<table>
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<tr>
<th><strong>Program Name:</strong></th>
<th>New Approaches to Smoking Cessation: A focus on Nicotine Replacement Therapy</th>
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<tbody>
<tr>
<td><strong>Planning Committee:</strong></td>
<td>Ron Pohar, BScPharm, APA</td>
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<td><strong>Accreditation Information:</strong></td>
<td>This version of the program is unaccredited and intended for informational purposes only. An accredited version is available online at <a href="http://www.rxBriefCase.com">www.rxBriefCase.com</a> until May 2, 2017</td>
</tr>
<tr>
<td><strong>Sponsor:</strong></td>
<td>This case study is supported by an educational grant from Johnson &amp; Johnson</td>
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Learning Objectives

Upon completion of the lessons, participants will understand

- Tobacco use disorder and why “cold turkey” is generally not an effective means of smoking cessation
- The role of the health care provider in supporting a quit attempt
- The rationale for using combination nicotine replacement therapy (NRT) in smoking cessation
- The efficacy of pre-cessation and combination NRT in smoking cessation
Pre-Test Survey

1. Please rate your level of knowledge of the approved combinations of nicotine replacement therapies available in Canada (i.e., nicotine patch with a short-acting nicotine replacement therapy) (1 = limited, 5 = excellent).

2. Please rate your level of comfort in recommending combination NRT for smoking cessation when indicated? (1 = completely uncomfortable / 5 = completely comfortable).

3. Please rate your level of understanding of the rationale for combining a long-acting nicotine replacement therapy (i.e. nicotine patch) with a short-acting nicotine replacement therapy (e.g., gum, lozenge, inhaler) for smoking cessation (1 = limited, 5 = excellent).

4. Please rate your level of knowledge of reduce to quit strategies using short-acting nicotine replacement therapies (1 = limited, 5 = excellent).

5. Please rate your level of comfort in recommending short-acting nicotine replacement therapies using of reduce to quit strategies (1 = completely uncomfortable / 5 = completely comfortable).

6. Please rate your level of comfort in recommending nicotine replacement therapy to patients who may continue to smoke while using it (1 = completely uncomfortable / 5 = completely comfortable).
Introduction - Smoking in Canada Today

Despite efforts to reduce smoking rates in Canada, about 4.2 million Canadians (14.6% of the population) continue to smoke, with most being daily smokers (10.9%). With smoking comes ongoing risk for smoking-related illnesses and associated costs. Tobacco remains a leading factor contributing to preventable death in Canada, with an estimated social cost of $17 billion dollars annually. While the prevalence of smoking has reached its lowest since Health Canada and Statistics Canada began conducting national surveys of the patterns and trends in tobacco use in Canada, the rate at which the prevalence has been declining has slowed.

Figure 1: Smoking prevalence in Canada, adults aged 15+, 1965 - 2013

Further, smoking rates remain relatively high in young adults with rates of 17.9% in those aged 20 to 24 and 18.5% in those aged 25 to 34. These observed trends are likely driven by many factors, and do not necessarily reflect a lack of desire on the part of smokers to quit. When asked about quitting, about two-thirds of smokers reported that they were seriously considering quitting in the next six months and 30% were considering quitting in the next month. One-half of smokers had tried to quit in the past year, with one-third having tried more than once.
The chronic nature of tobacco dependence is now well-established, and the need for repeated intervention and multiple quit attempts prior to achieving long-term abstinence is recognized in treatment guidelines. In fact, most smokers try quitting 5 to 7 times prior to successfully stopping long-term. Nicotine replacement therapy (NRT) is one of the recommended first-line pharmacotherapies for smoking cessation in a number of clinical practice guidelines, including those from the US Department of Health and Human Services and the Canadian Action Network for the Advancement, Dissemination and Adoption of Practice-informed Tobacco Treatment (CAN-ADAPTT). Recently, there have been changes to the approved labelling (licenses) of NRT products in Canada, which include use in combination with one another (i.e., nicotine patch in combination with a short acting form of NRT such as gum or lozenge) and use while still smoking as part of a “reduce to quit” strategy or a “pre-quit NRT.” This lesson will focus on the updated approved product labelling of long and short acting NRT products, in particular with their use in combination, to help healthcare providers better understand how these products can be used to assist smokers with a quit attempt.

Role of the Health Care Provider

Test Yourself

Typically without any form of support or assistance, what percentage of smokers will stop smoking and stay smoke-free over the course of a year?

a) 1% to 2%
b) 7%
c) 10%
d) 12%

Quitting smoking and remaining smoke free can be extremely difficult to achieve in both the short- and long-term, particularly without some form of assistance or support. Typically, without assistance or support from a health care provider, less than 2 to 5% of smokers will manage to stop smoking and remain smoke-free over the course of a year. Advice to quit smoking from a health care provider can increase the chances of a smoker engaging in a quit attempt and with behavioral support and pharmacotherapy, quit rates at one-year can increase considerably, up to three-fold depending on the approach. Community pharmacist interventions have been shown to increase abstinence rates in smokers approximately two-fold (RR: 2.21, 95% CI: 1.49 to 3.29), based upon pooled data from five controlled trials. Thus, it is critical that health care professionals accept the responsibility for providing smoking cessation counseling to patients, are confident in their abilities to deliver cessation strategies and are proficient in referring patients to appropriate cessation resources.

Health care professional support can be vital during a quit attempt. Many smokers have repeated contacts with a number of different health care providers on a regular basis. Pharmacists in community-based and institutional-based practice settings come into contact on a daily basis with smokers, some of whom are prepared to quit smoking and are actively seeking support and guidance in their quit attempts. In fact, almost three-quarters of pharmacists (73%) report that at least once a day smokers ask their advice about quitting, while almost one-half (47%) are asked at least twice per day. Smokers appreciate having access to smoking cessation information and resources through community pharmacies and perceive having a pharmacist discuss with them various aspects of quitting (e.g., importance of quitting, different medications and strategies for quitting, effects of continued tobacco
In a survey of non-prescription NRT users, two-thirds of study participants felt that a pharmacist’s advice and assistance would increase a smoker's likelihood of successfully quitting. This evidence suggests that many patients who smoke are likely to be open and accepting of pharmacists’ interventions into tobacco use and would appreciate the additional support a pharmacist could provide them with.

**Practice Point:**
Two-thirds of NRT users feel that pharmacist advice and assistance would increase their chances of quitting.

**The 5 As**
Healthcare providers have a professional responsibility to identify tobacco use in their patients and offer assistance to help them in addressing it. The 5 As model (Table 1) for identifying and treating tobacco use is recommended in evidence-based guidelines from both US Department of Health and Human Services and CAN-ADAPTT, a Canadian expert group.

