventive Services Task Force (USPSTF) concluded that the current evidence was insufficient to assess the balance of benefits and harms of pharmacological interventions, including NRT, for tobacco cessation in pregnant or breastfeeding women.[71] The American College of Obstetricians and Gynecologists (ACOG) recommends using NRT only after a detailed discussion with the patient of the known risks of continued smoking, the possible risks of NRT, and need for close supervision.[159]

» In the UK, the National Institute for Health and Care Excellence (NICE) recommends that NRT be considered alongside behavioural support in pregnant women who use tobacco, as most smoking-related health problems are caused by other components in tobacco smoke, not by

Ongoing

the nicotine.[63] Use of NRT instead of smoking reduces their nicotine exposure.[160]

» One Cochrane review determined that NRT used for smoking cessation in pregnancy may increase smoking cessation rates in late pregnancy; however, the evidence is of low certainty and there was no conclusive evidence on either positive or negative effects on birth outcomes.[158] There is insufficient evidence on either the effectiveness or the safety of bupropion or varenicline for smoking cessation in pregnancy.[158] NICE advises against using other pharmacotherapy options for smoking cessation, such as varenicline or bupropion, during pregnancy and breastfeeding.[63]

» In adolescents, the USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of primary-care feasible interventions for smoking cessation in children and adolescents younger than 18 years.[62] The American Academy of Pediatrics (AAP) recommends that smoking cessation pharmacotherapy (with NRT) may be considered for adolescents who are moderately to severely dependent on tobacco, in conjunction with behavioural support.[60]

» UK guidance from NICE recommends that clinicians consider NRT for children and adolescents aged 12 years and over who are smoking and dependent on tobacco, in conjunction with behavioural support.[63]

» In one Cochrane review, there was no clear evidence for the effectiveness of pharmacological treatment (including NRT) in young people.[161] However, a review of studies of pharmacotherapy for smoking cessation in adolescents concluded that if an adolescent shows signs of dependence, a nicotine patch may be prescribed in addition to a behavioural intervention.[162] One trial suggested that a combination of NRT and cognitive behavioural therapy is associated with significantly higher abstinence rates in adolescent smokers at 6 months.[163]

» Use of other types of pharmacotherapy for smoking cessation (e.g., varenicline, bupropion) is not recommended in those under the age of 18 years.[63]

» Consult a specialist for guidance on selection of treatment in pregnant/breastfeeding women and adolescents.

Ongoing

active smokers not ready to stop

1st brief intervention for smoking cessation

- » A brief advice intervention for smoking cessation may be given in as little as 30 seconds, and involves: 1) Asking about current and past smoking behaviour. 2) Advising on the risks of smoking and the benefits of stopping smoking by providing verbal and written information. 3) Advising on the options for stopping smoking, including behavioural support and evidence-based medication for smoking cessation. 4) Dependent on local service arrangements, referring the person to a specialist service (e.g., local smoking cessation service, tobacco dependence specialist, and/or telephone quitline) if they wish to stop smoking.[63]
- » Explain that a combination of drug treatment and behavioural support has been shown to improve smoking cessation rates and may be the best option.[63]
- » Physicians may be more effective in promoting attempts to stop smoking if they offer assistance to all smokers rather than only those who are motivated to stop smoking.[107] If the offer of a brief advice intervention for smoking is declined, it may still be offered at future consultations, as brief advice interventions are designed to be given repeatedly without antagonising the patient.[63] It is not uncommon for life events and changes in circumstances to precipitate stopping attempts even by people who appear to be entrenched smokers.[108]
- » People should be advised with clear, strong, and personalised messages: for example, 1) smoking cessation is the most important action for future health, 2) tie to current medical problems if applicable, and 3) mention risks of second-hand smoke to family.
- » 'Quitting tobacco use is the most important action you can take to improve your health and increase the quality and length of your life. If you currently smoke, when you stop, your loved ones will have less exposure to second-hand smoke - a known cause of asthma, respiratory infections, heart disease, and lung cancer. In addition, you will save money, improve your sense of taste, and keep your clothes, car, and house smelling fresher'.

