

General Clinical Practice Update

Canadian Cardiovascular Society Clinical Practice Update
on Contemporary Approaches to Smoking CessationHassan Mir, MD, MHI, MPH (Co-chair),^{a,b} Mark J. Eisenberg, MD, MPH (Co-chair),^cNeal L. Benowitz, MD,^{d,e} Emily Cowley, PharmD,^f Javad Heshmati, PhD,^aPrabhat Jha, MD, DPhil,^g Milan Khara, MBChB,^h Kerri-Anne Mullen, PhD,^{a,i}Sandra N. Ofori, MBBS, MSc, PhD,^j Nancy A. Rigotti, MD,^{k,l} and Richard San Cartier, NP^m

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ABSTRACT

Smoking tobacco is the leading cause of preventable disease and death in Canada. Life expectancy of those who smoke is on average 10 years shorter than those who do not smoke. It is the most important modifiable risk factor for cardiovascular disease (CVD), doubling the risk of abdominal aortic aneurysm, coronary artery disease, ischemic stroke, and peripheral arterial disease. Smoking cessation is the single most powerful preventative intervention in clinical practice. Within 1 year of smoking cessation, the risk of CVD events decreases by 50%; after 15 years, the risk is the same as that of someone who has never smoked. Those who quit by age 40 have a life expectancy similar to that of people who have never smoked. Smoking cessation is a fundamental responsibility of every health care provider and must be a priority in all clinical settings. All patients must be systematically identified, treated, and have sufficient follow-up arranged. Advice

RÉSUMÉ

Le tabagisme est la principale cause de maladies et de décès évitables au Canada. L'espérance de vie des fumeurs est en moyenne de 10 ans plus courte que celle des non-fumeurs. C'est le facteur de risque modifiable le plus important pour les maladies cardiovasculaires (MCV), doublant le risque d'anévrisme de l'aorte abdominale, de maladie coronarienne, d'AVC ischémique et de maladie artérielle périphérique. Le renoncement au tabac est la mesure de prévention la plus efficace qui soit sur le plan clinique. Moins d'un an après l'abandon du tabac, le risque d'événements liés aux MCV diminue de 50 %; et après 15 ans, le risque est le même que celui d'une personne n'ayant jamais fumé. Ceux qui arrêtent de fumer avant l'âge de 40 ans ont d'ailleurs une espérance de vie comparable à celle de ceux n'ayant jamais fumé. La cessation du tabagisme est une responsabilité fondamentale de chaque professionnel de la santé et doit être une priorité, quel que soit le

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This statement was developed following a thorough consideration of medical literature and the best available evidence and clinical experience. It represents the consensus of a Canadian panel comprised of interdisciplinary experts on this topic. The statement is not intended to be a substitute for physicians using their individual judgement in managing clinical care in consultation with the patient, with appropriate regard to all the individual circumstances of the patient, diagnostic and treatment options available and available resources.

I. Background

Current state of tobacco use in Canada

Tobacco use remains the leading cause of preventable disease and death in Canada because of an increased risk of cancer, cardiovascular disease (CVD), respiratory disease, and many other health conditions.^{1,2} The prevalence of smoking in Canada has steadily declined since the 1960s, and with it, mortality associated with CVD.³ This decline is largely because of health promotion and smoking cessation programs, labelling and advertising regulation, smoking bans in public places, and taxation policy.^{3,4} In 2022, according to the Canadian Tobacco and Nicotine Survey (CTNS), 10.9% of

should be brief, clear, and unambiguous to inform people who smoke about the harms of smoking and the benefits of cessation, in a personalized and nonjudgemental manner. It should be combined with pharmacotherapy because this can increase the likelihood of success by almost threefold. Health care practitioners should be as comfortable managing smoking cessation and initiating pharmacotherapy as they would be managing other CVD risk factors like hypertension or dyslipidemia.

Canadians aged 15 years or older were current tobacco users (12.9% of men and 9.1% of women—with the highest prevalence in those aged 25-44 years).⁵

Certain populations have disproportionately high smoking prevalence rates. For example, smoking rates are higher among those who are unmarried (21.4%), have lower levels of education (40.5%),⁶ are unskilled workers (17.6%),⁷ identify as First Nations, Inuit, or Métis (36%),⁸ or have mental or substance use disorders (61%).^{9,10} The current federal strategy to address tobacco use in Canada was designed to help achieve a target of < 5% tobacco use by 2035.²

Harms of smoking

Cigarette smoking accounts for up to 30% of CVD deaths, and is the most common and harmful form of tobacco use; it reduces the lifespan by an average of 10 years compared with nonsmokers.¹¹ It more than doubles the risk of all types of CVD—abdominal aortic aneurysm, coronary artery disease (CAD), ischemic stroke, and peripheral arterial disease—and changing smoking behaviour is a cornerstone for improved cardiovascular health.^{12,13} Exposure to second-hand smoke also causes CVD in nonsmokers.¹⁴ Other forms of combusted tobacco use including cigar, pipe, and waterpipe are also associated with CVD, but the overall effect is less than that of cigarette smoking.^{15,16}

The morbidity and mortality of CVD caused by smoking increases on the basis of the number of cigarettes smoked per day, duration of smoking, and age at the time of cessation.¹⁷ This relationship is nonlinear and smoking any cigarettes can be harmful. Cigarette smoking is associated with many forms of acute and chronic CVD, as shown in Table 1. In the case of acute myocardial infarction, smokers have a greater thrombus load compared with nonsmokers.

Combustion of tobacco results in high levels of oxidant chemicals and particulates, which causes oxidative stress and inflammation resulting in platelet activation and thrombosis, endothelial dysfunction, and accelerated atherosclerosis. Carbon monoxide reduces oxygen-carrying capacity of blood, which reduces myocardial oxygen supply. Nicotine contributes to CVD primarily by causing compulsive use and addiction. Nicotine might also contribute to acute cardiovascular events by activating the sympathetic nervous system and releasing catecholamines, which produce hemodynamic stress, and can also promote arrhythmogenesis, insulin resistance, and lipid abnormalities.

contexte clinique. Tous les patients doivent être systématiquement repérés, traités, et avoir un suivi adéquat. Les conseils doivent être brefs, clairs et sans ambiguïté, afin d’informer les fumeurs sur les dangers du tabagisme et des bienfaits liés à son abandon, et ce de manière personnalisée et sans jugement. Ces conseils doivent être accompagnés d’une pharmacothérapie, car celle-ci peut presque tripler les chances de succès. Enfin, les professionnels de la santé doivent être à l’aise avec la prise en charge du renoncement au tabac et l’initiation d’une pharmacothérapie comme ils le feraient pour d’autres facteurs de risque de MCV, comme l’hypertension ou la dyslipidémie.