**Table 1: The 5 As**
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<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td><strong>Ask:</strong> Ask every client if he or she uses tobacco</td>
<td></td>
</tr>
<tr>
<td><strong>Advise:</strong> Advise all patients who smoke or use smokeless tobacco to quit</td>
<td></td>
</tr>
<tr>
<td><strong>Assess:</strong> Assess the willingness of patients who use tobacco to make an attempt to quit at present</td>
<td></td>
</tr>
<tr>
<td><strong>Assist:</strong> Assist all patients in their quit attempts</td>
<td></td>
</tr>
<tr>
<td><strong>Arrange:</strong> Arrange for follow-up and ongoing support</td>
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</table>

The CAN-ADAPTT guidelines recognize the effectiveness of 1 to 3 minute interventions for tobacco users and state that such interventions should be offered to every smoker. Using a structured approach in the assessment of tobacco use (such as the 5 As) ensures that all tobacco users are:

- Identified
- Advised to quit
- Offered evidence-based treatments to assist them

Regardless of the willingness of a tobacco user to quit, the first three steps (Ask, Advise and Assess) of the 5 As model are applicable to all patients. The manner in which the last two steps (Assist and Arrange) are applied will depend on an individual’s willingness to make an attempt to quit and will be covered later in this lesson, as will be approaches to assessing readiness to quit.

**Ask the Expert**
What tips can you offer clinicians for integrating screening for tobacco use into their practice? What can be done to help reduce barriers?
Why is Quitting Smoking so Hard?

Which of the following is correct regarding tobacco use and cessation?

a. “Cold turkey” is an effective means of quitting for most smokers
b. The abstinence rate with “cold turkey” is about 33% after two days
c. Nicotine addiction results from the action of nicotine on acetylcholine receptors in the brain and other non-dopaminergic structures and the ability of nicotine to trigger the dopamine reward system
d. B and C
e. A, B and C are correct

While “cold turkey” is commonly attempted as a method for smoking cessation, it is generally met with limited success. In a study of smokers who were motivated to quit and attempted to do so “cold turkey”, abstinence rates after two days had already fallen to 33%. The poor success rates with smoking cessation unassisted with pharmacotherapy or other forms of support may be related to the addictive nature of nicotine. Nicotine is the key addictive component in tobacco smoke and is rapidly delivered to the brain (within 10 to 16 seconds) when tobacco smoke is inhaled. Addiction to nicotine is believed to result from its interaction with acetylcholine receptors in the brain and other non-dopaminergic structures and its ability to trigger the dopamine reward system, similarly to other drugs of abuse. When nicotine levels decrease, dopamine levels (and the associated reward) decrease as well, resulting in symptoms of withdrawal, which can occur quite quickly. Nicotine withdrawal symptoms (irritability, difficulty concentrating, feeling anxious and restless, cravings) are distracting, unpleasant and stressful to experience and reinforce the desire to continue to smoke, making cessation difficult. This is precisely why quitting smoking is so hard. The discomfort created by withdrawal can be rapidly reversed simply by administering nicotine (i.e. smoking). These withdrawal symptoms are a strong source of motivation to continue smoking, making quitting challenging. In fact, severity of withdrawal symptoms is an important predictor of relapse during a quit attempt.

When cigarettes are smoked, plasma nicotine levels vary throughout the day. The background nicotine level rises with sharp peaks immediately following cigarette consumption. (Figure 2). When cigarettes are smoked, plasma nicotine levels vary throughout the day. The background nicotine level rises with sharp peaks immediately following cigarette consumption. (Figure 2).
Cigarettes and other forms of tobacco allow consumers to: (i) sustain high daily plasma nicotine concentrations; and (ii) obtain acute increases in plasma nicotine concentrations on demand as cravings emerge throughout the day with falling nicotine levels. Pharmacotherapy for smoking cessation can be tailored to replace both the background level of nicotine, as well as address acute cravings.

**Barriers to Quitting with Pharmacotherapy**

**Test Yourself**

Which of the following is correct regarding the use of pharmacotherapy for smoking cessation?

- a. The odds of smoking cessation with NRT are reduced if it is used for less than 5 weeks.
- b. The odds of smoking cessation with non-NRT medication are reduced if it is used for less than 5 weeks.
- c. Both A and B are correct.

Pharmacotherapy is often a key treatment component of a smoking cessation attempt; however, in order for smokers to achieve the full benefit of pharmacotherapy it is important that it is used at an optimal dose, for an appropriate duration of therapy. Unfortunately, it is often the case that neither dosing nor duration of treatment are adequate. NRT, for example, is available without a prescription and because of this, it can be obtained in the absence of counselling from a pharmacist or healthcare provider. This may mean that the opportunity to develop a personalized quit plan and receive advice on dosage, duration, and ongoing counselling, support and follow-up are lost. Evidence suggests that smokers frequently take less than the prescribed dosage of NRT, are frequently prescribed inadequate dosages of NRT and fail to complete treatment courses, despite evidence that using higher NRT dosages increases quit rates.

Using data from the 2010–2011 Tobacco Use Supplement to the US Current Population Survey, self-reported smoking cessation rates were analyzed based upon duration of pharmacotherapy use in individuals who were 1) current daily smokers who made a quit attempt in the past year or 2) former smokers one year prior to the survey. Using pharmacotherapy for less than five weeks was associated with lower quit rates for both NRT and oral prescription medications (bupropion SR and varenicline) (Figure 3). Further, while most of those who used prescription medication did so for five or more weeks, the majority of NRT users remained on pharmacotherapy for 2 weeks or less, thereby compromising its efficacy.
Figure 3: Adjusted cessation rate by duration of pharmacotherapy use

Similar results were observed with data from the Ontario Tobacco Survey, which suggested use of NRT for a duration of four weeks or longer compared to not using NRT was associated with an increased likelihood of smoking cessation:

- NRT for 4.0 – 7.9 weeks: OR = 2.26, P < 0.0001
- NRT for 8.0 – 11.9 weeks: OR = 3.84, P < 0.0001
- NRT for ≥12 weeks: OR = 2.80, P < 0.0001.

In addition to these studies, it has been found that only 1 in 8 people will use NRT for the full recommended eight weeks of therapy. These findings suggest there is an opportunity for healthcare providers to intervene and optimize pharmacotherapy to maximize a patient's likelihood of success. Further, these findings underscore the importance of remembering that nicotine addiction is a chronic disease and must be managed as such, requiring ongoing treatment and support.

Who is a Candidate for Pharmacotherapy?

Pharmacotherapy is often a key component of a quit attempt and should be offered to all individuals who are attempting to quit smoking, except where a contraindication exists or in populations where research evidence is insufficient to support its use (such as in light smokers or pregnancy). Given that evidence suggests that the combination of pharmacotherapy and counselling is more effective than either used alone, both US Department of Health and Human Services and CAN-ADAPTT guidelines endorse a combination of the two where feasible. Specifically, the CAN-ADAPTT guidelines state:

Combining counselling and smoking cessation medication is more effective than either alone, therefore both should be provided to patients/Patients trying to stop smoking where feasible.
However, readiness for abstinence must first be assessed to determine if an individual is indeed willing to make a quit attempt. Returning to the 5A’s model (Table 1)

Table 1: The 5 As

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<table>
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</table>

Readiness for smoking cessation can be assessed using tools such as readiness rulers:

It may be helpful to visualize responses using “rulers” where patients can mark their place along a continuum, like Figure 4. Such rulers have been shown to predict the likelihood of a change in smoking behaviour.

**Figure 4: Readiness Ruler**

Assessment of willingness to quit can be carried out using basic questions and/or basic tools such as readiness rulers. The US Department of Health and Human Services guidelines recommend the following question:

- “Are you willing to give quitting a try?”

