ERS School Course
Smoking Cessation
The process of stopping smoking

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Educational aims

- To provide healthcare professionals and respiratory physicians with a practical set of information based on the recommendations made by recent relevant guidelines to facilitate the treatment of tobacco dependence.

Summary

The potential health benefits of smoking cessation are substantial; however, many people find it very difficult to quit. The main physiological obstacle is addiction to nicotine. This article aims to describe the "5 As" for effective intervention for smoking cessation that should be followed in current smokers. In addition, some baseline and follow-up assessments to be performed during a smoking cessation programme are proposed.

Tobacco use is the leading preventable cause of death, and is responsible for one out of every five deaths [1]. Hence, the potential health benefits of smoking cessation are substantial [2]. Approximately 70% of smokers worldwide report that they want to quit; however, only one third of them try to stop smoking each year, and fewer than 5–6% are successful in the long term when they attempt to quit on their own [3–5]. The main physiological obstacle to quitting smoking is the addictive action of nicotine. Nicotine causes tolerance and physical dependence. Psychological factors also contribute to the difficulties that smokers have when they try to quit. Stopping smoking is an incremental and very difficult process, in which attempts to quit may end in the resumption of smoking many times until complete abstinence is achieved. Smokers must learn new coping skills and try to break old patterns in order to have a successful quit attempt. This can be helped by counselling. Effective medical treatments are also available that can produce long-term or even permanent abstinence of tobacco use [6–9] (see Nicotine replacement).

As tobacco dependence is a chronic condition that often requires repeated interventions, it is essential that health professionals provide ongoing counselling, support and appropriate pharmacotherapy, in a similar fashion as for other chronic diseases, such as hypertension or hypercholesterolaemia. An estimated 70% of smokers see a physician each year, providing medical doctors with the opportunity to influence smoking behaviour [3]. To help smokers, physicians must be familiar with the spectrum of effective therapies. They must also appreciate that tobacco use has complex physiological

and psychological determinants, and understand that changing any behaviour is a gradual process [9–13].

Stages in the process of smoking cessation

The following steps are recommended as the "5 As" for effective intervention for smoking cessation in current smokers (figure 1) [6, 7].

Step 1: ASK (identify the smokers)

The first step in treating tobacco use and dependence is to identify smokers. Healthcare professionals have to ask the patient about smoking at every clinic visit. This can be done effectively by expanding the number of vital signs to include smoking status in the patient's notes for each patient at every clinic visit. Two questions are important: whether the person smokes currently and, if so, whether he/she is currently interested in stopping.

Step 2: ADVISE (give advice)

Smokers should be advised of the value of stopping smoking and the health risks of continuing smoking. Even brief advice from a healthcare professional can double the chances of a successful attempt to quit smoking, and such brief advice represents one of the most cost-effective healthcare interventions.

While not every smoker who presents to a clinic is willing to commit to an attempt to quit smoking during their visit, brief counselling interventions should be offered at every visit to maximise the patient's chance of a successful attempt. It is important that the clinician helps smokers to understand how the facts about smoking and health harm apply to them personally, and to consider smoking implications in a personalised manner.