Benefits of smoking cessation

The benefits of smoking cessation have been widely studied and are undisputed. Quitting at any age is associated with prolonged survival. Those able to quit before age 40 have life expectancy similar to those who have never smoked. Even quitting for a short duration (< 3 years) can significantly improve life expectancy.¹⁸

Quitting smoking produces a rapid reduction in the risk of CVD events.¹⁹ Within 1 year, the risk of CVD events is reduced by approximately 50%, and the risk declines progressively over 15 years to the same risk as nonsmokers.²⁰ A smoker with preexisting CVD who quits will experience a 30% reduction in future events, a benefit greater than that of other preventive measures, including antiplatelet drugs or statins.²¹ In light of these benefits, smoking cessation should be a high priority for primary and secondary prevention of CVD.

II. Evidence-based Approach to Smoking Cessation

Smoking cessation is the single most powerful preventative intervention in clinical practice.²² Assisting people who smoke

Table 1. Cardiovascular disorders caused by cigarette smoking

Vascular disease
Accelerated atherosclerosis
Acute myocardial infarction
Shorter exercise time to angina
Coronary spasm
Stroke
Aortic aneurysm
Peripheral obstructive arterial disease
Stent thrombosis after percutaneous coronary intervention
Graft occlusion after coronary bypass surgery
Arrhythmias
Sudden cardiac death
Atrial fibrillation
Implantable defibrillator shocks
Myocardial disease
Increases risk and aggravation of heart failure
Hypertensive heart disease
Inducing cardiac risk factors
Diabetes, type 2
Dyslipidemia
Hypertension, including malignant hypertension
Hypertensive renal disease
Others
Impaired wound healing
Erectile dysfunction
Reproductive disorders
Macular degeneration

Modified from Benowitz et al.¹²⁷

to reduce or quit is a fundamental responsibility of any practitioner who sees patients who smoke. Because of the effect of smoking and benefits of cessation, management of smoking should be a priority and standard of care. It should be managed with the same intensity as managing other cardiovascular risk factors. Every person who smokes should be offered pharmacotherapy because this increases the likelihood of success up to threefold compared with counselling alone.²³ For a simple and practical approach to smoking cessation, see Figure 1.

System-based interventions

It is vital to incorporate systematic approaches to smoking cessation so that it becomes a part of routine care. This simplifies the delivery of care for health care providers while ensuring these services are offered to all patients who smoke. The Ottawa Model for Smoking Cessation (OMSC) is the most widely implemented evidence-based approach to treating nicotine dependence within clinical settings in Canada.²⁴ This program is aimed at health care providers and administration to combine practice change processes with implementation of evidence-based clinical tools and protocols.

The OMSC is a simple, systematic approach for clinicians to: (1) identify the smoking status of all patients; (2) provide brief, practical cessation advice; (3) initiate pharmacotherapy to manage acute withdrawal and support long-term quitting; and (4) refer patients for ongoing follow-up. The program leverages automated telephone follow-up and live calls with nicotine addiction treatment specialists according to the patient needs and preferences. OMSC's automated follow-up has been shown to be effective for cardiac patients.²⁵ Referrals can be passive (opt-in) or automated (opt-out) on the basis of the health care setting. Significant improvements in referrals, follow-up, and cessation rates are obtained by using an "opt-out" rather than an "opt-in" approach.²⁶ Beyond this, the program has been shown to improve cessation rates (15% absolute increase), health care utilization such as all-cause readmission (11.6% absolute reduction at 2-year follow-up), clinical outcomes such as mortality (7.3% absolute reduction at 2-year follow-up) and cost-effectiveness.²⁷ The model has been implemented in > 500 sites across Canada, supported > 500,000 Canadians in their journey to reduce or quit, and been adopted in countries around the world.

Behavioural interventions

Behavioural counselling, a cornerstone of smoking cessation intervention, involves encouraging patients to reflect on their smoking, and thus increase their motivation and confidence. Clinicians should assess a patient's readiness to quit at every visit. The "5 A's" model is commonly used to encourage clinicians to **ask** the patient about smoking, **advise** them to quit, **assess** their readiness to quit, **assist** them through prescription of evidence-based pharmacotherapy, and **arrange** appropriate follow-up supports. During the advise stage, the "5 R's" can be used to motivate individuals to reduce or quit. This includes a discussion of why it is **relevant** for the patient to quit smoking, the **risks** of smoking, the **rewards** of cessation, the **roadblocks** they might experience including withdrawal symptoms, and **repeating** this process at future visits until they are ready to quit.

Counselling can be offered to patients in a variety of ways including brief (< 5 minutes), intensive (30 or more minutes, often multiple visits), or group-based (large group activities and peer-to-peer support) sessions. Busy clinicians are most likely to provide brief counselling, who rapidly and clearly advise about the harms of smoking and benefits of cessation in a personalized, unambiguous, and nonjudgemental manner. It should ideally be combined with initiation of pharmacotherapy and referral for continued support for interested patients because these are vital in achieving smoking cessation.

The 2021 Cochrane network meta-analysis of behavioural interventions showed a high degree of certainty for the benefit of counselling in clinical and nonclinical populations.²⁸ The highest-certainty evidence was for individual counselling compared with usual care, brief advice, or self-help materials. More intensive counselling is more effective than less intensive counselling. However, even printed self-help materials can be helpful toward cessation when no other support is available.

Different delivery modes of counselling including text, telephone, videoconferencing, Web-based interventions, and smartphone applications are discussed in a later section. Quit lines, automated text messaging, and interactive internet-based interventions are effective in achieving smoking cessation. Long-term quit rates are significantly higher when counselling is combined with pharmacotherapy and is considered standard of care.²⁹