This, however, is a close-ended question, which yields a ‘yes’ or ‘no’ response. Simply responding ‘yes’ or ‘no’ may not illicit a response which allows the healthcare provider to assess how ‘strongly’ a client feels about continued smoking or quitting.

Other recommended approaches involve the use of “scaling questions”. It may be useful to ask the patient a broader question such as “What do you think about quitting?” and then follow-up with the scaling questions that follow.
• On a scale from 0 to 10, how important is it for you to make a change at this time?

• On a scale from 0 to 10, how confident are you that you can quit smoking at this time?

• On a scale from 0 to 10, how ready are you to make this change?

The Stages of Change or Transtheoretical Model can also provide useful information on a smoker’s willingness or preparedness to quit smoking, which can help to tailor smoking cessation interventions. More information on this model and its application to smoking cessation can be found at the link below:

• Transtheoretical Model

For those who are ready to quit smoking, the next step may be a quit plan that involves pharmacotherapy. For those who are not ready, motivational interviewing may be the next step to help move them towards a quit attempt (Figure 5).

Figure 5: Algorithm for Pharmacotherapy in Primary Care

Ask the Expert
What tools or approach do you find the most useful for assessing readiness to quit smoking in your practice?

Motivational Interviewing
Not all smokers are motivated, willing or prepared to quit smoking. There are a number of reasons why a smoker may not be motivated to quit. Patients may be unwilling to quit smoking when they perceive the benefits of smoking to outweigh the risks associated with continued smoking. Having fears or
concerns about smoking cessation can decrease the motivation to quit. For example, patients may feel smoking:

- Helps with relaxation
- Boosts energy levels or improves concentration
- Helps control weight
- Helps with social or interpersonal relationships

Some patients may be reluctant to initiate a quit attempt because they fear that they are incapable of overcoming nicotine addiction. These individuals lack the self-efficacy required to attempt a change in behaviour, given the likelihood of not being successful. Previous unsuccessful quit attempts or relapses may leave patients feeling demoralized, which can discourage the desire to try again. Other reasons for not being motivated to quit smoking include a lack of knowledge of the harmful effects of smoking and/or the benefits of quitting. While this seems surprising, in a population-based survey, 36.5% of smokers did not believe that smoking was a big problem in their lives. Further, a Canadian survey found that 27% of respondents who were at risk for COPD did not agree or were unaware that smoking was associated with the disease.

When patients who are unwilling to quit smoking are identified, trying to convince them to set a quit date and stop smoking is not likely to be successful. For patients who lack motivation to quit smoking, the key objective of an intervention is to increase their motivation so that they are more likely to be willing to try quitting at some point in the future.

Guidelines recommend the use of interventions that are designed to promote the motivation to quit. These interventions follow the principles of Motivational Interviewing (MI), which is a non-confrontational, non-prescriptive counseling intervention designed to enhance the motivation to quit smoking.

Motivational interviewing has been shown to increase the likelihood of a future attempt at smoking cessation even in those individuals with low motivation or intention to quit smoking. Motivational interviewing has been shown to be more effective than using a directive, advice-giving approach to counselling.

**Training in Motivational Interviewing and Other Resources**

Motivational interviewing is a specialized counselling technique which is more effectively applied when the healthcare provider has training in this area. Advanced training in motivational interviewing provides healthcare providers with another tool to effectively intervene into tobacco use with their patients. Training in motivational interviewing is available through web-based and in-person sessions. Links to selected resources for training in motivational interviewing are provided below:

- Center for Addiction and Mental Health Motivational Interviewing 1: Introduction Course
- Motivational Interviewing Training
- Motivational Interviewing in Practice - Level 1
- Motivational Interviewing - Canadian Mental Health Association
Oral Pharmacotherapy for Smoking Cessation

Test Yourself

Which of the following are oral first-line pharmacotherapies for smoking cessation?

- a. Varenicline
- b. Bupropion SR
- c. Clonidine
- d. A and B only
- e. A, B and C

Bupropion sustained release and varenicline are both oral, prescription medications that are approved for use for smoking cessation in Canada. Guidelines from US Department of Health and Human Services[^3] and CAN-ADAPTT guidelines[^9] recognize bupropion, varenicline and NRT as first-line treatment options for smoking cessation. CAN-ADAPTT’s treatment algorithm is shown in Figure 6.
Figure 6: Algorithm for Pharmacotherapy in Primary Care

However, in 2013 the labelling of both products was revised by Health Canada to include a statement that nicotine replacement therapy (NRT) should be considered prior to their use as follows:

- “Prior to a decision to prescribe a non-nicotine treatment, [varenicline] or [bupropion SR], thorough consideration should be given to the treatment option of nicotine replacement therapy.
- In many cases, nicotine replacement therapy should be tried before prescribing [varenicline] or [bupropion SR].” (Health Canada, 2013)

Practice Point:
Bupropion SR and Varenicline are considered first-line oral treatment options for smoking cessation according to guidelines; however, Health Canada approved product labelling recommends consideration be given to a trial of nicotine replacement therapy prior to their use.

**Bupropion**

Bupropion SR is an inhibitor of the neuronal reuptake of norepinephrine, serotonin, and dopamine and non-competitive inhibitor of the nicotinic receptors α3β2 and α4β2 that has been shown to improve rates of smoking cessation after 6 months and 12 months of follow-up compared to placebo. Its mechanism of action in smoking cessation is largely unknown. Bupropion SR is approved for use alone and in combination with NRT for smoking cessation. The odds of successfully quitting smoking with bupropion are about twice that of placebo when used as monotherapy (OR: 2.0; 95% CI 1.8 to 2.2). Table 2 summarizes the key points related to dosing, adverse effects, contraindications and warnings with respect to the use of bupropion SR for smoking cessation. Given the potential for co-addictions or concurrent substance use or misuse disorders amongst smokers, it is important to ask patients about alcohol use with bupropion given the increased risk of seizures with alcohol and bupropion SR. Other factors that increase the risk of seizures should also be considered (Table 2).

**Table 2:** Dosing, Adverse Effects, Precautions, and Contraindications with Bupropion SR

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Most Common Adverse Effects</th>
<th>Precautions and Contraindications</th>
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</table>
| Starting one to two weeks prior to the target quit date:  
- 150 mg in the morning for 3 days, followed by 150 mg twice daily, with dosages at least 8 hours apart.  
- Treatment should continue for 7 to 12 weeks with duration based on the relative benefits and risks for individual patients. | - Dry mouth  
- Insomnia | Pregnancy3  
- Pregnant smokers should be encouraged to quit without medication.  
- Bupropion has not been shown to be effective for tobacco cessation in pregnant smokers.  
- Bupropion has not been evaluated in breastfeeding patients.  
**Cardiovascular disease**2  
- Generally well-tolerated; occasional reports of hypertension.  
**Seizure risk**3  
- Contraindicated in history of seizures or eating disorders, with concurrent use of another form of... |
bupropion, or use of a MAO inhibitor in the past 14 days.