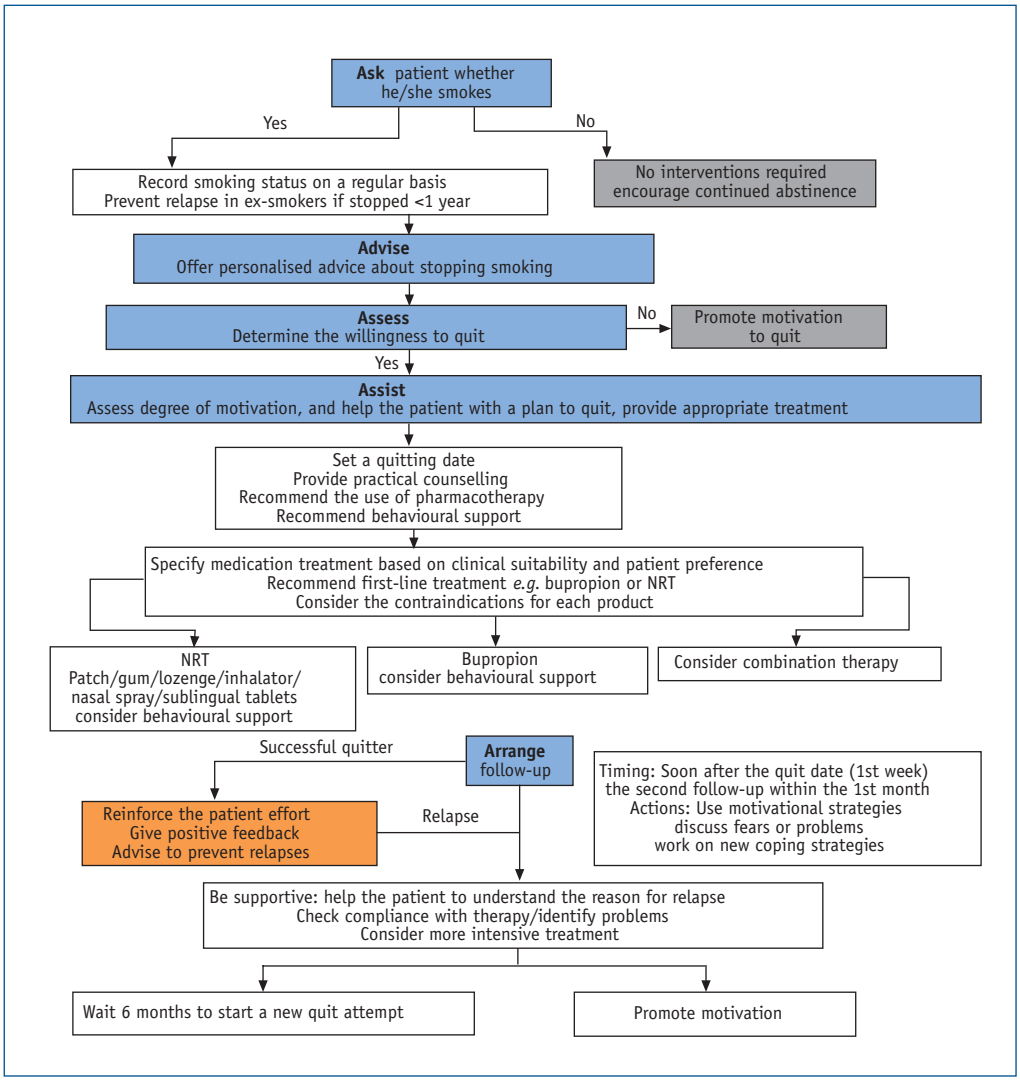

Figure 1
An illustration of the recommended smoking cessation steps and approved first-line interventions. NRT: nicotine replacement therapy.

Step 3: ASSESS (assessment of motivation to quit smoking)

One important step in the process of stopping smoking is to identify the motivated quitters and assist them to stop smoking.

The three following questions will help health professionals to recognise motivated quitters and get them started on an appropriate action plan:

1. Does the patient want to stop smoking?
2. How important is it for the patient to stop smoking?
3. Would the patient be prepared to stop smoking in the next 2 weeks?

There are three main types of patients regarding tobacco use:

1. Current smokers who are willing to make an attempt to quit smoking.
2. Current smokers who are unwilling to make an attempt to quit.
3. Ex-smokers who have recently quit.

However, other different types of smokers may be characterised according to the answers to these questions. Smokers may be in a pre-contemplation stage if they have no intention of giving up smoking within 6 months, and they may be in the preparation stage if they are planning to give up within a 1-month time period.