Smoking cessation pharmacotherapy

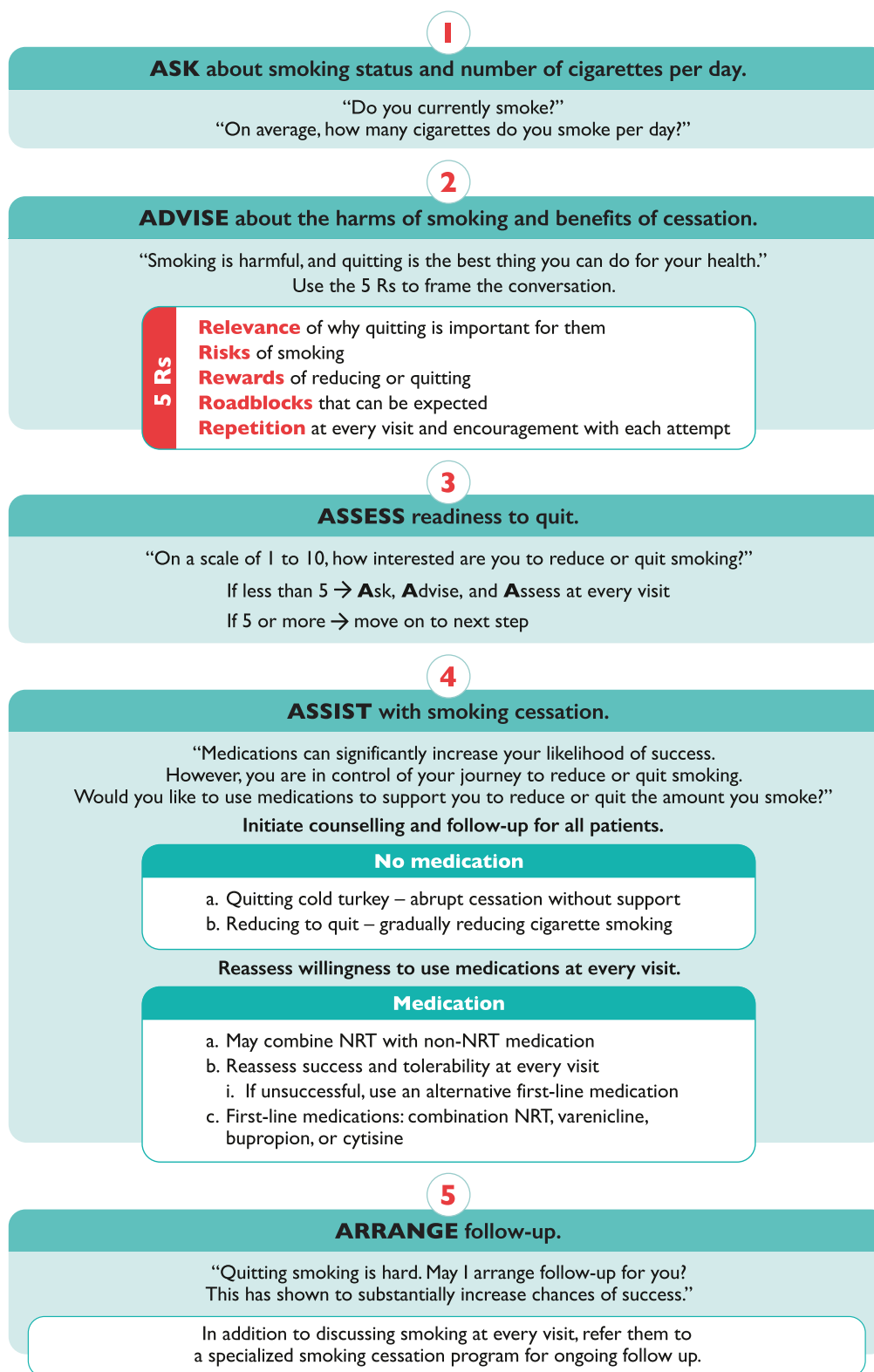
Pharmacology. Cigarette smoking is sustained by addiction to nicotine. Nicotine acts primarily on $\alpha 4\beta 2$ nicotinic cholinergic receptors in the brain to facilitate the release of several neurotransmitters including dopamine and serotonin. These produce pleasure, enhanced vigilance and cognitive function, and reduction of stress and anxiety.

With regular exposure to nicotine, the brain adapts, resulting in tolerance, associated with changes in brain structure and function. When nicotine is no longer consumed, withdrawal symptoms occur, which might include anxiety, irritability, depression, trouble concentrating, and increased appetite.

Compulsive use of nicotine products is driven by the positive effects and avoidance of negative effects of withdrawal. Smokers typically inhale nicotine throughout the day to modulate mood and arousal and to deal with stress and other negative emotions. There is a similar pattern and amount of nicotine consumed day-to-day.

Medications that are approved to promote smoking cessation in Canada include nicotine replacement therapy (NRT; gum, patches, lozenges, sprays, and inhalers), bupropion, varenicline, and cytisine. Medications help make smokers more comfortable during the quitting process. Medications act by 3 main mechanisms: (1) relief of withdrawal symptoms; (2) desensitization or blocking of nicotinic receptors, thereby reducing the rewarding effects of nicotine from tobacco; and (3) serve as a less harmful source of nicotine for positive reward instead of smoking.

NRT can act by all 3 mechanisms. The efficacy of NRT as a substitute for smoking depends on the product. Products that deliver nicotine quickly, such as sprays, gums, and lozenges, can satisfy the smoker when used in place of a cigarette.



NRT – Nicotine Replacement Therapy

Figure 1. One-minute approach to smoking cessation. NRT, nicotine replacement therapy.

Nicotine patches reduce withdrawal symptoms and reduce the reward of nicotine from smoking.

Bupropion, marketed for depression and smoking cessation, is a sympathomimetic drug. It blocks neuronal uptake of dopamine and norepinephrine thereby simulating some of the desirable effects of nicotine. Bupropion also has antagonistic activity of the $\alpha 4\beta 2$ nicotinic cholinergic receptors, which might blunt the rewarding effects of nicotine from the cigarette.

Varenicline and cytisine are partial agonists of $\alpha 4\beta 2$ nicotinic cholinergic receptors. Activation of the receptors results in reduction of withdrawal symptoms.

Pharmacotherapy. Quitting smoking is difficult. Studies have shown that most smokers would like to quit and that most have tried and failed.³⁰ Without behavioural therapy and/or pharmacotherapy to aid in cessation efforts, the likelihood of successful smoking abstinence is exceedingly low.³¹ In this section we summarize the smoking cessation pharmacotherapies that are available and how to use them to help your patients quit smoking (Table 2).

Pharmacotherapies can be divided into 2 major groups: NRT or non-NRT.^{23,30} NRTs are used to replace the nicotine consumed when smoking conventional cigarettes.³² When used appropriately, nicotine patches provide the individual with approximately the same amount of nicotine that they consume when smoking, thus avoid withdrawal symptoms and cravings during smoking cessation.³¹ Most pharmacotherapies are prescribed for 12 weeks, but there is emerging evidence that longer periods of treatment might be more successful.³³

NRT. Before discussing specific NRTs, it is important to assess how much nicotine an individual is consuming daily. Smoking 1 cigarette typically delivers 1-2 mg of nicotine (this might vary according to factors such as the frequency and depth of inhalation). A pack of cigarettes contains 20-25 cigarettes. Thus, a person who smokes 1 pack per day consumes at least 20 mg per day of nicotine. When prescribing NRT it is important to personalize the dosages. Inadequate dosage of NRT is a frequent cause of cessation failure. For clarity, the gum, lozenge, spray, and inhaler forms of NRT are considered “short-acting,” whereas the patch is classified as “long-acting.”

