Smoking cessation

**Tobacco dependence:**
Is an addiction to tobacco caused by the drug nicotine. The smoker suffering from tobacco dependence cannot stop using the substance despite the fact that it causes him/her harm. Inhaled nicotine is known as a drug able to induce an addiction at least as strong as that of heroin or cocaine. Tobacco users who took up smoking as teenagers are usually more addicted than those who took up tobacco use as adults. Nicotine, a substance with psycho-active properties, creates the cravings for cigarettes, cigars, pipes, making smokers unable to quit easily and causes smokers to have physical and psychological symptoms when abstaining from smoking. While the nicotine contained in tobacco causes the nicotine dependence, the toxic effects are mainly due to other substances contained in the tobacco smoke.

**Smoking status:**
It is recommended that all clinicians appropriately assess of current and past tobacco use with patients.

The following definitions are used for the classification of smoking status:
- **Non-smoker** is a person who has not smoked more than 100 cigarettes in his/her lifetime (or 100 g of tobacco, in the case of pipes, cigars or other tobacco products).
- **Daily smoker** is a person who has smoked on a daily basis for at least three months.
- **Occasional smoker** is a person who has smoked, but not on a daily basis.
- **Ex-smoker** is a person who has quit smoking for at least six months.

**Smoking severity scale:**

<table>
<thead>
<tr>
<th>&lt; 20 cigarettes/day or &lt;8 pack/year</th>
<th>Mild</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-40 cigarettes/day or 8-30pack/year</td>
<td>Moderate</td>
</tr>
<tr>
<td>&gt;40 cigarettes/day or &gt;30pack/year</td>
<td>High</td>
</tr>
</tbody>
</table>
Assessment/diagnosis of tobacco use and dependence:
Assessing smokers is a process consisting of a clinical and biological assessment of tobacco smoke exposure, assessment of tobacco dependence, assessment of psycho-behavioral profile and health consequences of tobacco use.

- Clinical diagnosis of tobacco use and dependence:
Clinical diagnosis is based on:
1. Smoking status (non-smoker, occasional smoker, daily smoker, ex-smoker).

2. Type of tobacco product used: it gives an idea about the level of addiction, since nicotine dependence is more severe in cigarette consumers, compared to those who use cigars, 19 pipes, water pipes, e-cigarettes or oral tobacco.

3. Tobacco consumption: the number of cigarettes smoked per day; number of cigarette packs/years.
The number of pack/years is calculated by multiplying the number of cigarettes packs smoked/day by the number of years of smoking (e.g. if someone smokes 15 cigarettes per day for 15 years, this 15 equals 15x15/20 = 11.2 PY).

- Tobacco dependence assessment:
Tobacco dependence could be diagnosed in accordance with the WHO definition:
Tobacco dependence is defined by the presence of at least 3 out of 7 definition criteria, if present at a moment during the past 12 months.

- Strong desire to smoke
- Difficulty in controlling quantity
- Withdrawal symptoms when reducing or quitting tobacco
- Continued consumption despite obvious harmful effects
- Priority of smoking over other activities
- High tolerance
- Physical tobacco withdrawal symptoms

Nicotine/cigarette dependence is mainly assessed using the Fagerström nicotine dependence test, FTND that provides not only a yes/no answer but also a final score, which categorizes tobacco users as having either low, medium, or high levels of nicotine dependence. The higher the score, the higher the nicotine dependence of an individual. The level of nicotine dependence can be used to guide the design of treatment plan for patient.
Fagerström Test for Nicotine Dependence

<table>
<thead>
<tr>
<th>Questions</th>
<th>Response Options</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How soon after you wake up do you smoke your first cigarette?</td>
<td>Within 5 minutes</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>6-30 minutes</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>31-60 minutes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>After 60 minutes</td>
<td>0</td>
</tr>
<tr>
<td>2. Do you find it difficult to refrain from smoking in places where it is forbidden, e.g., in church, at the library, in cinema, etc.?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>3. Which cigarette would you hate most to give up?</td>
<td>The first one in the morning</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>All others</td>
<td>0</td>
</tr>
<tr>
<td>4. How many cigarettes per day do you smoke?</td>
<td>10 or less</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>11-20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>21-30</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>31 or more</td>
<td>3</td>
</tr>
<tr>
<td>5. Do you smoke more frequently during the first hours after waking than during the rest of the day?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>6. Do you smoke if you are so ill that you are in bed most of the day?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
</tr>
</tbody>
</table>

Score 0-3: no or low tobacco dependence
Score 4-6: medium tobacco dependence
Score 7-10: high tobacco dependence

Low: patient **not need** NRT
Low/moderate: treated with **single** agent NRT
Moderate: treated with a combination of NRT (long acting with short acting)
High: can be treated with a combination of NRT with oral agent

**Smoking cessation:**

Quitting smoking can be difficult due to physical and psychological dependence; both the habit and nicotine addiction are hard to break. There may be some immediate withdrawal symptoms that are difficult to overcome such as: agitation, anxiety, insomnia, even weight gain and depression. However, withdrawal symptoms are temporary.