plus motivational messages

Ongoing

Treatment recommended for ALL patients in selected patient group

- » Open-ended questions are asked to encourage the smoker to move towards thinking about stopping.
- » Relevance: patient is asked how tobacco use relates to their own situation.
- » Risks: patient is asked about risks of continued tobacco use.
- » Rewards: patient is asked about benefits of stopping.
- » Roadblocks: patient is asked to identify barriers to stopping and possible solutions.
- » Repetition: advice to stop and motivational messages should be repeated every time the patient is seen.
- » Conversation should end with a statement that many people have successfully stopped and that most people who smoke make repeated stopping attempts before they are successful. Help is available and they can be connected with resources when they are ready to try.^[73]

adjunct harm-reduction measures

Treatment recommended for SOME patients in selected patient group

Primary options

- » **nicotine transdermal**: 21 mg once daily for 6 weeks initially, followed by 14 mg once daily for 2 weeks, followed by 7 mg once daily for 2 weeks
Can start patient on 14 mg/day if smoke <10 cigarettes/day. Other strengths may be available.

OR

- » **nicotine gum**: 2-4 mg gum every 1-2 hours for 6 weeks, then taper gradually over 6 weeks, maximum 24 gum pieces/day

Secondary options

- » **varenicline**: 0.5 mg orally once daily for 3 days initially, followed by 0.5 mg twice daily for 4 days, followed by 1 mg twice daily for 12-24 weeks

Ongoing

- » Many smokers are unable or unwilling to stop smoking abruptly even when offered pharmacotherapy. Harm reduction measures may be considered for this group.[63] [129]
- » Approaches to harm reduction vary and include: cutting down before stopping smoking, with or without pharmacotherapy (varenicline or nicotine replacement therapy [NRT]); smoking reduction, with or without pharmacotherapy (varenicline or NRT); or temporary abstinence from smoking, with or without pharmacotherapy (varenicline or NRT).[63]
- » Shared decision making allows selection of the most suitable approach for the individual.
- » Reviews of randomised studies of 'NRT-assisted reduction to stop' (also known as cut down to stop) demonstrate that the long-term abstinence rates among smokers provided with NRT for this purpose are double those among smokers given placebo, and that adverse events are not increased despite receiving nicotine from both NRT and cigarettes.[151] [152] [153] Forms of NRT that have been studied include the use of nicotine gum or inhaler for up to 18 months and the use of nicotine patches for 6 weeks before a stopping date.[151] [152] [153] Many of these studies included behavioural support.
- » For people who are not willing to stop in the next month, but are willing to reduce cigarette consumption and stop in 3 months, varenicline therapy for 24 weeks has been shown to significantly increase smoking cessation rates.[154]
- » However, neither reduction-to-stop nor abrupt stopping interventions result in superior long-term stopping rates when compared with one another.[155]
- » Note that NRT may be considered in some circumstances in pregnancy, and for adolescents, depending on local guideline recommendations; however, use of other medicines including varenicline is not recommended for pregnant or breastfeeding women, or adolescents.[62] [63] [71] [159]
Consult a specialist for guidance on selection of treatment in pregnant/breastfeeding women and adolescents.
- » The choice of nicotine delivery method is guided by patient preferences, prior experience, and availability. In most countries, the patch and gum are available without a prescription.

Ongoing

Product literature should be consulted for further guidance on dosage of specific brands of NRT products.

» NRT should be started at the same time as the planned stopping date. Varenicline is relatively slow-acting, and so should be started 1-2 weeks in advance of the stopping date.^[63]

Emerging

Cytisinicline (cytisine)