Patch. NRT should be used with a combination of long-acting patches and short-acting gum, lozenge, spray, or inhaler. Nicotine patches are the most commonly used formulation and typically come in 3 different dosages: 7, 14, and 21 mg (Table 2).³⁴ Clinicians should aim to replace the nicotine consumed 1:1 by long-acting NRT. This might require using multiple patches concurrently to avoid withdrawal symptoms. Some studies suggest that tapering the dosage of nicotine over 12 weeks or more can help the individual quit cigarettes and stop NRT as well.³⁵

Gum. Nicotine gum is commonly used for smoking cessation, but if inadequately used, is often unsuccessful. Nicotine gum usually comes in 2 mg and 4 mg dosages (Table 2). Importantly, only approximately half the dose is systematically absorbed,³⁶ so a 2-mg piece of gum will deliver 1 mg, and a 4-mg piece of gum will deliver 2 mg. Thus, 1 piece of gum

delivers a nicotine dose equivalent to approximately 1-2 cigarettes.³⁷ Nicotine gum may be used as monotherapy (solo agent) in individuals who smoke < 10 cigarettes per day. For individuals who smoke more than 10 cigarettes per day, nicotine gum should be used as an adjunct with a long-acting nicotine patch or in conjunction with a non-NRT. The gum can then be used to “top up” nicotine levels when the individual starts developing withdrawal symptoms.

When counselling individuals about the use of nicotine gum, the “chew and park” method is preferred. The gum should be chewed 2-3 times and then “parked” between the gum and the buccal mucosa. This method allows the nicotine to be absorbed and is often accompanied by a peppery taste. The gum should be “parked” for 15-30 minutes. Just chewing the gum without “parking” it will not allow for sufficient nicotine absorption and might result in gastrointestinal symptoms.

Lozenge. Nicotine lozenges are similar to nicotine gum. They come in 2 strengths: 2 mg and 4 mg. The lozenge should be “parked” between the gum and the buccal mucosa and should be left in place until it dissolves. Up to 20 lozenges can be consumed per day and titrated as needed (Table 2).³⁸

Spray and inhaler. Nicotine can also be administered in the form of a nasal spray, mouth spray, or via inhalation. These are also available over the counter. Each spray of the mouth spray delivers 1 mg of nicotine. Similar to nicotine gum, nicotine spray could be used as a single agent in individuals who smoke < 10 cigarettes per day. For individuals who smoke more than this, nicotine spray is best used in conjunction with a long-acting nicotine patch or with a non-NRT.

Nicotine inhalers deliver nicotine via a small plastic tube similar to a cigarette. Nicotine is absorbed in the mouth and upper airway. Individuals can self-titrate to the level of nicotine they need.

Practical considerations. NRT is among the most effective pharmacotherapies available for smoking cessation. For all of the NRTs, it is important to personalize the dosage according to the individual’s daily nicotine consumption.³¹ Combination NRT is superior to use of a single form of NRT.³⁵ Most studies of NRTs for smoking cessation used a treatment period of 12 weeks. Some studies used the full dose during the 12 weeks and others a tapered regimen (tapering by no more than 7 mg per week). Some studies suggest that treatment periods longer than 12 weeks are more successful for smoking cessation.

Nicotine overdose is rare. In most cases, cigarette smokers are easily able to self-titrate the dosage of nicotine they require. Symptoms of nicotine overdose include bradycardia, dyspnea, headache, syncope, tachycardia, vomiting, or weakness. Cases of nicotine overdose have been reported among children and pets, so NRTs should be kept in secure areas.

Non-NRT

Bupropion. Bupropion, commonly known by its trade names Zyban (GlaxoSmithKline; Brentford, United Kingdom) or

Table 2. Summary of smoking cessation medications

Drug	Dosing	Quit date	Typical treatment duration	Caution
NRT				
Nicotine patch: 7, 14, and 21 mg patches	1 Patch every 24 hours for 4-6 weeks, then taper 7 mg every 2-4 weeks (< 10 cigarettes per day, initiate 14 mg patch, > 10 cigarettes per day initiate 21 mg patch)	Same day or up to 14 days after initiation of NRT	12-24 Weeks	Vivid dreams, insomnia
Nicotine inhaler: contains 10 mg nicotine per cartridge	6-12 Cartridges per day for 3 months, reduce usage to 1-2 cartridges per day			Hiccups, dyspepsia, and mouth and/or throat irritation
Nicotine spray: contains 1 mg nicotine per spray	1-2 Sprays every 30-60 minutes (maximum of 4 sprays per hour)			
Nicotine lozenge: 2 and 4 mg lozenge	1 Lozenge every 1-2 hours (Use 2 mg if < 25 cigarettes per day; use 4 mg if > 25 cigarettes per day)			
Nicotine gum: 2 and 4 mg gum	Chew 1 piece every 1-2 hours (2 mg if ≤ 25 cigarettes per day; 4 mg if > 25 cigarettes per day)			
Bupropion				
Bupropion (Sustained Release)	Days 1-3: 150 mg daily Ongoing: 150 mg BID; quit date 1 week after initiation	7 to 14 days during therapy	7-12 Weeks; can be used up to 6 months	Dry mouth, constipation, agitation. Contraindicated in those with history of seizure disorder
Nicotinic acetylcholine receptor partial agonist				
Varenicline	Days 1-3: 0.5 mg daily Days 4-7: 0.5 mg BID Day 8-later: 1 mg BID; quit date 1 week after initiation	7 to 14 days during therapy	12 Weeks, can extend up to 6 months	Nausea, vivid dreams, and insomnia
Cytisine	3 mg 3 times per day or: Days 1-3: 1 capsule every 2 hours (maximum 6 capsules per day) Days 4-12: 1 capsule every 2.5 hours (maximum 5 capsules per day) Days 13-16: 1 capsule every 3 hours (maximum 4 capsules per day) Days 17-20: 1 capsule every 5 hours (maximum 3 capsules per day) Days 21-25: 1-2 capsules per day	Day 5 during therapy	25 days, can extend up to 12 weeks	Vivid dreams, insomnia, and nausea (but less nausea than varenicline)

BID, twice per day; NRT, nicotine replacement therapy.

Wellbutrin (Bausch Health, Canada Inc, Laval, Quebec), is used to treat depression and smoking cessation.³⁹ It is usually prescribed in its long-acting form to reduce withdrawal symptoms and nicotine craving. One tablet of 150 mg is given daily for 3 days and then increased to twice a day (Table 2). The target quit date should only be set for 1 week after bupropion is begun with the treatment period being 12 weeks. Bupropion is often combined with short-acting NRTs. Seizures have rarely been reported with bupropion, so its use is contraindicated in individuals with a history of seizure or in those with a history of recent major head trauma. Minor side effects have been reported with bupropion, but these resolve with stopping the medication. If insomnia occurs, the dose can be reduced to 1 pill a day in the morning.⁴⁰

Varenicline. Like bupropion, varenicline (trade name, Champix in Canada and Chantix in the United States; both manufactured by Pfizer, New York, NY) reduces withdrawal symptoms and nicotine cravings. It is prescribed as follows: 0.5 mg daily for 3 days, then 0.5 mg twice a day for 4 days, and then 1 mg twice a day for the remainder of the 12-week treatment period (Table 2). The target quit date should also be set for 1 week after treatment initiation, and varenicline can be used in combination with short-acting NRTs. Minor side effects have been noted with varenicline including nausea, insomnia, and vivid dreams. These effects may be alleviated by reducing the dosage to once a day in the morning and they will resolve entirely with the cessation of the medication.³³

Cytisine. Cytisine is a plant-based alkaloid that has been used in Europe for decades and available over the counter as a natural health product in Canada. It has gained attention as an effective smoking cessation aid.⁴¹ It works through the same mechanism as varenicline. It is the least expensive smoking cessation medication available.⁴² Recent studies have confirmed that cytisine is superior to placebo and NRT. The latest Cochrane component network meta-analysis showed that cytisine more than doubled the odds of long-term smoking cessation (ie, for 6 months or longer) compared with placebo.⁴³ Cytisine is similar in efficacy to varenicline, but its milder side effect profile makes it an attractive alternative.⁴⁴ Its currently approved dosing schedule is complex and described in Table 2. However, in a recent randomized controlled trial (RCT) a simplified dose of cytisine (3 mg 3 times a day) was used and shown to be safe and effective for smoking cessation (Table 2).⁴¹ This might increase uptake by patients and clinicians.