- Extreme caution in those with risk factors for seizures
  - Excessive alcohol use
  - Concurrent drug abuse
  - History of head trauma, CNS tumour,
  - Presence of severe hepatic impairment
  - Use of concomitant medications that lower seizure threshold, including but not limited to: antipsychotics, antidepressants, lithium, amantadine, theophylline, systemic steroids, quinolone antibiotics, and antimalarials
  - Use of over-the-counter stimulants or anorectics
  - Diabetes treated with oral hypoglycemics or insulin

Psychiatric Warnings

- Agitation-type events have been reported in both pediatrics and adults, of severe agitation-type adverse events coupled with self-harm or harm to others.
- The agitation-type events include: akathisia, agitation, disinhibition, emotional lability, hostility, aggression, depersonalization.
- In some cases, the events occurred within several weeks of starting treatment.
- Clinical monitoring for psychiatric symptoms is recommended

Varenicline

Varenicline is an agent with partial agonist activity at the α4β2 nicotinic acetylcholine receptor. It exerts an agonist activity at the receptor to a lesser degree than nicotine, while simultaneously preventing nicotine binding. In Canada, varenicline is approved for use as a smoking cessation treatment in adults in conjunction with smoking cessation counselling. The odds of successfully quitting smoking with varenicline are about three times that of placebo (3.1; 95% CI 2.5 to 3.8). Varenicline and Bupropion can be taken in combination. However, while varenicline has been used in combination with NRT in clinical studies, the current product labelling carries the following statements about co-administration:

- “Due to the partial agonist nicotinic activity of varenicline, it is not anticipated that co-administration with NRT would confer additional benefits compared with varenicline alone, and may result in increased side effects.”
- “The concomitant use of NRT with varenicline tartrate) may result in an increase in adverse reactions. In a clinical drug interaction study (N=24), the incidences of nausea, headache, vomiting, dizziness, dyspepsia and fatigue were greater for the combination of NRT and varenicline than for NRT alone. The safety and efficacy of the combination treatment with
Varenicline and NRT have not been studied. Due to the proposed mechanism of action of varenicline, it is not anticipated that co-administration with NRT would confer additional benefit compared with varenicline alone.

A randomized controlled trial, however, found that the combination of varenicline with NRT was more effective than varenicline alone.

In terms of dosing of varenicline, there are two dosing options, both of which begin with a dose of 0.5mg once daily on days 1 to 3 and 0.5mg twice daily on days 4 to 7. At Day 8, the dose either remains at 0.5 mg twice daily or increases to 1.0 mg twice daily (Table 3). The dose selection is based upon a number of clinical factors, the discussion of which is beyond the scope of this lesson. Generally, treatment is continued for 12 weeks and for those who have stopped smoking at the end of this time, an additional 12 weeks of treatment course may be considered.

**Table 3: Dose titration of varenicline**

<table>
<thead>
<tr>
<th>Day</th>
<th>Dosing Regimen</th>
<th>Options*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5 mg BID Regimen</td>
<td>1.0 mg BID Regimen</td>
</tr>
<tr>
<td>Days 1–3:</td>
<td>0.5 mg once daily</td>
<td>0.5 mg once daily</td>
</tr>
<tr>
<td>Days 4–7:</td>
<td>0.5 mg twice daily</td>
<td>0.5 mg twice daily</td>
</tr>
<tr>
<td>Days 8–onward</td>
<td>0.5 mg twice daily</td>
<td>1.0 mg twice daily</td>
</tr>
</tbody>
</table>

* Selection of dosage from day 8 onward is based upon a number of clinical factors.

**Table 4** summarizes the key points related to dosing, adverse effects, contraindications and warnings with respect to the use of varenicline for smoking cessation.

**Table 4: Dosing, Adverse Effects, Precautions, and Contraindications with Varenicline**

<table>
<thead>
<tr>
<th>Most Common Adverse Effects</th>
<th>Precautions and Contraindications</th>
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<tbody>
<tr>
<td>Nausea, abnormal dreams,</td>
<td>Pregnancy&lt;sup&gt;3&lt;/sup&gt;</td>
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<tr>
<td>constipation, flatulence,</td>
<td>• Pregnant smokers should be encouraged to quit without medication.</td>
</tr>
<tr>
<td>and vomiting</td>
<td>• Varenicline has not been shown to be effective for tobacco cessation in pregnant smokers.</td>
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<tr>
<td></td>
<td>• Varenicline has not been evaluated in breastfeeding patients.</td>
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<tr>
<td></td>
<td><strong>Renal Impairment&lt;sup&gt;3&lt;/sup&gt;:</strong></td>
</tr>
<tr>
<td></td>
<td>• Caution in patients with significant renal impairment (creatinine clearance &lt; 30mL/min) or who are on dialysis.</td>
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<tr>
<td></td>
<td>• Dose should be reduced with these patients.</td>
</tr>
<tr>
<td></td>
<td><strong>Activities</strong></td>
</tr>
<tr>
<td></td>
<td>• May experience impairment of the ability to drive or operate heavy machinery.</td>
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</tbody>
</table>
Psychiatric Warnings and Recommendations

- The benefits and risks of all options for quitting smoking should be discussed with the patient before initiating treatment.
- All patients attempting to quit smoking with varenicline, as well as their families and caregivers, should be alerted about the need to monitor for depressed mood, agitation, aggression, hostility, suicidal ideation or behavior, or changes in behavior or thinking that are not typical for the patient.
- Patients should be instructed to stop taking varenicline immediately and contact their doctor if they experience, or if others observe, these symptoms. In many post-marketing cases, resolution of symptoms after discontinuation of varenicline was reported, although in some cases the symptoms persisted; therefore, ongoing monitoring and supportive care should be provided until symptoms resolve.
- Regarding alcohol intake: Patients should be advised that alcohol intake may increase the risk of experiencing psychiatric adverse events during treatment with varenicline.
- Regarding patients with psychiatric history: Patients with concomitant psychiatric conditions, even if well controlled, or with a history of psychiatric symptoms, should be diligently monitored by a healthcare professional for new or worsened psychiatric events.

Cardiovascular Disease

Patients should be advised to notify a health care provider of new or worsening symptoms of cardiovascular disease.

Nicotine Replacement Therapy

Test Yourself

Nicotine replacement therapy

a. Increases the odds of quitting about 1.5 to 2.3-fold
b. Provides a clean source of nicotine to smokers while preventing withdrawal symptoms
c. Is available in short-acting and long-acting formulations
d. All of the above are correct

Nicotine replacement therapy is a treatment option for smoking cessation that is available without a prescription; however, it still requires adequate support and follow-up to ensure it is used appropriately to maximize the chances of success. Nicotine replacement therapy provides a ‘clean source’ of nicotine, to help reduce the symptoms of nicotine withdrawal associated with smoking cessation and increase the success rate.
In Canada, there are a number of different formats of NRT available which provides flexibility in terms of dosage and format. This may be helpful with the tailoring of pharmacotherapy to meet individual need and preferences.

Available dosage forms include

- Transdermal Patch
- Gum
- Inhaler
- Lozenge
- Mouth spray

Tailoring pharmacotherapy may involve using the individual’s preferred format or formats of NRT as monotherapy or using various combinations of NRT that best controls their cravings and withdrawal symptoms. Further, some individuals may prefer to initiate pharmacotherapy prior to their quit attempt, using ‘reduce to quit’ gum or a ‘pre-cessation’ patch. These approaches will be reviewed in greater detail in the sections that follow. Details of the approved dosages, common adverse effects and contraindications and precautions can be found in Table 5.