The key components of successful cessation (remission) are combinations of therapeutic education, behavioral support and pharmacotherapy. A tobacco user’s preparation, motivation to quit, nicotine dependence, age, comorbidity and numerous personal factors will affect the chances of success.

**Health Benefits of Stopping Smoking:**

Most people who smoke are aware that smoking damages health. They may not be aware
that most adverse health effects from smoking decline dramatically after quitting.

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Health Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within 20 Minutes</td>
<td>Blood pressure drops, pulse rates drops to normal, body temperature of hands and feet return to normal</td>
</tr>
<tr>
<td>Within 8 Hours:</td>
<td>Carbon Monoxide levels in the blood return to normal</td>
</tr>
<tr>
<td>Within 24 Hours:</td>
<td>Risk of heart attack decreases</td>
</tr>
<tr>
<td>Within 48 Hours</td>
<td>Ability to smell and taste improves</td>
</tr>
<tr>
<td>Within 72 Hours:</td>
<td>Breathing gets easier as bronchial tubes relax, lung capacity increases</td>
</tr>
<tr>
<td>Within 3 Weeks:</td>
<td>Mucus in the lungs loosens, lung function and circulation improves</td>
</tr>
<tr>
<td>Within 2 Months:</td>
<td>Blood flows more easily to arms and legs, lung function increases up to 30%</td>
</tr>
<tr>
<td>After 3 Months</td>
<td>Lungs become more healthy, you breathe more easily, you get fewer colds</td>
</tr>
<tr>
<td>After 1 Year:</td>
<td>Risk of sudden death from heart attack is almost cut in half</td>
</tr>
<tr>
<td>After 5 Years:</td>
<td>Lung cancer death rate for the average smoker decreases nearly 50%</td>
</tr>
<tr>
<td>Within 10 Years:</td>
<td>Risk of sudden heart attack and strokes becomes almost the same as a nonsmoker, risk of cancer drop significantly</td>
</tr>
</tbody>
</table>

(Breen, G., Spiers, A., Wintzides, W. Help Smokers Quit Kit. Ulster Cancer Foundation, Northern Ireland.)

**Smoking cessation treatment:**

The initial aim of the treatment is to quit tobacco.

- A quitter is a smoker who has voluntarily not smoked a single cigarette.
- Abstinence has to be monitored when possible together with monitoring of expiratory carbon monoxide (CO).
- The maximum recommended level of CO in breath required to validate abstinence is 7 ppm.

1. **Convince** smokers to quit and assess their willingness for that by using the 5A’s approach:
   - **Ask**: all patients about smoking status
   - **Advice**: patients who smoke to quit
   - **Assess**: willingness to quit at every visit
   - **Assist**: quitting within 2 weeks with pharmacotherapy or counseling
   - **Arrange**: follow-up
2. **Therapeutic education:**
- Explain tobacco dependence disease
- Explain the health consequences of smoking
- Explain the benefits of quitting smoking
- Explain tobacco cessation treatment
- Explain chronic tobacco dependence management to prevent relapse
- Present tools available locally to smokers.

3. **Cognitive-behavioral therapy (CBT)**
The principles of CBT are as follows: initiating a collaboration relationship between doctor and patient; avoiding conflicts; active listening – which refers to re-phrasing what the patient says; valuing success; creating positive appreciation skills concerning the benefits of quitting smoking.

Using CBT in smoking cessation centers helps smokers learn to take note of their smoking behavior and evaluate themselves, given that smoking is a learned behavior, subsequently maintained through a dependence constantly influenced by environment stimuli.

This technique developed from treatments for anxiety and depression (so-called cognitive behavioral therapy) attempts to change habitual ways of thinking and feeling about smoking and oneself and provides encouragement and advice on ways of minimizing and managing the desire to smoke.

4. **Medications:**

4.1 **Nicotine replacement therapy (NRT):**
The goal of nicotine replacement therapy (NRT) is to relieve nicotine withdrawal symptoms by providing nicotine without the use of tobacco, while the smoker breaks the behavior of cigarette smoking.