Effectiveness. Combination NRT (short- and long-acting), varenicline and cytisine are the most effective smoking cessation aids. A recent Cochrane Review of > 300 RCTs including > 150,000 patients showed that these medications increase the likelihood of smoking cessation by 2 to 3 times compared with placebo. The odds ratio of smoking cessation with these medications are provided in Table 3.²³

Safety. Early case reports suggest that bupropion and varenicline might be associated with suicidal ideation, suicidal behaviour, and adverse cardiac effects. These anecdotal reports were investigated in depth and debunked with evidence from multiple clinical trials and meta-analyses. The most persuasive

Table 3. Effectiveness of smoking cessation pharmacotherapies

	Smoking cessation (6 or more months), odds ratio (95% confidence interval)
Control	1.0 (Referent)
Combination NRT	1.93 (1.61-2.32)
Bupropion	1.43 (1.26-1.62)
Varenicline	2.33 (2.02-2.68)
Cytisine	2.21 (1.66-2.97)
Nicotine e-cigarette	2.37 (1.73-3.24)

NRT, nicotine replacement therapy.

Modified from Lindson et al.²³

evidence comes from the 2016 Evaluating Adverse Events in a Global Smoking Cessation Study (EAGLES) trial, in which > 8000 smokers were randomized (half with a psychiatric history and half without) in a blinded placebo-controlled manner to varenicline, bupropion, nicotine patch, and placebo.⁴⁵ There was no evidence of increased neuropsychiatric events in any of the active treatment arms compared with placebo. A substudy of EAGLES also showed that there was no evidence of an increase in cardiac events in any of the treatment arms.³² Thus, NRT, bupropion, and varenicline are safe to use and are considered first-line agents for smoking cessation.

III. Approaches in Specific Populations

Smoking cessation in hospitalized and acutely ill cardiac patients

Those who are hospitalized are up to twice as likely to smoke compared with the general population.²⁷ People who smoke are known to have more prolonged and complicated hospitalizations than those who do not. Hospitalization provides a “window of opportunity” or a “teachable moment” for smoking cessation. In hospital, patients have access to educational information, counselling through health care providers, free cessation aids, and are more receptive to the idea of cessation because of their acute illness.^{30,46} Family members are also supportive of smoking cessation because of the circumstances. The OMSC program has been widely applied in Canadian hospitals since the early 2000s.²⁴ This systematic, evidence-based smoking cessation program provides counselling, follow-up, and pharmacotherapy after discharge to patients at partnered sites.

Among hospitalized patients, acute coronary syndrome (ACS) patients have been well studied with 20%-30% of them being a smoker at the time of their event.⁴⁷ Without intervention, more than two-thirds continue to smoke 1 year post ACS. Behavioural therapy has been shown to be effective for smoking cessation in hospitalized patients and postdischarge. However, it is more effective when combined with pharmacotherapy.⁴⁸ NRT is safe to use in the ACS population and is widely prescribed to reduce acute withdrawal symptoms. Nonrandomized data suggest that prescribing NRT at discharge might lead to improved long-term abstinence rates. Although bupropion is effective in generalized outpatient populations, results have been less convincing among patients with ACS.⁴⁹ Evidence to date suggests that varenicline might be the most effective pharmacotherapy in the post-ACS population. A recent Canadian RCT showed that almost half of the participants had quit smoking at 6-month follow-up

compared with one-third in the control group (number needed to treat of 6.8).⁵⁰

Although patients typically refrain from smoking in-hospital, most relapse post-discharge.⁴⁶ As such, counselling, pharmacotherapy, and follow-up should be initiated before discharge. Post-discharge support for smoking cessation is critical. Referral and attendance at cardiac rehabilitation or at least 1 month follow-up in a smoking cessation clinic and/or program have been shown to significantly increase the likelihood of quitting and should be prioritized.⁴⁷

Smoking cessation in perioperative care

Smoking rates among surgical patients are higher than in the general population and ranges from 14% to 26% in noncardiac surgery and up to 51% among cardiac surgery patients.⁵¹ With more than 1 million surgeries performed annually in Canada, the reach achieved by targeting smoking cessation in this population is significant.

Smoking cessation interventions around the time of surgery increase short- and long-term smoking abstinence. The evidence is strongest for intensive strategies that combine multiple face-to-face counselling sessions with or without NRT. This increases the odds of abstinence by the time of surgery by up to 10 times and long-term abstinence 12 months post surgery by almost 3 times compared with standard care.⁵² Brief interventions increased abstinence by the time of surgery but not long-term. Varenicline has been reported to increase long-term abstinence but there is limited evidence on bupropion.⁵²

There are no RCT data to determine the minimum duration of preoperative abstinence required to reduce perioperative complications. Intensive smoking cessation interventions 4-8 weeks before surgery have been shown to reduce postoperative complications.⁵²⁻⁵⁴ However, smoking cessation interventions can be implemented at any time before or after surgery without increasing complication risk.

A systematic review and meta-analysis of 25 studies (2 of which were RCTs) showed that the risk of respiratory complications was similar among those who quit smoking < 2 weeks or between 2 to 4 weeks before surgery compared with current smokers.⁵⁵ However, compared with current smokers, those who quit > 4 weeks or > 8 weeks before surgery experienced significantly lower risks of respiratory complications and lower risk of wound-healing complications.

Smoking cessation in those with mental illness and substance use disorder

The high smoking prevalence rates observed among those with mental illness and/or substance use disorders (SUDs) indicates that these populations are disproportionately affected by tobacco-attributable illness and premature death compared with the general population. It has been estimated that almost half of all cigarettes are bought and consumed by those with mental illness.⁵⁶ People with schizophrenia lose 25 years of life compared with the general population and most of this is attributable to tobacco use.⁵⁷

Despite this, there has been a reluctance among clinicians to offer and initiate evidence-based tobacco treatments for these patients. Many plausible explanations exist for why this might be so, varying from a belief that they are uninterested or

unable to quit or that cessation will make their mental illness and/or SUD worse. These beliefs are inaccurate. In fact, evidence suggests cessation leads to better outcomes in those with SUD and improved symptomatology in those with mental illness.^{58,59} Major national guidelines recommend clinicians screen for tobacco use and offer treatment to these populations as a standard of care.^{60,61} Effective, evidence-based methods to treat tobacco use disorder are available; combinations of these treatments should be considered the optimal approach.⁶¹ As described previously, specific concerns about neuropsychiatric side effects caused by these smoking cessation medications were allayed by the EAGLES study.