**Table 5: Forms of NRT Available in Canada and Their Dosages**

<table>
<thead>
<tr>
<th>Dosage Form</th>
<th>Dosage</th>
<th>Common Adverse Effects</th>
<th>Precautions and Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine patch</td>
<td>21mg, 14mg and 7 mg per 24 hours</td>
<td>skin irritation, vivid dreams, insomnia, headache, nausea</td>
<td>Contraindications: Previous acute hypersensitivity reaction, Immediate post-myocardial infarction period, Life-threatening arrhythmias, Severe or worsening angina pectoris, Recent cerebral vascular accident, Active temporomandibular joint disease (gum).</td>
</tr>
<tr>
<td></td>
<td>21mg/24 hours for 6 weeks, then 14 mg/24 hours for 2 weeks followed by 7mg/24 hours for 2 weeks. A starting dose of 14mg/24 hours may be used in patients with CVD, who weight &lt; 45 kg or who smoke less than ½ pack of cigarettes a day.</td>
<td></td>
<td>Precautions: Pregnancy, Nursing mothers, Generalized skin disorders (patch), Active peptic ulcer disease (gum, lozenge, inhaler, mouth spray), Bronchospastic diseases such as asthma (inhaler).</td>
</tr>
<tr>
<td>Nicotine gum</td>
<td>2mg gum for those who smoke one pack per day or less</td>
<td>mouth or throat soreness, jaw ache</td>
<td></td>
</tr>
<tr>
<td>2mg, 4mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Appropriate Use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------------</td>
<td>-----------------</td>
<td></td>
</tr>
<tr>
<td>4mg gum for those who smoke more than one pack per day</td>
<td>First two weeks: 10 to 20 pieces per day</td>
<td>hiccups</td>
<td></td>
</tr>
<tr>
<td>Next two weeks: 8 to 15 pieces per day</td>
<td>Month 2: 4 to 10 pieces per day</td>
<td>flatulence</td>
<td></td>
</tr>
<tr>
<td>Month 3: 2 to 5 pieces per day</td>
<td>Month 4: 1 piece if the urge to smoke returns</td>
<td>upset stomach</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>insomnia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>headache</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>nausea</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Nicotine lozenge 2mg, 4mg</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2mg lozenge for those who smoke one pack per day or less</td>
<td>Weeks 1 to 6: 8 to 15 lozenges per day</td>
<td>mouth or throat soreness</td>
</tr>
<tr>
<td>4mg lozenge for those who smoke more than one pack per day</td>
<td>Weeks 7 to 9: 4 to 8 lozenges per day</td>
<td>hiccups</td>
</tr>
<tr>
<td>Weeks 10 to 12: 2 to 4 lozenges per day</td>
<td>Next 3 months: 1 to 2 lozenges per day if the urge to smoke returns.</td>
<td>upset stomach</td>
</tr>
<tr>
<td></td>
<td></td>
<td>insomnia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>nausea</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Nicotine inhaler 10 mg cartridge that delivers 4 mg of nicotine</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 12 weeks: minimum of 6/maximum of 12 cartridges per day.</td>
<td>mild local irritation of mouth, sinus or throat</td>
<td>cough</td>
</tr>
<tr>
<td>12 to 24 weeks: Reduce the number of cartridges gradually. When down to 1 – 2 cartridges per day, stop using the inhaler.</td>
<td></td>
<td>dry mouth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hiccups</td>
</tr>
<tr>
<td></td>
<td></td>
<td>insomnia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>nausea</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Nicotine mouth spray 1mg per spray</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1 to 6: 1 to 2 sprays every half hour</td>
<td>hiccups</td>
<td>throat irritation</td>
</tr>
<tr>
<td>Week 7 to 9: Reduce average number of sprays</td>
<td></td>
<td>increased salivation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>tingling sensation of the mouth/lips</td>
</tr>
</tbody>
</table>
per day by half
Week 10 to 12: 2 to 4 sprays per day
After 12 weeks: Stop
Maximum: 2 sprays at a time
4 sprays per hour
64 sprays per day

• insomnia
• headache
• nausea

Based on a systematic review of the literature used to develop the US Department of Health and Human Services’ guidelines, it was found that a single form of NRT can increase the odds of cessation about 1.5 to 2.3 times when compared to placebo (Table 6).

**Table 6**: Efficacy of single dosage forms of NRT for smoking cessation

<table>
<thead>
<tr>
<th>Medication</th>
<th>Odds Ratio (95% CI)</th>
<th>Abstinence Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>1.0</td>
<td>13.8</td>
</tr>
<tr>
<td>Nicotine Nasal Spray</td>
<td>2.3 (1.7–3.0)</td>
<td>26.7 (21.5–32.7)</td>
</tr>
<tr>
<td>Nicotine Gum (&gt;14 weeks)</td>
<td>2.2 (1.5–3.2)</td>
<td>26.1 (19.7–33.6)</td>
</tr>
<tr>
<td>Nicotine Inhaler</td>
<td>2.1 (1.5–2.9)</td>
<td>24.8 (19.1–31.6)</td>
</tr>
<tr>
<td>Nicotine Patch (6–14 weeks)</td>
<td>1.9 (1.7–2.2)</td>
<td>23.4 (21.3–25.8)</td>
</tr>
<tr>
<td>Nicotine Patch (&gt;14 weeks)</td>
<td>1.9 (1.7–2.3)</td>
<td>23.7 (21.0–26.6)</td>
</tr>
<tr>
<td>Nicotine Gum (6–14 weeks)</td>
<td>1.5 (1.2–1.7)</td>
<td>19.0 (16.5–21.9)</td>
</tr>
</tbody>
</table>

A Cochrane Collaboration systematic review with network meta-analysis used indirect treatment comparison methods to compare the efficacy of a number of pharmacotherapies for smoking cessation. Using these methods, NRT as monotherapy was found to have similar efficacy to bupropion SR, but was less effective than varenicline in achieving smoking cessation for six months or longer (Table 7).³⁰

**Table 7**: Odds of achieving smoking cessation for six months or longer³⁰
Comparison between pharmacotherapies

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion vs nicotine patch</td>
<td>0.97 (0.83, 1.13)</td>
</tr>
<tr>
<td>Bupropion vs nicotine gum</td>
<td>1.1 (0.93, 1.3)</td>
</tr>
<tr>
<td>Bupropion vs other NRT</td>
<td>0.91 (0.75, 1.09)</td>
</tr>
<tr>
<td>Varenicline vs Nicotine patch</td>
<td>1.51 (1.22, 1.87)</td>
</tr>
<tr>
<td>Varenicline vs Nicotine gum</td>
<td>1.72 (1.38, 2.13)</td>
</tr>
<tr>
<td>Varenicline vs Other NRT</td>
<td>1.42 (1.12, 1.79)</td>
</tr>
</tbody>
</table>

Pre-cessation NRT – Approved Monotherapy

There are two ‘on-label’ or approved NRT dosing strategies (one for the patch and one for the gum) in which NRT can be initiated prior to stopping smoking completely. These strategies allow for a reduction in smoking while using NRT. While both are based on the same general concept and involve the use of NRT pre-cessation, they have been referred to with different terminology in the literature, with the patch being termed “pre-quit” and the gum being termed “reduce to quit”.