A plant derivative, cytisinicline (also known as cytisine) is a partial agonist at the alpha-4 beta-2 nicotinic acetylcholine receptor, with a similar mechanism of action to varenicline. Evidence for cytisinicline looks very promising, and suggests that it may be more effective than single-agent nicotine replacement therapy (NRT) as well as placebo.[127] [197] [198] Results from one phase 3 randomised controlled trial (RCT) suggest that 32.6% of people randomised to receive 12 weeks of cytisinicline were abstinent during weeks 9-12 of treatment (compared with 7.0% in the placebo group), and 21.1% were abstinent during weeks 9-24 (compared with 4.8% in the placebo control group).[198] Adverse effects included nausea, headache, and insomnia, with 2.9% of study participants discontinuing the drug due to tolerability problems. One Cochrane review found cytisinicline to be similar in efficacy to varenicline.[125] Cytisinicline has a long history of use in Eastern Europe, but its use is limited across most of Europe, and it has not received US Food and Drug Administration (FDA) or European Medicines Agency (EMA) approval, although the FDA has granted breakthrough designation to the drug in order to expedite its review and approval. However, it is approved for use in the UK by the Medicines and Healthcare products Regulatory Agency (MHRA), and is recommended by the National Institute for Health and Care Excellence (NICE) in the UK as one of a number of options for smoking cessation when combined with behavioural support. Healthcare professionals are encouraged to discuss the available options with patients to determine the most suitable treatment based on individual needs and preferences. Regarding the decision to recommend cytisinicline, the NICE committee states that, despite moderate to very low-quality evidence, cytisinicline appears to be effective for smoking cessation with behavioural support, outperforming placebo and NRT, and demonstrating similar effectiveness to varenicline. Cytisinicline is only recommended for those between the ages of 18 and 65 years, and is not recommended during pregnancy or breastfeeding. NICE advises setting a stopping date within the first 5 days of treatment.[63]

Pharmacogenetics

Association studies on genetic polymorphisms and smoking cessation following NRT and/or bupropion therapy have been carried out, but only a few candidate genes or regions were analysed, requiring further research.[54] [199] Evidence to support the use of pharmacogenetic tests in routine smoking cessation therapy is still lacking, though continuously growing.[200]

Nicotine vaccine

Antibodies formed against nicotine may prevent this molecule from crossing to the reward centres of the brain, and thereby prevent the positive reinforcing effects of smoking. To be effective, high antibody levels would need to be achieved and maintained. Early studies suggested that three vaccines in testing were safe and well tolerated. In a randomised trial, nicotine-Q beta has been shown to increase 12-month cessation rates in smokers in the highest tertile of antibody response compared with those who received placebo.[201] However, overall cessation rates were not different between vaccinated and placebo groups.[201] To date, no nicotine vaccines have enhanced long-term smoking cessation. There has been no further development in recent years, and it may be that nicotine vaccines are no longer under active investigation.

Transcranial magnetic stimulation

Animal models have shown that repeated transcranial magnetic stimulation (TMS) of the dorsal prefrontal cortex can cause lasting reductions in drug craving and consumption. One small study suggested that application of high-frequency TMS treatment reduced nicotine consumption and dependence, yielding a 33% abstinence rate at 6-month follow-up.[202] One larger multicentre, double-blind RCT suggested that abstinence was achieved in 28% of participants compared with 11.7% in the sham group.[203] The FDA has given marketing clearance to one particular device using TMS as an aid for short-term smoking cessation in adults. It is currently unclear whether there is a particular subsection of people who are more likely to benefit from treatment.[204]

Alternative therapies

Several alternative therapies have been advertised for smoking cessation, most in an anecdotal fashion. One Cochrane database review for hypnotherapy, for example, reviewed 14 studies and suggested that there is insufficient evidence to determine whether hypnotherapy is more effective for smoking cessation than other forms of behavioural support or unassisted stopping.[205] One meta-analysis of 24 trials looking at acupuncture for smoking cessation suggested a statistically significant abstinence rate with acupuncture versus no intervention, but there was no statistically significant comparison between real acupuncture and sham acupuncture, suggesting a placebo effect.[206] One RCT using 8 weeks of yoga therapy compared with general wellness classes as controls showed a statistically significant improvement in abstinence rates up to 6 months later in a dose-response manner, presenting an interesting potential adjunct to treatment.[207] However, one systematic review found no clear benefit or harm of yoga on stopping rates.[208]