There is evidence that those with mental illness and/or SUD might find cessation more difficult and might therefore require more intensive approaches with closer monitoring, extended duration of treatment, and combination of pharmacotherapies.⁶² This might require referral to specialist services (when available) but does not preclude those in all clinical settings providing "brief intervention" and initiation of pharmacotherapy. The evidence that supports smoking cessation in primary and secondary prevention of CVD should make intervention a standard of care in this population.

Smoking cessation among Indigenous Peoples (First Nations, Inuit, Metis)

Many Indigenous people have a long history of using unprocessed tobacco traditionally, which might be used for ceremonial, medicinal, or spiritual purposes. This is in contrast to commercial tobacco use, which refers to the use of processed, commercially packaged products like cigarettes.

Smoking is still the norm in many First Nation communities and is linked to many aspects of everyday life, positive and negative.⁶³ The First Nations Regional Health Survey showed that > 50% of First Nations adults smoke cigarettes.⁶⁴ This highlights an urgent need to address the misuse of tobacco among the Indigenous community.

Although there have been a few epidemiological, qualitative, and policy-related studies conducted, little has been published on the implementation of smoking cessation interventions among Indigenous populations in Canada. Previous studies have shown that locally and culturally tailored, intensive, multidimensional smoking cessation interventions are more effective to achieve smoking cessation compared with nontailored current best practices.⁶⁵

As with the general population, all members of Indigenous communities should be screened for tobacco misuse and offered help. Lack of consistent access to health care providers further emphasizes the need to address tobacco misuse at every visit. Predictors of smoking cessation among Indigenous people who smoke have included the use of pharmacotherapy and cessation counselling and/or coaching.⁶⁶

Consistent recommendations for success across most studies of smoking cessation interventions in Indigenous communities include ensuring local development, ownership and participation; cultural tailoring; worker professional development and support; and operating within a framework of trust and cultural safety.⁶⁷

It is important to recognize the inequities experienced by Indigenous peoples. Unaddressed intergenerational trauma adds to the challenges that face Indigenous peoples and results

in a general mistrust of health services. Using a team-based approach in which one member of the team is a trusted individual in the Indigenous community might foster more rapid acceptance and help build trust for the whole team.

Sex and gender considerations in smoking cessation

Smoking prevalence is higher among male (12.1%) compared with female (8.6%) Canadians.⁶⁸ E-cigarette use in the past 30 days is also more prevalent among men (5.7%) than women (3.6%) overall; however, among individuals aged 15–19 years, there are no sex differences in e-cigarette ever use (34.9% male vs 35.3% female individuals) or 30-day prevalence (14.7% male vs 13.9% female individuals).^{69,70}

Smoking confers a greater risk of CVD in women compared with men. A meta-analysis of more than 2.4 million subjects showed that women who smoked had a 25% increase in the risk for CAD compared to men who smoked.⁷¹ Moreover, women who smoke and concurrently use oral contraceptives have a 10-fold increased risk of myocardial infarction and a threefold increased risk of stroke.⁷² Although the exact mechanisms are not fully understood, it has been suggested that the effects of smoking on sex hormones, arginine vasopressin, and arterial hypertension and endothelial dysfunction are factors that contribute to these sex differences.⁷³

Women might be more likely than men to use recommended cessation resources, including pharmacotherapy, counselling, and self-help materials.⁷⁴ Despite this, studies have consistently shown that women have more difficulty quitting smoking than men due because of sex- and gender-related factors.⁷⁵ Nicotine patch, bupropion, and varenicline are all effective cessation aids compared with placebo among men and women.⁷⁶

Sexual and gender minorities

Smoking prevalence among sexual minority (eg, lesbian, gay, bisexual, asexual, or pansexual) and gender minority (eg, transgender and nonbinary) individuals is between 10% and 25% higher than heterosexual and cisgender men and women.^{77–79} Because of the higher prevalence of smoking, co-occurring drug use, and anxiety and depression, sexual and gender minority (SGM) individuals are at increased risk for CVD. SGM individuals have identified that the tailoring of smoking cessation interventions to meet their needs (eg, led by or co-designed to consider characteristics shared by SGM individuals) would be preferable and increase accessibility⁸⁰; however, recent RCTs suggest that SGM-tailored interventions produce similar cessation rates as nontailored interventions.⁸¹

Pregnancy

More than half of women who smoke before pregnancy quit smoking before or during pregnancy.⁸² Among those who quit, nearly half relapse back to smoking postpartum. Clinicians should support patients with quitting smoking during pregnancy, and in the postpartum period to prevent relapse.

The Society of Obstetricians and Gynecologists of Canada clinical practice guidelines recommend that non-pharmacological cessation support be considered first-line

during pregnancy. Pregnant individuals unable to quit smoking with nonpharmacological approaches may use NRT, bupropion, or varenicline.⁸³ Nicotine metabolism increases during pregnancy, particularly from week 18 onward, which is thought to explain why NRT might not be as effective during pregnancy.⁸⁴ Higher doses of NRT and NRT combination therapy might be required during pregnancy to offset the higher rate of nicotine metabolism, manage nicotine withdrawal, and prevent relapse.⁸⁵ Bupropion might be a reasonable cessation option, specifically for pregnant women with depression.⁸⁶

Breastfeeding

The safety and effectiveness of smoking cessation pharmacotherapies while breastfeeding has not been adequately studied. Smoking cessation aids are preferable to continued smoking during breastfeeding.⁸⁷ Additional sufficiently powered safety and effectiveness studies on peripartum smoking cessation treatments are needed. However, there is a dearth of these studies because of potential ethical concerns with conducting clinical trials during pregnancy and breastfeeding.⁸⁸

IV. Emerging Technologies

Digital health technologies offer a novel and innovative means of supporting smoking cessation. Interventions such as smartphones, mobile applications, telephone calls, video calls, text messages, video conferences, chatbots, virtual reality tools, and artificial intelligence have gained traction as viable tools.^{89–91} These tools are convenient, personalized, and accessible for users. The COVID-19 pandemic resulted in increased acceptance and adoption of digital health in clinical care.⁹²

Web-based interventions have been shown to be effective at increasing rates of smoking cessation at 6-month follow-up compared with information booklets or e-mail interventions.⁹³ Computer-generated programs have also been shown to increase quit rates compared with self-help materials or no intervention.⁹⁴ However, this type of intervention is less popular with the increasing use of social media and smartphone applications.