Pre-quit NRT Patch

In addition to the standard dosing, an alternate “pre-quit” or pre-cessation treatment approach can be used with nicotine 21mg/24 hour patches. Using this pre-quit approach, a quit date is set and the patch is started two weeks prior to this time. The number of cigarettes smoked is then gradually reduced over the two weeks leading up to the quit date. The smoker then quits on the quit date and patches are continued for the remainder of the quit attempt as usual (typically 10 more weeks). Using nicotine patches pre-quit has been shown to be an effective approach to smoking cessation. Based upon pooled data from four studies, it was found that compared with starting nicotine patches on the quit day, pre-cessation treatment with nicotine patches increased the odds of quitting by 1.96 after six weeks (95% CI: 1.31 to 2.93) and 2.17 after six months (95% CI: 1.46 to 3.22).31

Ask the Expert

What has been your experience using pre-cessation NRT? If you have not yet used this approach, what type of patient do you think this approach might appeal to?
“Reduce to Quit Strategy” - Gum

Some studies suggest that up to one-half of smokers prefer a gradual reduction in smoking to abrupt cessation\(^2\) and that almost half of those planning to quit in the next 12 months (44%) preferred to quit by gradually reducing the amount smoked.\(^3\) Further, it has been found that up to 68% of smokers felt that they may consider using a product to assist them with reducing the amount that they smoked.\(^3\) Strategies such as these are referred to as “reduce to quit.” The “reduce to quit” strategy involves gradually reducing the cigarette intake while using nicotine gum to help manage nicotine cravings and withdrawal symptoms until the smoker reaches a point where he or she can quit smoking completely. Using less tobacco per day can be achieved by reducing the number of cigarettes per day, taking fewer drags/inhales per cigarette, waiting an hour longer each day before lighting up the first cigarette or smoking only during odd or even hours.

The rationale behind this approach is that it

- May increase confidence in the ability to quit
- Nicotine physical dependence decreases as cigarettes are reduced, so final quit might be easier
- Environmental cues for smoking are diminished as certain cigarettes are cut out each day

Practicing behaviours (saying no, avoiding situations) leads to these behaviours becoming more natural and automatic. The effectiveness of reduce to quit strategy that involves that use of NRT has been assessed in a number of research studies with positive results.\(^3\) Across five studies, which used various forms of NRT (gum, inhaler, patch or combination) as part of a reduce to quit strategy, the likelihood of making a quit attempt and succeeding in quitting was increased by approximately 2.5 times (95% CI: 1.7 to 3.7) compared to placebo.\(^3\) Clearly, complete cessation from tobacco use remains the ultimate goal. However, using a reduce to quit strategy is worth trying compared to not intervening at all. Further, “reduce to quit” may, indeed, be the most widely used quit method. Reducing the number of cigarettes was cited by nearly two-thirds of Canadian smokers as a quit method, with the second most common method being pharmacotherapy.\(^1\)

**Practice Point:**
The gradual reduction in smoking with the "reduce to quit" approach may be appealing to smokers who may not have been willing to try an abrupt cessation approach and may increase the odds of smoking 2.5 times.

**Ask the Expert**
In what types of patients do you find the Reduce to Quit Strategies most effective?

**Approved Labelling for Reduce to Quit with Gum**

0 to 6 weeks
- Identify the cigarettes that matter the least in the daily routine and replace them with nicotine gum.

6 to 16 weeks – Cut Down By 50%
- Set goals to try and get rid of some of the cigarettes that are more difficult to give up – first of the day, after a meal etc. – while using nicotine gum to manage cravings and withdrawal symptoms
• By 16 weeks, should aim to be smoking half the amount of daily cigarettes as when started the program.

16 to 24 weeks
• Continue to eliminate cigarettes from daily routine while managing cravings and withdrawal symptoms with Gum.
• Within last 3 months, should be ready to give up cigarettes entirely.

Combination NRT Therapy

Test Yourself
Combination nicotine replacement therapy
  a. Is contraindicated
  b. Usually involves two forms of short acting NRT
  c. Generally refers to the simultaneous usage of a nicotine patch in conjunction with an oral nicotine replacement product such as gum, lozenge, inhaler, or mouth spray.
  d. None of the above are correct

Combination NRT therapy usually refers to the simultaneous usage of more than one format of nicotine replacement therapy, generally a nicotine patch used in conjunction with an oral nicotine replacement product such as gum, lozenge, inhaler, or mouth spray. As previously outlined, smoking cigarettes may produce a background nicotine level with additional nicotine levels peaking with consumption. No single form of NRT ideally mimics both categories of nicotine delivery to which cigarette smokers become accustomed and may require if they are to avoid symptoms of withdrawal and sustain abstinence from tobacco. Monotherapy with a single, short-acting NRT may not adequately replace the levels of nicotine to which a smoker may be accustomed. In theory, using an oral, short acting NRT in addition to a patch enables smokers to relieve acute cravings as well as manage their other tobacco withdrawal symptoms (Figure 7).
Figure 7: Replacing nicotine with combination NRT

Efficacy of Combination NRT
Based upon the systematic review that was used to develop the US Department of Health and Human Services smoking cessation guidelines, it was found that the combination of patch and inhaler for less than 14 weeks increased the odds of smoking cessation more than two-fold and that long-term patch combined with either gum or spray as needed increased the odds of quitting almost four-fold (Table 8) when compared with placebo.

Table 8: Efficacy of different combinations of NRT based upon the US Department of Health and Human Services guidelines

<table>
<thead>
<tr>
<th>Medication</th>
<th>Odds Ratio (95% CI)</th>
<th>Abstinence Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine patch (long-term; &gt; 14 weeks) with NRT 2mg gum or spray</td>
<td>3.6 (2.5–5.2)</td>
<td>36.5 (28.6–45.3)</td>
</tr>
<tr>
<td>Nicotine patch* + inhaler</td>
<td>2.2 (1.3–3.6)</td>
<td>25.8 (17.4–36.5)</td>
</tr>
</tbody>
</table>

* Dose of nicotine patch was 15mg

Another systematic review that used a network meta-analysis approach found that compared with placebo, combination NRT increased the quit rate almost three fold (OR: 2.73; 95% CrI: 2.07, 3.65). As well, efficacy of combination NRT was estimated relative to monotherapy NRT and oral first-line monotherapies in this network meta-analysis. The odds of successfully quitting for at least six months can be found in Table 9 and were greater with combination NRT relative to the patch or gum alone or
with bupropion.\textsuperscript{30} For the comparison of combination NRT and varenicline, however, there appeared to be no statistical difference in the odds of quitting.\textsuperscript{30} The evidence from this review suggests that the most efficacious options for smoking cessation are either varenicline or combination NRT.