Primary prevention

Prevention of smoking in children and adolescents has the potential to substantially reduce smoking rates in adults, given that nearly 90% of adult daily smokers smoke their first cigarette by the age of 18 years, and approximately 80% of regular adolescent smokers will carry on smoking into adulthood.[14] [59] Although older teens are more likely to smoke than younger teens, the earlier a person starts smoking or using any addictive substance, the more likely they are to develop an addiction. According to the American Academy of Pediatrics (AAP), tobacco prevention messaging should start no later than 11 or 12 years of age.[60] Boys are more likely to take up smoking in adolescence than girls.[56]

Overall, the evidence suggests that high-intensity, family-based interventions have a positive effect on preventing children and adolescents from starting to smoke.[61] According to the US Preventive Services Task Force (USPSTF), there is moderate certainty that behavioural interventions carried out in primary care to prevent tobacco use in school-aged children and adolescents have a moderate net benefit. Interventions listed by the USPSTF as being effective include behavioural support, face-to-face or telephone interaction with a healthcare clinician, print materials, and computer applications. No harms of behavioural support interventions were noted by the USPSTF.[62] The AAP echoes this approach and recommends that paediatricians include tobacco and nicotine use prevention as part of anticipatory guidance for children and adolescents.[60]

Experimentation or regular use of e-cigarettes by young people should be discouraged.[63] A number of studies have found a strong association between e-cigarette use and subsequent smoking initiation among adolescents and young adults, although it is unclear whether this relationship is causal.[37] [38] [39] Evidence on strategies for preventing e-cigarette use in children and adolescents is currently lacking.[64]

Prevention can also take place at the school or community level, including peer-led interventions.[63] In addition to education, successful evidence-based interventions aim to reduce smoking, alcohol use, and illicit drug use by reducing or mitigating modifiable risk factors and bolstering protective factors.[65]

Population-level interventions are effective in reducing smoking.[66] Increased excise taxes on cigarettes, smoke-free legislation, and regional and national comprehensive tobacco control programmes decrease cigarette consumption and smoking prevalence. Restriction on advertising and mandatory health warnings on packages have also been shown to work.[67] [68]

Media anti-smoking or counter-advertising campaigns can have significant impact. In the US, the 'Tips from Former Smokers (Tips)' campaign used impactful imaging of real-life smokers with dramatic physical changes from smoking-induced harm and surgeries. Following the campaign there was an immediate, sustained, and dramatic spike in calls to the smoking quitline and visits to the website.[69] In a longitudinal survey of the US adults who smoke cigarettes, aged 18 years or older in 2012-2018, the US Centers for Disease Control and Prevention estimates 16.4 million quit attempts and over 1 million successful quits because of the Tips campaign.[70]

Secondary prevention

Providing free cessation resources to smokers significantly increases the proportion of smokers who attempt to stop, use drug treatments, and stop smoking.[221]

Measures like promoting smoke-free homes are also important in decreasing consumption and smoking cessation in adults. They also reduce exposure to second-hand smoke.[222]

Involving parents in school-based strategies for smoking cessation as part of the patient's support system has also been effective.[223]

Patient discussions

The following brief message (STAR) to the patient provides guidance on planning a stopping attempt.

S: Set a stop date within 2 weeks.

T: Tell family, friends, and co-workers about your plans and ask for support.

A: Anticipate ways to deal with times you are at high risk for smoking.

R: Remove cigarettes, matches, and ashtrays from your home, car, work, and other places where you smoke.

The patients should follow up with the clinic or with a behavioural support service (quitline, group, or other) within a week of the stopping date.