Mobile-based interventions such as text messaging have been shown to increase rates of smoking cessation in clinical trials.⁹⁵ Smartphone applications are a promising tool because of their ubiquitous use. Although there are many smartphone applications for smoking cessation, few have been rigorously evaluated in clinical trials.⁹⁶ As such, currently there is insufficient evidence to support their use.

Video-based platforms enable real-time counselling for smoking cessation. During the COVID-19 pandemic, it was a primary means of communication, which was acceptable and well received.⁹⁷ However, focused clinical trials of its effectiveness are lacking. Alternatively, video games and virtual reality are emerging as innovative means of delivering cessation programming.⁹⁸ They offer immersive and engaging experiences for users, which could help distract them from common triggers for relapse.^{99,100} Additional research is necessary to evaluate the effectiveness and cost-effectiveness of such tools.

Artificial intelligence tools such as ChatGPT (OpenAI, San Francisco, CA) have emerged as a revolutionary tool. There is

exciting potential to harness the power of such tools to provide personalized, high-fidelity, real-time support for patients while leveraging predictive analytics to enhance the effectiveness of smoking cessation programs.¹⁰¹ Currently there are limited tools and evaluations of their effectiveness.

V. Electronic Cigarettes

Background

Electronic cigarettes (e-cigarettes) are hand-held, battery-operated devices that heat a liquid containing nicotine, propylene glycol, and/or glycerin, and flavorings, producing an aerosol that users inhale ("vape").¹⁰² Unlike combustible tobacco products, e-cigarettes do not burn tobacco to produce smoke. These devices vary in design and evolve rapidly. Newer-generation products deliver nicotine to the lungs in a manner similar to cigarettes. Most products now use nicotine salts rather than unprotonated nicotine, which allow users to tolerate inhaling higher doses of nicotine.¹⁰³ E-cigarettes pose a risk of nicotine addiction for young nonsmokers, but for adults already addicted to cigarettes, they are a less hazardous alternative to continued smoking.¹⁰⁴ Using an e-cigarette permits people who smoke to sustain nicotine dependence but avoid or reduce their exposure to the many toxic chemicals in tobacco smoke.^{102,103}

In Canada, no e-cigarette is licensed as a medical product by the Food and Drugs Act. Instead, e-cigarettes are regulated as consumer products by the Tobacco and Vaping Products Act, which limits maximum nicotine concentration to 20 mg/mL.¹⁰⁵ Health Canada lists e-cigarettes as potential alternatives for smokers who cannot quit with cessation medications.¹⁰⁶

E-cigarettes for smoking cessation

E-cigarettes are potentially valuable harm reduction tools for adults who smoke, especially those who are unable to use or quit with conventional evidence-based tobacco cessation treatments. Meta-analyses of randomized trials report strong evidence that e-cigarettes are effective to help people to quit smoking, with minimal harms when used short-term (6-12 months).¹⁰⁷ Nicotine-containing e-cigarettes are effective for smoking cessation, and increase the odds of quitting by 2-3 times compared with placebo.²³

Harms of vaping e-cigarettes

E-cigarette aerosol contains oxidizing chemicals but fewer and at lower levels than cigarette smoke.¹⁰⁸ The levels of oxidants depend on the heating temperature of the device.¹⁰⁹ E-cigarettes can deliver nicotine at similar levels to that of a tobacco cigarette.¹¹⁰ Nicotine from e-cigarette inhalation produces similar sympathomimetic effects as smoking, which can induce cardiac ischemia in people with CAD and could, via release of catecholamines, increase the risk of lethal events.^{111,112} E-cigarette use can acutely induce endothelial dysfunction, but when smokers switch completely from cigarettes to e-cigarettes, endothelial function improves.¹¹³

To date, there are no data to suggest that e-cigarette use is associated with an increased risk of clinical CVD events or mortality.¹⁰³ This is in part because e-cigarettes have been

used for short durations of time and because most e-cigarettes users are former smokers. This makes it difficult to distinguish whether events that occur are because of past smoking or more recent e-cigarettes use. Because of the toxicant profile of e-cigarette aerosol, it is expected that e-cigarette use would pose a lower risk of CVD than cigarette smoking. Although the health risks of long-term e-cigarette use cannot yet be directly measured, existing evidence suggests that potential long-term harms are likely to be less than those associated with smoking.^{102,103}

Vaping among youth, often recreational, has increased dramatically. In 2022, according to the CTNS, 30% of youth aged 15-19 years and nearly half (48%) of young adults aged 20-24 years reported having tried vaping in their lifetime. Younger Canadians were more likely to have vaped in the past 30 days (14% of youth aged 15-19 years and 20% of those aged 20-24 years) compared with 4% of Canadians aged 25 and older.⁵ Although the long-term health risks are unclear, this might be a cause for concern because of the risk of developing nicotine addiction, the effect of nicotine on the developing brain, and the potential of tobacco co-use.¹¹⁴ People of all ages who do not use any combustible tobacco products should be discouraged from recreational e-cigarette use. E-cigarettes are not harmless to health and can lead to nicotine addiction among people who do not use nicotine products.

Practical considerations

There are no clear guidelines on how to use an e-cigarette to quit smoking. However, if doing so, the minimum effective dose should be used to manage cravings. Individuals should switch completely to e-cigarettes and stop smoking all cigarettes. There might be a period of using both products (dual use) before complete cessation, but this should be minimized because there is risk of increased nicotine addiction. Eventually, the goal is also to quit e-cigarettes when the individual is confident that they will not relapse to smoking combustible cigarettes. E-cigarettes should not be used recreationally and should not be tampered with or modified in any way.

Vaping cessation programs

Whether for recreational use or as a smoking cessation aid, use of e-cigarettes has dramatically increased over the past decade.¹¹⁵ The increase has been particularly noted in young adults and adolescents.¹¹⁶ Because of the addictive nature of nicotine in e-cigarettes, there is a need to develop evidence-based strategies and interventions to support vaping cessation. Recent studies show a high interest in vaping cessation among e-cigarette users but there is limited evidence of how best to support such individuals.¹¹⁷ A review of the literature showed that vaping cessation interventions such as pharmacotherapy (NRT, varenicline, cytisine), educational materials, and digital health interventions such as text messaging might increase rates of vaping cessation.¹¹⁸⁻¹²¹ More high-quality evidence is needed. However, combination NRT might be an appropriate first step with an emphasis on rapid titration using short-acting NRT to address nicotine withdrawal symptoms. It is imperative for clinicians advising vaping cessation to former smokers to ensure that this does not lead to relapse back to cigarette smoking. The current consensus is