Table 9: Odds of successfully quitting for at least six months with combination NRT compared with other forms of NRT and first-line oral therapies\textsuperscript{30}

<table>
<thead>
<tr>
<th>Comparison between pharmacotherapies</th>
<th>Odds Ratio (95% CrI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination NRT vs NRT Patch</td>
<td>1.43 (1.08, 1.91)</td>
</tr>
<tr>
<td>Combination NRT vs NRT Gum</td>
<td>1.63 (1.21, 2.2)</td>
</tr>
<tr>
<td>Combination NRT vs Other NRT</td>
<td>1.34 (1, 1.8)</td>
</tr>
<tr>
<td>Bupropion vs Combination NRT</td>
<td>0.68 (0.5, 0.91)</td>
</tr>
<tr>
<td>Varenicline vs Combination NRT</td>
<td>1.06 (0.75, 1.48)</td>
</tr>
</tbody>
</table>

Who May be a Candidate for Combination Therapy?
Combination NRT is endorsed in smoking cessation guidelines from Canada, the United States and the United Kingdom; however, until recently NRT products in Canada carried contraindications and warnings regarding the concurrent use of more than one product.

In early 2016, the licenses of NRT products in Canada were updated to remove contraindications and warnings about using more than one form of NRT concurrently and warnings about concurrent smoking while using NRT.\textsuperscript{34-38} Specifically, the licenses for NRT patches, gum, lozenge and mouth spray now contain the following statements:

“If the amounts of Patch/gum you are taking do not help you stop smoking, talk with your healthcare provider about using more than one type of nicotine replacement therapy at the same time.”

Statements cautioning about concurrent use of other forms of NRT, such as gum, and smoking while wearing patches have been removed.\textsuperscript{34-38}

Consistent with the changes to the Canadian licenses, combination therapy may be indicated for smokers who fail to respond to monotherapy, despite being adherent to an optimized dose of medication according to treatment guidelines. The CAN-ADPATT algorithm suggests two forms of NRT (Patch plus short acting agent) as one option for individuals who do not respond to optimized pharmacotherapy (Figure 8).
Figure 8: Algorithm for Pharmacotherapy in Primary Care

Source: https://www.nicotinedependenceclinic.com/English/teach/resources/Visual%20Aids/Tobacco%20Algorithm%20updated%20Nov%202013.pdf
Guidelines from the USTFPS suggest that combination pharmacotherapy may be indicated for initial treatment, rather than first trying monotherapy and then progressing to combination therapy. For example, patients who are highly nicotine dependent or experience severe withdrawal symptoms may benefit from the initial use of combination NRT. The Fagerström Test for Nicotine Dependence can be used to help identify patients who may be highly nicotine dependent.

Thus, a suitable candidate for combination NRT may be a smoker who

- Has used NRT in a previous quit attempt but relapsed while using it
- Feels he or she needs something more than a patch or other single form NRT
- Heavier smokers

**Ask the Expert**

What do you feel are the key challenges or barriers to using combination NRT in your practice?

**Suggested Dosing for Combination NRT**

While the prescribing of combination NRT is no longer considered “off-label”, the new licensing of NRT products does not provide guidance with respect to dosing of short and long acting NRT when used simultaneously. The new labelling simply refers consumers to their healthcare providers for advice about using more than one type of NRT at the same time. Dosing algorithms for combination NRT vary across different jurisdictions, with some sources suggesting lower daily maximums with the short acting agent than when it is used as monotherapy. Consensus, based upon the best available evidence, is needed in the future. Links to a number of different algorithms used in clinics and hospitals in Canada and the United States can be found below:

- **Mayo Clinic**

- **Winnipeg Regional Health Authority**

- **Centre for Addiction and Mental Health**

- **Grand River Hospital**
Meet Tom
- Tom is 47 years old, has been a smoker for 25 years, and smokes about 20 to 30 cigarettes per day.
- Tom has no chronic medical conditions, other than osteoarthritis for which he takes acetaminophen.
- Tom has tried to quit smoking three times, twice “cold turkey” and most recently (starting about four weeks ago) using an NRT patch.
- With his past quit attempts, Tom suffered from intense cravings and found himself ready to cave to his cravings almost immediately.
- With his current quit attempt, he still smoking in situations that are triggers for him (in the car when driving, when he goes out for beer with his friends).
- He feels the patch is helping him most of the time but not when these occasional strong cravings hit.

Case Question
Would a trial of combination NRT be an appropriate treatment option for Tom?
- a) Yes
- b) No

Meet Sarah
- Sarah is 27 years old, with a seven year history of smoking. She smokes about 25 cigarettes a day. Sarah has no medical conditions and is not currently taking any medications.
- Sarah is currently using a nicotine patch, which she started four weeks ago using the pre-quit approach. She has been almost smoke free for two weeks having the occasional slip as she misses the hand to mouth sensation of cigarette smoking.

Case Question
Would a trial of combination NRT be an appropriate treatment option for Sarah?
- a) Yes
- b) No
- Sarah is considering trying an e-cigarette and wonders if they work and if they are safe to use.

An electronic cigarette (e-cigarette) is a battery powered device containing a liquid substance that is vaporized and then inhaled in a manner analogous to a traditional cigarette. The ‘e-liquid’ may or may not contain nicotine. This is an important distinction as the nicotine content determines regulation of e-cigarettes in Canada. In Canada, an e-cigarette that contains nicotine would be regulated under the
Food and Drug Act, requiring market authorization from Health Canada as a new drug prior to importation, marketing, or sale. No such product has received authorization to date and, as such, sale of any nicotine containing e-cigarette in Canada remains illegal. Conversely, e-cigarettes that do not contain nicotine and do not make health claims remain legal to sell. Health Canada has, however, advised against the use of these products in the past and has not provided any updates to its warning against their use, as they have not been “fully evaluated for safety, quality, and efficacy”.

Systematic literature reviews of e-cigarettes have produced conflicting results, with two reviews showing that they increase the chances of smoking cessation and the most review recent showing that e-cigarette use is associated with reduced cessation. However, it is also important to consider that majority of the literature assessed nicotine-containing e-cigarettes, and is not directly applicable to the non-nicotine containing e-cigarettes which can be legally sold in Canada. Thus, the efficacy and safety of these products over the long-term remains uncertain; however, they are, in all likelihood, to be safer than smoking cigarettes. While there are positive experiences with e-cigarettes from other countries, such as the UK, the products available there are unlikely to be reflective of those available in Canada and there continues to be concerns with e-cigarettes here. New provincial and municipal regulations soon coming into effect are reflective of such concerns. In Quebec, for example, e-cigarettes and other similar devices, including their components and accessories, are now subject to the same rules as tobacco products. Until more is known about the safety and efficacy of non-nicotine containing e-cigarettes, health care providers are encouraged to recommend evidence-based treatments to their patients.

Rationale: A. Yes. An inhaler combined with a patch may help her craving. It may specifically replace the hand to mouth ritual and could reduce the chances of further slips and returning to smoking.

Meet Richard

- Richard is 63 years old and is a tradesman who works on the oilfields. He smokes 25 to 30 cigarettes per day and has been smoking about 40 years.
- He has high cholesterol and hypertension, which are currently controlled with atorvastatin and ramipril.
- Richard’s has found quitting difficult, especially at work where many of his coworkers smoke. When he has tried to quit in the past, they have given him a rough time about it – they hassle him, smoke around him and offer him cigarettes.
- Richard has tried to quit in the past with oral pharmacotherapies and does not want to try these again. He quit about one week ago, using nicotine lozenges but does not feel his cravings are being adequately controlled, especially at work.
- He would like something discreet and easy to use during the day.
Case Question
Would a trial of combination NRT be an appropriate treatment option for Richard?

a) Yes
b) No

Rationale: A. Yes. Lozenges can relieve acute cravings discreetly; however, adding a patch to provide a background level of nicotine may be beneficial for him.