Online web-based resources for patients are available in most countries. Examples include the following:

- [\[Staying smoke free \(UK\)\] \(https://www.nhs.uk/better-health/quit-smoking/staying-smoke-free\)](https://www.nhs.uk/better-health/quit-smoking/staying-smoke-free)
- [\[Smokefree.gov \(US\)\] \(https://smokefree.gov\)](https://smokefree.gov)

Explain to patients that even 'light' smoking (i.e., fewer than 5 cigarettes per day) still carries health risks. Smoking one cigarette per day carries around 40% to 50% of the excess risk for developing coronary heart disease and stroke of smoking 20 cigarettes per day, and smoking 5 cigarettes per day has around 55% to 65% of the excess risk.[16] Smokers can expect positive changes as soon as 2 weeks after stopping, and people with heart disease who stop smoking are likely to experience a decreased risk in future heart attacks or other events linked to the heart or blood vessels, such as stroke.[220]

People may have questions about the role of e-cigarettes as potential smoking cessation aids. It is important to inform people about the variety of products and services available to help them stop smoking, and be involved in a discussion of the risks and benefits of each. Professional medical bodies in different countries have varying stances on the use of e-cigarettes for smoking cessation based on the available evidence and public health considerations, and so clinicians should be familiar with local guideline recommendations. Use of e-cigarettes for smoking cessation is not typically recommended by guidelines or professional medical bodies in the US or Europe (excluding the UK).[146] [147] In the UK, the National Institute for Health and Care Excellence (NICE) and the Royal College of Physicians (RCP) support the use of nicotine e-cigarettes as a smoking cessation tool in adults in certain circumstances: for example, when licensed treatments are not sufficient.[63] [148] [149]

There is universal agreement among professional medical bodies worldwide that e-cigarettes should be discouraged in people who have never smoked, and that they should not be used for smoking cessation in children and adolescents, owing to potential safety risks in this age group, as well as to a lack of evidence supporting their efficacy compared with behavioural support and nicotine replacement therapy.

Monitoring

Monitoring

Patients attempting to stop smoking are at a high risk for relapse. Only about 3% to 5% of smokers stopping on their own achieve prolonged continuous abstinence, usually defined as 6-12 months of not smoking. The highest risk of relapse is within 8 days of the stop attempt. Therefore, behavioural support should focus on that first week of a stop attempt.^[209]

If the smoker does not succeed on a stop attempt, it should not be viewed as a failure but as a learning experience.

The motivational intervention should be repeated every time an unmotivated patient visits the clinic setting. Tobacco users who have been unsuccessful in previous stop attempts should be told that most people make repeated stop attempts before they are successful.

The circumstances of the relapse should be reviewed and new strategies, and alternative or additional pharmacotherapy, should be tried.^{[2] [73]}

Complications

Complications	Timeframe	Likelihood
nicotine withdrawal symptoms	short term	high
It is common during a cessation attempt for patients to experience symptoms of nicotine withdrawal, including dysphoric or depressed mood, irritability, frustration, anger, anxiety, increased appetite, and weight gain.[2] [73] [132]		
changes in glycaemic control in diabetes	short term	medium
Both smoking and NRT increase insulin resistance. The effect of NRT on insulin resistance is less than that of smoking. Patients with diabetes whose blood sugars are very tightly controlled should have their blood glucose levels monitored for hypoglycaemia when they stop smoking or when they stop NRT use, as insulin resistance will decrease.		
increased blood levels of theophylline and some psychiatric medicines	short term	medium
Polycyclic aromatic hydrocarbons in cigarette smoke lower the blood levels of theophylline and some psychiatric medicines, including alprazolam, chlorpromazine, clomipramine, clozapine, diazepam, fluphenazine, fluvoxamine, haloperidol, imipramine, lorazepam, olanzapine, and oxazepam. Smoking cessation can thus result in 10% to 40% increases in blood levels of these medicines. Careful monitoring is required, and may require dose reductions to avoid toxicity.[219]		
alterations in heart rate and BP due to NRT	short term	medium
NRT can cause acute, but clinically minimal, fluctuations in heart rate and BP in patients with hypertension. However, studies demonstrate that NRT is safe in these patients. In patients presenting with untreated or uncontrolled hypertension and desiring smoking cessation, both problems can be treated simultaneously (beginning both NRT and antihypertensives at the same time).		
weight gain	variable	high
<p>Stopping smoking is often accompanied by weight gain of 4-6 kg due to a combination of increased energy intake from the need to substitute food for cigarettes in hand-to-mouth habits and oral gratification, and decreased metabolic rates.[213] Concerns about weight gain particularly among women smokers may reduce the motivation to stop, although the health risks of weight gain are small in comparison with the risks of continued smoking.</p> <p>One study showed that an increase in body mass index after smoking cessation had no moderating effect on the protective association of smoking cessation with myocardial infarction and stroke.[214] It is not recommended to advise smokers to limit their calorie intake during stopping attempts, as hunger may trigger cravings and reduce stopping rates. This approach has not been effective in reducing weight gain.[215] Individualised behavioural weight control plans, exercise programmes, very low-calorie diets, and cognitive behavioural therapy may reduce weight gain without reducing stopping rates, but the effects of these interventions are modest.[216] Further research is needed. No pharmacological interventions specifically to reduce weight gain have shown evidence of long-term benefit, although nicotine replacement therapy (NRT), antidepressants, and probably varenicline for smoking cessation all reduce weight gain in the short term.[215] Data suggest that a combination of smoking cessation medications results in less short-term post-cessation weight gain compared with monotherapy or placebo.[217] In people with serious mental illness, adjunctive behavioural support for weight gain (e.g.,</p>		