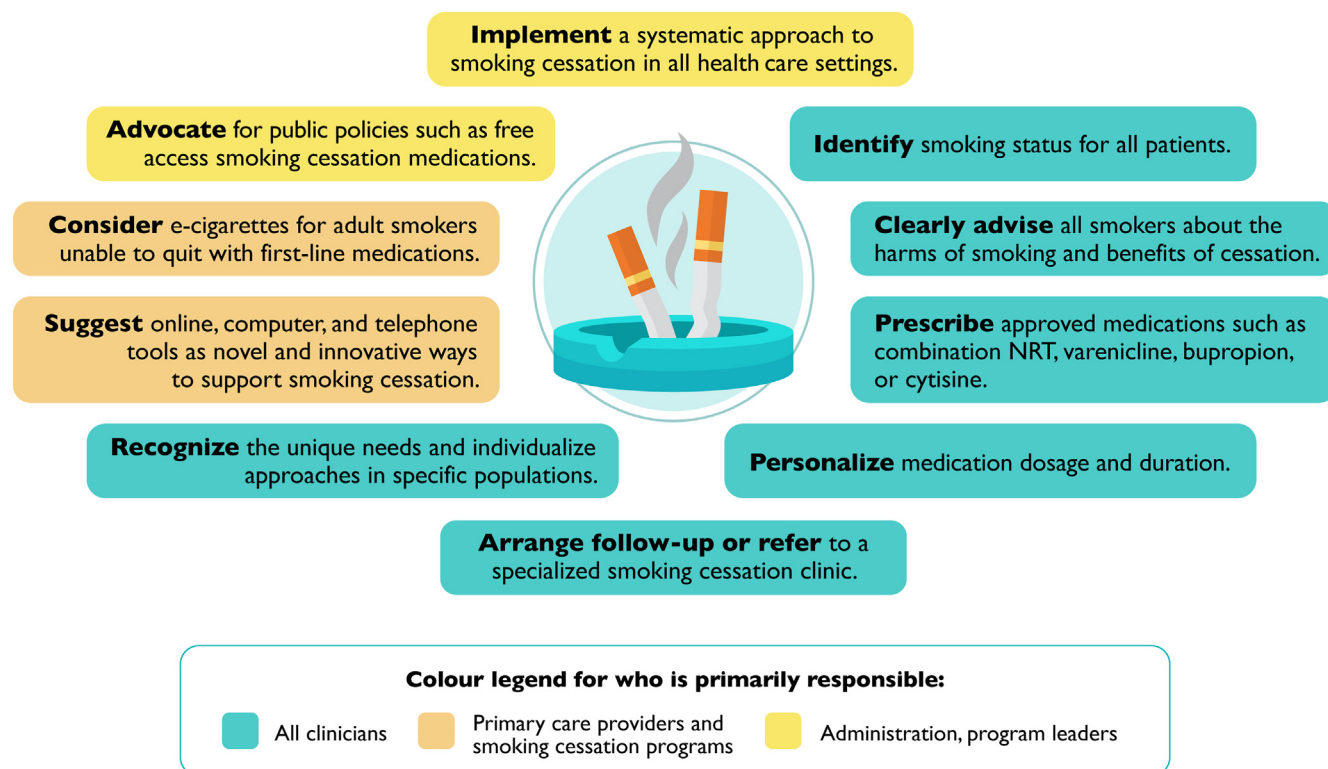


Figure 2. Smoking cessation summary of key takeaways and practical tips. NRT, nicotine replacement therapy.

that this would have a worse effect on long-term health compared with continued e-cigarette use.¹²²

VI. Tobacco and Vaping Policy

Drug approval

Health Canada has authorized 2 prescription medicines, bupropion and varenicline, for the purposes of smoking cessation. NRTs and cytisine are also approved as natural health products and thus do not require a prescription for purchase.¹²³ Nicotine pouches were recently authorized as a natural health product and available in 2- and 4-mg doses; however, there are few data on their efficacy for smoking cessation. In August 2024, Health Canada announced regulations aimed at reducing recreational use of nicotine pouches including behind-the-counter pharmacy sales, restrictions on advertising and packaging, restriction on flavours (mint/menthol only), and the addition of a warning label.¹²⁴ E-cigarettes are not approved or regulated as a cessation aid, but their contents, sale, and marketing is regulated by Health Canada.¹²⁵ E-cigarettes and nicotine pouches are owned by tobacco companies, which has led to some clinicians having concerns about recommending their use.

Universal coverage

Across Canada, many provinces have expanded the prescribing privileges to initiate smoking cessation therapy to include nurse practitioners, pharmacists, and dentists. Numerous provincial programs and national initiatives exist to

increase accessibility for smoking cessation. However, significant gaps exist in terms of coverage for the cessation therapies. Most provinces and territories provide financial coverage for prescription smoking cessation medications (bupropion and varenicline). Coverage for NRT and cytisine, which are available without prescription, varies greatly. For example, provincial programs in Ontario and Alberta do not offer coverage for NRT. The duration of treatment coverage also differs across Canada, with many programs approving up to 12 weeks. This time restriction does not allow for gradual “reduce to quit” cessation attempts or support patients who require multiple attempts to succeed. Smoking cessation can be challenging because of the provincial differences in coverage and Canada’s Tobacco Strategy should prioritize a universal coverage for approved cessation aids. For a summary of financial coverage of smoking cessation medications in Canada, visit <https://s22457.pcdn.co/wp-content/uploads/2021/11/Financial-coverage-smoking-cessation-medications-map-2021-EN.pdf> from the Canadian Partnership Against Cancer.¹²⁶

VII. Summary of Key Updates

Since the last update on this topic by the Canadian Cardiovascular Society (CCS) in 2011, there have been several significant developments in the field of smoking cessation, particularly concerning new pharmacotherapies, the use of e-cigarettes, and other innovative strategies.

1. **Cytisine** is approved as a natural health product and has been shown to be safe and effective for smoking cessation. Its milder side effect profile, lower cost, status as a

natural health product, and recently tested simplified dosing will make it an attractive choice for patients.

2. **E-cigarettes** are potentially valuable harm reduction tools for adults who smoke, especially those who are unable to quit with first-line tobacco cessation treatments. They are effective for smoking cessation and adverse events are infrequent within 1-year follow-up. There are no e-cigarettes licensed or regulated as a medical product, but they are available as a consumer product. There is growing concern about the recreational use of e-cigarettes by non-smokers, especially youth, who initiate nicotine use through e-cigarettes.
3. **Digital health technologies** such as Web-based, computer-based, and telephone-based have shown a significant increase in rates of smoking cessation compared with usual care. Additional clinical trials are required to evaluate smartphone applications, video-based platforms, and AI platforms. Nonetheless, these formats hold promise in providing equitable approaches to smoking cessation by enabling more accessible and personalized support.

Conclusion

Smoking cessation is the single most powerful preventative intervention in clinical practice. It is a fundamental responsibility of every health care provider and must be a priority in all health care settings. The 10 key takeaways from this clinical practice update (CPU) are summarized in Figure 2.

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Ethics Statement

All research reported in the current article adheres to the relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article because this is a CPU document; no patients were involved in the development of the CPU.

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