**Safety of NRT:**
Side effects common among all NRT products include gastrointestinal symptoms (nausea, vomiting, abdominal pain, diarrhea), headache, and local irritation depending on the delivery method. Smokers who experience side effects from NRT products can titrate use of the product to minimize side effects or change products. NRT is safe to use in patients with known stable cardiovascular disease (CVD).

**Administration of NRT:**
The initial dosing of most NRT products is based on the number of cigarettes smoked daily, NRT dose is then gradually tapered. In general, NRT use is recommended for **two**
to three months after smoking cessation, though NRT use for as long as a smoker is at high risk for relapse is acceptable because NRT is much safer than continuing to smoke. Some smokers may need to use the products indefinitely. NRT products can also be used while the smoker is still smoking.

1. **Nicotine transdermal patch (long-acting):** The nicotine patch provides the most continuous nicotine delivery among all NRT products and is the simplest NRT to use. The patch has a long-acting, slow-onset pattern of nicotine delivery, which produces relatively constant relief from withdrawal over 24 hours but requires several hours to reach peak levels. Compliance with the patch is high; however, the user cannot adjust the dose of nicotine being released to respond to nicotine cravings and withdrawal symptoms. The patch is available over the counter and by prescription.

**Dosing:**
Determined by the number of cigarettes smoked daily:
- **>10 cigarettes per day and weight >45 kg:** Start with the highest dose nicotine patch (21 mg/day) for six weeks, followed by 14 mg/day for two weeks, and finish with 7 mg/day for two weeks.
- **≤10 cigarettes per day or weight < 45 kg:** Start with the medium dose nicotine patch (14 mg/day) for six weeks, followed by 7 mg/day for two weeks.

**Instructions on how to use:**
- Apply one patch each morning to any non-hairy skin site; rotate the site daily to avoid skin irritation (the most common side effect)
Over-the-counter hydrocortisone 1% cream or ointment topically may be used to relieve skin irritation if it occurs.

- Remove and replace the patch with a new one at bedtime. However, if leaving the patch on overnight is causing the frequently reported side effects of insomnia and vivid dreams, replace the patch the next morning.

- If the patch is removed at night and morning nicotine cravings occur, use a short-acting NRT (e.g., gum, lozenge) while waiting for the nicotine patch to take effect.

**Adjusting duration:**
- longer duration (more than 8 to 10 weeks) of treatment with the nicotine patch may lead to improved smoking cessation rates. Generally, NRT is used until a patient feels that he or she has stabilized as a nonsmoker. The patch may be continued longer, even indefinitely if needed, as NRT is safer than continued smoking. NRT is often used for a longer period in patients with co-morbid psychiatric illness or other substance use disorders.

2. **Short-acting nicotine replacement therapy:**
A short-acting form of NRT (lozenge, gum, inhaler, or nasal spray) can be used as a single agent or can be added to daily nicotine patch therapy to help control cravings and withdrawal symptoms. However, short-acting forms require repeated use throughout the day, lead to more variable nicotine levels than the patch, and require more instructions for correct use.

Smokers may be instructed to use the product when they have a craving, but this generally leads them to underuse the products. An alternative approach is to have the smoker use the short-acting NRT product at least once every hour while awake and more often as needed.

The choice of a short-acting agent depends on patient preference and co-morbidities. The nicotine patch, lozenge, and gum are available without a prescription; nasal spray and oral inhaler require a prescription.

A. **Nicotine gum:**
Chewing the gum releases nicotine to be absorbed through the oral mucosa, resulting in peak blood nicotine levels 20 minutes after starting to chew. Nicotine gum is available in several flavors that most users find preferable to the original flavor.
Dosing:
Determined by the number of cigarettes smoked daily.

≥ 25 cigarettes per day: 4 mg dose of gum is recommended

< 25 cigarettes per day: 2 mg dose of gum is recommended

-Chew at least one piece of gum every one to two hours while awake and also whenever there is an urge to smoke.

- Use up to 24 pieces of gum per day for six weeks.

- Gradually reduce use over a second six weeks, for a total duration of three months.

- Gastric and esophageal irritation can occur if the gum is chewed too rapidly, because nicotine is released faster than it can be absorbed by the buccal mucosa and the nicotine is thus swallowed. Nicotine absorbed from the gastrointestinal tract is largely metabolized by the liver and is therefore relatively ineffective for smoking cessation.