Complications	Timeframe	Likelihood
weight management counselling and support for physical activity) may be beneficial in addition to standard treatment for smoking cessation.[218]		

Prognosis

Relapse

Habitual smokers find it extremely difficult to successfully stop smoking. Although 70% of smokers would like to stop, and 40% make at least 1 stop attempt per year, only 3% to 4% of smokers per year are successful in stopping long term on their own.[18]

The highest risk for relapse is within the first 8 days after stopping. Active smoking cessation interventions by the physician, a clinic staff member, or a behavioural support service (in-person or telephone behavioural support) should be initiated before or within the initial week after the planned stop date.[209]

- Behavioural interventions used to help people avoid relapse usually focus on teaching the skills to cope with temptations to smoke.
- Randomised trials have not demonstrated that skills training interventions are helpful, although the studies may not have been large enough to detect possible small effects.[210]
- Internet- and mobile-phone-based interventions are increasingly available to help patients avoid relapse.[115] [211] Mobile-phone interventions have been shown to have a beneficial impact on 6-month cessation outcomes.[117]

Responses to relapse

Relapse after stopping is common. Patients should be encouraged to learn from the experience and try again. Most smokers must make several attempts to stop. The circumstances of the relapse should be reviewed, and new strategies and alternative or additional pharmacotherapy should be tried.[2] [73]

Extending medicine duration has been examined in a limited number of trials.

- Two trials of nicotine gum showed some effect, but extending the duration of bupropion use delayed but did not prevent relapse. Further studies of extended treatment with nicotine replacement are needed.[210]
- Limited evidence supports the use of varenicline as an aid to relapse prevention.[127]
- Extended-duration transdermal nicotine therapy (24 weeks) has been shown to increase success rates and decrease relapse when compared with standard-duration therapy (8 weeks) in adults.[212]

Treatment guidelines

United Kingdom

Tobacco: preventing uptake, promoting quitting and treating dependence (<https://www.nice.org.uk/guidance/ng209>)

Published by: National Institute for Health and Care Excellence

Last published: 2025

Hiding in plain sight: treating tobacco dependence in the NHS (<https://www.rcp.ac.uk/improving-care/resources/hiding-in-plain-sight-treating-tobacco-dependency-in-the-nhs>)

Published by: Tobacco Advisory Group of the Royal College of Physicians

Last published: 2018

Nicotine without smoke: tobacco harm reduction (<https://www.rcp.ac.uk/improving-care/resources/nicotine-without-smoke-tobacco-harm-reduction>)

Published by: Royal College of Physicians

Last published: 2016

North America

NCCN clinical practice guidelines in oncology: smoking cessation (https://www.nccn.org/guidelines/category_3)

Published by: National Comprehensive Cancer Network

Last published: 2024

Smoking and tobacco use: clinical cessation tools (<https://www.cdc.gov/tobacco/hcp/patient-care/clinical-cessation-tools.html>)