Summary of Key Learning Points
- While the prevalence of smoking has reached its lowest in Canada since surveys began, the rate at which the prevalence has been declining has slowed, demonstrating the ongoing need for healthcare providers to continue to identify and address tobacco use in their patients.
- Screening for tobacco use with the 5A’s approach and assessing readiness to quit smoking can help identify potential candidates for pharmacotherapy for smoking cessation.
- Nicotine replacement therapy is a first-line option for smoking cessation and can be used with different dosing strategies, all of which have been shown to significantly increase the chances of successfully quitting.
- Compared to monotherapy, combination NRT may better mimic the pattern of nicotine delivery to which cigarette smokers are accustomed. This could potentially help to minimize symptoms of withdrawal and sustain abstinence from tobacco.
- Based upon systematic reviews, combination NRT has been shown to increase cessation rates almost three-fold compared to placebo and had better efficacy than monotherapy NRT and bupropion. Efficacy is similar to that of varenicline.
Resources

Guidelines

CAN-ADAPTT

Tools
https://www.albertaquits.ca/helping-others-quit/healthcare-providers

Ontario Ministry of Health and Long-Term Care Pharmacy Smoking Cessation Program
Nicotine Dependence Clinic Change Plan Workbook
   CAMH Knowledge Exchange Addiction Toolkit
   Alberta Quits Toolkit
   Health Canada On the Road to Quitting Guide
   Fagerström Test for Nicotine Dependence

Discussion forum questions

1. What are the most common barriers you encounter to using combination nicotine replacement therapy in practice?
2. What types of patients do you feel are the most appropriate candidates for the Reduce to Quit Strategy?
Post-Test Questions

1. Which of the following is correct regarding quitting smoking?
   a. About 10% of smokers who quit will remain smoke free without any form of support over the course of one year.
   b. Most smokers require multiple quit attempts to remain smoke free.
   c. Intensive interventions from health care providers are needed to increase the chances of successful quitting. Brief interventions are ineffective.
   d. None of the above are correct.

2. Which of the following is correct regarding the 5A’s approach to identifying and treating tobacco use?
   a. The 5A’s process works through the following steps (in order): Ask, Assist, Arrange, Advise and Assess.
   b. The 5A’s process works through the following steps (in order): Ask, Advise, Assess, Assist, and Arrange.
   c. The three steps of Ask, Advise and Assess of the 5 As model are applicable to all patients who smoke.
   d. B and C are both correct

3. Which of the following is correct regarding nicotine and smoking?
   a. When nicotine levels decrease, dopamine levels increase, resulting in symptoms of withdrawal.
   b. Smoking provides a background level of nicotine, in addition to peak levels immediately following smoking.
   c. Nicotine affects the dopamine reward system of the brain, similar to other drugs of abuse.
   d. B and C are correct
   e. All of the above are correct

4. Which of the following is correct regarding the motivation to quit smoking
   a. Patients will be willing to quit smoking when they perceive that the benefits of smoking outweigh the risks associated with continued smoking.
   b. Having fears or concerns about smoking cessation can increase the motivation to quit.
   c. When patients who are unwilling to quit smoking are identified, it is important to try to convince them to set a quit date and stop smoking.
   d. Motivational Interviewing (MI), is a non-confrontational, non-prescriptive counseling intervention designed to enhance the motivation to quit smoking.

5. Which of the following is correct regarding first-line therapies for smoking cessation?
   a. Bupropion SR, varenicline, and NRT are all considered first-line treatments according to American and Canadian Guidelines for smoking cessation.
   b. Bupropion SR is not approved for use in combination with NRT
c. Varenicline is metabolized by the liver and requires no dosage adjustment in severe renal dysfunction.

d. All of the above are correct

6. The efficacy of NRT for smoking cessation therapy

a. May be reduced if taken for less than five weeks duration.

b. May be similar to varenicline when used as a combination of short-acting agent and patch.

c. May be similar to bupropion SR when used as monotherapy, but greater than bupropion SR when used as a combination of short-acting agent and patch.

d. Is almost three times greater than placebo when a short acting NRT is combined with a patch.

e. All of the above are correct

7. Pre-cessation nicotine replacement therapy (NRT)

a. Is started four weeks prior to the quit date with the number of cigarettes smoked being gradually reduced over the four weeks leading up to the quit date.

b. Is started two weeks prior to the quit date with the number of cigarettes smoked being gradually reduced over the two weeks leading up to the quit date.

c. Pre-cessation treatment with NRT patches has been shown to increase the odds of quitting approximately two fold compared with compared with starting nicotine patches on the quit day.

d. A and C are both correct

e. B and C are both correct

8. The reduce to quit strategy with NRT

a. Is an approach to smoking cessation that appeals to a small proportion of smokers.

b. May decrease the patient’s confidence in the ability to quit.

c. Increases the odds of successfully quitting approximately 2.5 times compared with placebo.

d. May increase environmental cues for smoking as certain cigarettes are cut out each day.

e. All of the above are correct

9. Combination NRT therapy

a. Generally refers to using a nicotine patch in conjunction with an oral nicotine replacement, such as gum, lozenge, inhaler or mouth spray.

b. Provides nicotine to help relieve ongoing and acute cravings and provides background nicotine to help manage nicotine withdrawal symptoms.

c. Has been shown to be more effective than NRT patch or gum alone and bupropion SR.

d. All of the above are correct

10. Which of the following is correct regarding the contraindications with NRT?

a. Smoking while using NRT is contraindicated
b. Patients who experience “a slip” and smoke while using the nicotine patch should immediately stop using it.
c. Using nicotine gum while on the nicotine patch is contraindicated.
d. None of the above are correct
Post-test Survey

1. Please rate your level of knowledge of the **approved** combinations of nicotine replacement therapies available in Canada (i.e., nicotine patch with a short-acting nicotine replacement therapy) (1 = limited, 5= excellent).

2. Please rate your level of comfort in recommending combination NRT for smoking cessation when indicated? (1=completely uncomfortable / 5 = completely comfortable).

3. Please rate your level of understanding of the rationale for combining a long-acting nicotine replacement therapy (i.e. nicotine patch) with a short-acting nicotine replacement therapy (e.g., gum, lozenge, inhaler) for smoking cessation (1 = limited, 5= excellent).

4. Please rate your level of knowledge of **reduce to quit strategies** using short-acting nicotine replacement therapies (1 = limited, 5= excellent).

5. Please rate your level of comfort in recommending short-acting nicotine replacement therapies using of **reduce to quit strategies** ( 1=completely uncomfortable / 5 = completely comfortable).

6. Please rate your level of comfort in recommending nicotine replacement therapy to patients who may continue to smoke while using it (1=completely uncomfortable / 5 = completely comfortable).
References


5. Sutherland, G. Smoking: Can we really make a difference? Heart; May 2003; 89, ii25 – ii27.