"Chew and park" is recommended: chew the gum until the nicotine taste appears, then "park" the gum in the buccal mucosa until the taste disappears, then chew a few more times to release more nicotine. Repeat this for 30 minutes, then discard the gum (because all nicotine in the gum has been released).

-Acidic beverages (e.g. coffee, carbonated drinks) should be avoided before and during gum use, as acidic beverages lower oral pH, which causes nicotine to ionize and reduces nicotine absorption.

Side effects are mostly a consequence of excess nicotine release with overly vigorous chewing and consist of nausea, vomiting, abdominal pain, constipation, hiccups, headache, excess salivation, a sore jaw, and mouth irritation or ulcers.
Chewing gum may exacerbate temporomandibular joint disease and the gum can damage or adhere to dental appliances. Smokers with temporomandibular joint disease, with poor dentition, or who use dental appliances may do better with an alternative short-acting form of NRT such as the lozenge or inhaler.

**B. Nicotine lozenge:**
Nicotine lozenges are a commonly used short-acting NRT product, with pharmacokinetics similar to nicotine gum. Lozenges are easier to use correctly than nicotine gum and are also available in different flavors.

- **Dosing**
  Determined by how soon the first cigarette is typically smoked upon awakening:

  - Smokers who smoke **within 30 minutes** of awakening: 4 mg dose recommended
  - Smokers who wait **more than 30 minutes** after awakening to smoke: 2 mg dose recommended

  - Use up to one lozenge every one to two hours for six weeks. The maximum dose is five lozenges every six hours or 20 lozenges per day.

  - gradually reduce number of lozenges used per day over a second six weeks.

- **Instructions on how to use:**
  - Place lozenge in the mouth and allow it to dissolve for 30 minutes. The lozenge does not need to be chewed.
Side effects include mouth irritation or ulcers, in addition to nicotine-related side effects of abdominal pain, nausea, vomiting, diarrhea, headache, and palpitations.

C. Nicotine inhalers: These consist of a mouthpiece and a plastic, nicotine-containing cartridge. The inhaler addresses not only physical dependence but also the behavioral and sensory aspects of smoking (i.e., having a cigarette between one's fingers and inhaling from the cigarette).

When the smoker inhales through the device, nicotine vapor (not smoke) is released, deposited primarily in the oropharynx, and absorbed through the oral mucosa. Nicotine vapor does not reach the lungs to an appreciable extent.

- **Dosing:**
  - Use 6 to 16 cartridges per day for the first 6 to 12 weeks
  - Gradually reduce dose over the next 6 to 12 weeks
Instruction on how to use:

- Take 1 cartridge out of the package.
- Put the cartridge into the inhaler device and push the pieces together.
- Twist so the markings do not line up.
- Gently draw air into your mouth through the inhaler.
- Puff into the cheeks, DO NOT inhale deeply.
- Hold the vapour in your mouth for a few seconds before breathing out.

**Side effects** occurring commonly include localized irritation of the mouth or throat, particularly during the early stages of use. Because inhaled nicotine may cause bronchospasm, it may be less appropriate for smokers with a history of severe airway reactivity.

**D. Nicotine nasal spray:** The nicotine nasal spray delivers an aqueous solution of nicotine to the nasal mucosa.

**Dosing:**

- Dose is one or two sprays per hour
- Use for about three months
- The maximum dose is 10 sprays per hour, **not to exceed 80 total sprays / day**

**Side effects** include nasal and throat irritation, rhinitis, sneezing, and tearing.
E. Nicotine mouth spray:

- **Dosing:**
  - 1 mg nicotine is delivered per spray
  - Use one or two sprays when cravings occur, up to four sprays per hour

**Side effects:** hiccups, throat irritation, and nausea.
F. Nicotine sublingual tablet:
● Dosing:

- Allow one 2 mg tablet to dissolve sublingually (typically over 30 minutes) every one to two hours
- Patients who are heavily nicotine-addicted can use two tablets sublingually (4 mg total) for each dose

Side effects occurring commonly include sore mouth or throat and dryness or burning in the mouth.

4.2 Oral drugs:

1. CHAMPIX:
   A prescription medicine, called Varenicline:
   It is a nicotinic acetylcholine receptor partial agonist and is thought to work by reducing the strength of the smoker's urge to smoke and relieving withdrawal symptoms.
Furthermore, if a person smokes a cigarette while using varenicline, it has the potential to diminish the sense of satisfaction associated with smoking. Unlike nicotine replacement therapies (e.g. nicotine patches, gum or inhalation devices), CHAMPIX does not contain any nicotine. It blocks the action of nicotine in your brain and helps to reduce cravings and withdrawal symptoms associated with giving up smoking.