Published by: Centers for Disease Control and Prevention

Last published: 2024

Tobacco smoking cessation in adults, including pregnant persons: interventions (<https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions>)

Published by: US Preventive Services Task Force

Last published: 2021

Tobacco use in children and adolescents: primary care interventions (<https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/tobacco-and-nicotine-use-prevention-in-children-and-adolescents-primary-care-interventions>)

Published by: US Preventive Services Task Force

Last published: 2020

Smoking cessation: a report of the Surgeon General (<https://www.cdc.gov/tobacco-surgeon-general-reports/reports/2020-smoking-cessation>)

Published by: United States Public Health Service Office of the Surgeon General; National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health

Last published: 2020

Initiating pharmacologic treatment in tobacco-dependent adults (<https://www.thoracic.org/statements/guideline-implementation-tools/index.php>)

Published by: American Thoracic Society

Last published: 2020

Tobacco and nicotine cessation during pregnancy (<https://www.acog.org/clinical/clinical-guidance/committee-opinion>)

Published by: American College of Obstetricians and Gynecologists' Committee on Obstetric Practice

Last published: 2020 (re-affirmed 2023)

Tobacco smoking in children and adolescents (<https://canadiantaskforce.ca/guidelines/published-guidelines>)

Published by: Canadian Task Force on Preventive Health Care

Last published: 2017

Integrating tobacco interventions into daily practice (https://rnao.ca/bpg/guidelines?f%5B0%5D=bpg_categories%3A1898)

Published by: Registered Nurses' Association of Ontario

Last published: 2017

North America

Treating tobacco use and dependence: 2008 update (<https://www.ahrq.gov/prevention/guidelines/tobacco/index.html>)

Published by: US Department of Health & Human Services

Last published: 2008

Oceania

Guidelines for preventive activities in general practice, 10th ed (<https://www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines>)

Published by: Royal Australian College of General Practitioners

Last published: 2024

The New Zealand guidelines for helping people to stop smoking update (<https://www.health.govt.nz/publications/the-new-zealand-guidelines-for-helping-people-to-stop-smoking-update>)

Published by: New Zealand Guidelines Group

Last published: 2021

Supporting smoking cessation: a guide for health professionals (<https://www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines>)

Published by: Royal Australian College of General Practitioners

Last published: 2021

Online resources

1. [PhenX Toolkit: protocol - Heaviness of Smoking Index \(https://www.phenxtoolkit.org/protocols/view/330201\)](https://www.phenxtoolkit.org/protocols/view/330201) (*external link*)
2. [National Institute on Drug Abuse: instrument - Fagerstrom Test for Nicotine Dependence \(FTND\) \(https://cde.nida.nih.gov/instrument/d7c0b0f5-b865-e4de-e040-bb89ad43202b\)](https://cde.nida.nih.gov/instrument/d7c0b0f5-b865-e4de-e040-bb89ad43202b) (*external link*)
3. [University of Ottawa Heart Institute: Ottawa model for smoking cessation \(https://ottawamodel.ottawaheart.ca\)](https://ottawamodel.ottawaheart.ca) (*external link*)
4. [Staying smoke free \(UK\) \(https://www.nhs.uk/better-health/quit-smoking/staying-smoke-free\)](https://www.nhs.uk/better-health/quit-smoking/staying-smoke-free) (*external link*)
5. [Smokefree.gov \(US\) \(https://smokefree.gov\)](https://smokefree.gov) (*external link*)

Key articles

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Images

Assess

How important is it for you to stop smoking now?

0 1 2 3 4 5 6 7 8 9 10

Not at all extremely

If you decide to stop, how confident are you that you can succeed?

0 1 2 3 4 5 6 7 8 9 10

Not at all extremely

Are you willing to try and quit in the next month?

Figure 1: Questionnaire to assess and improve motivation and self-confidence for stopping

From the collection of Dr Theodore W. Marcy

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This approach is in line with the guidance of the [International Bureau of Weights and Measures Service](#).

Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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