Patients should start taking your CHAMPIX tablets 1–2 weeks before you quit smoking and before you start taking your CHAMPIX you should set your quit date. This should be in the second week of treatment (between day 8 and day 14). It’s important to write this date on the pack as a reminder. If you are unable (or unwilling) to give up on your designated quit date, you can choose an alternative quit date within 5 weeks of starting treatment. Alternatively, you can choose to reduce smoking during the first 12 weeks of treatment and quit by the end of that treatment period. You should then continue to take CHAMPIX 1 mg film-coated tablets twice daily for a further 12 weeks, resulting in a total of 24 weeks of treatment.
2. Bupropion:
- Is an oral non-nicotine therapy to assist cessation, which affects neuronal re-uptake of noradrenalin and dopamine.
- It is available only on prescription and not to be used on those who is under 18 years old
- Bupropion is available as a PBS Authority item once per year ‘as short-term adjunctive therapy for nicotine dependence with the goal of maintaining abstinence in patients who have indicated they are ready to cease smoking and who have entered a comprehensive support and counseling program’. Support and counseling can be provided by the GP or through referral to other programs. Bupropion is supplied as a commencement quantity of 30 tablets then a continuation quantity of 90 tablets. Arrangement should be made at the first consultation to book patient in for the follow-up visit.

Table 6. Varenicline dosing guidelines

A course of varenicline requires two or three authority prescriptions.

- An initial 4 weeks of treatment (including dose titration)

Smokers should start varenicline and then set a quit date 1–2 weeks after starting, but a later quit date is sometimes appropriate. The exact date can be determined on the basis of perceived effects of the drug. The recommended dose of varenicline is 1 mg twice per day following a 1-week titration as follows:

- Days 1–3: 0.5 mg once per day
- Days 4–7: 0.5 mg twice per day
- Day 8 on: 1 mg twice per day until the end of the 4-week course

- A further 8 weeks of treatment: continue with 1 mg twice per day until the end of the standard treatment week course
- To reduce a relapse, a further 12 weeks of treatment for those who successfully quit at 12 weeks: continue with 1 mg twice per day until the end of the 12-week course
**Administration:**
Several formulations are available, including a sustained-release formulation (Zyban, which is licensed as an aid to smoking cessation and is identical to the antidepressant forms: generic sustained-release bupropion and Wellbutrin SR).

**Dosing, duration and instructions for use:**

- Bupropion sustained-release is started one week before a smoker’s target quit date, since it takes five to seven days to reach steady-state blood levels.

- The recommended dose is 150 mg/day for three days, then 150 mg twice a day thereafter.

- We recommend treating for **at least 12 weeks**.

**Adjusting dosing and duration:**

- Bupropion 150 mg/day (rather than 300 mg/day) is an option for smokers who do not tolerate the full dose due to side effects.

- Longer duration of treatment can be considered in individual cases, based on the patient’s previous quit attempts and patient preference. However, if the rationale for longer treatment is improved mood, it is important to assess the change in depressive symptoms from the initiation of treatment and to make dosing adjustments accordingly.

**Relapse management and prevention:**
After quitting smoking, relapse is defined as smoking ≥ 7 cigarettes for seven consecutive days or for two consecutive weeks. After the quit date, treatment should be tailored to the level of craving and risk of relapse. There is an urgent need for studies validating tools and treatments for this.
purpose. A high craving score is an important factor in predicting the risk of relapse.

For patients who successfully quit smoking and then experience relapse, we suggest restarting a pharmacologic agent that previously worked for the patient. This may be enhanced with more intensive behavioral support and/or intensified pharmacotherapy (e.g., adding another medication).

Once lapses have occurred, the following interventions may assist with preventing relapse:

- Increasing CBT sessions in time, format and number sustains the effectiveness of treatment
- Using nicotine patches for more than 14 weeks plus short acting NRT formulations when needed
- Prolonging the use of varenicline from 12 to 24 weeks
- Prolonging the use of bupropion
- Combing medications.

**Smoking cessation in pregnancy:**

All pregnant women should have their smoking status assessed throughout their pregnancy and offered support with quitting

- Intensive behavioral / psychosocial intervention are recommended for all pregnant women who smoke
- NRT is the only medication that has been tested among pregnant women. There is mixed evidence to support the use of NRT as an effective strategy to support cessation at the present time; however the risk to fetus when compared to continued smoking is sufficiently less than using NRT.

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