It is important to be able to identify those people who are motivated to quit. These smokers are most likely to succeed in stopping smoking and should be the target group for the immediate offer of a smoking cessation programme with support and treatment.

However, a smoking cessation intervention programme also has to focus on smokers who have not committed to the idea of giving up, in order to increase their motivation. Some smokers may be unwilling to make an attempt to quit either because they lack information about the harmful effects of tobacco or because they may not realise how these effects are relevant to their personal health history. They may also have fears or concerns about quitting, or they may be demoralised because of previous relapse experiences. Motivational information has the greatest impact if it is relevant to the patient's disease status, family (*e.g.* children at home) or social situation, or other patient characteristics (*e.g.* prior quitting experiences, other problems to find therapy). Clinicians have to provide appropriate information regarding the acute- and long-term risks of smoking and also the potential benefits of stopping smoking, whilst highlighting those that are the most relevant to the patient. A list of the potential benefits may help the smoker to identify the personal rewards of his attempt (*e.g.* improved health, food taste, better sense of smell, improvement in physical activity, reduction of wrinkling/ageing of skin, having healthier babies, setting a good example for the family, improved personal image, *etc.*).

The motivational intervention should be repeated every time an unmotivated patient visits the clinic. In the case of smokers who have failed in a previous quit attempt, reinforcement is needed to reassure them that most people make repeated quit attempts before they are successful.

The clinician has also to give time for discussion and identify barriers to quitting (*e.g.* withdrawal symptoms, fear of failure, weight gain, lack of support, depression, enjoyment of tobacco).

A patient's willingness to give up smoking may also be assessed by simply asking the patient to rate, on a 10-point scale, "how important is it to you to give up smoking?" and also "how confident are you that you would succeed if you were to decide to stop smoking?". If the rating for motivation is high but the self-efficacy is low, the treatment and the support are critical for success. If self-efficacy is high but the willingness to try is low, more effective health education is important. If both are low, both motivation and self-efficacy need to be built up by the clinician. In case of a high scores on both questions, a quit date could be set immediately.

Step 4: ASSIST (aid the smoker in quitting)

If the smoker does want to stop, the clinician has to help him with a plan to quit. The following points have to be covered:

- Set a quit date, ideally in 2 weeks (try to find a "special day" for commitment, to quit completely and abruptly).
- Provide practical counselling and skills training (*e.g.* review past quit experience and learn from it, *i.e.* What helped? What factors were related to relapses?).
- Discuss possible nicotine withdrawal symptoms and how the patient can successfully overcome them, particularly during the critical first few weeks.
- Identify other problems and plan how to cope with them.
- Ask family and friends for support (particularly a spouse or partner).
- Make a personalised action plan with treatment recommendations.

Information relating to how to stop can be

reinforced with leaflets, booklets or other self-help materials.

All smokers can be given information about pharmaceutical treatments (either nicotine replacement therapy or bupropion) and all those who smoke >10 cigarettes per day should be encouraged to try them (either attending a specialist smoking cessation clinic or a clinician's office). The clinician should explain how these medications increase smoking cessation success and reduce withdrawal symptoms, and explain that they are first-line pharmacotherapy for smoking cessation worldwide. Clinical examination and patient history are strongly suggested before any pharmaceutical treatment.

The importance of total abstinence should be strongly emphasised: "not even a single puff after the quit date".

Triggers or any challenges in an upcoming attempt should be anticipated; for example, drinking alcohol is highly associated with relapses and the smoker should consider limiting or abstaining alcohol during the quit process. The clinician should also discuss that the presence of other smokers in the household is associated with lower abstinence rates. Therefore, partners or spouses should be encouraged to make a common effort to quit smoking.

Table 1 The Fagerström Test for Nicotine Dependence

Question	*Options*	*Points*
How soon after you wake up do you smoke your first cigarette?	*≤5 min*	*3*
	6–30 min	*2*
	31–60 min	*1*
	>60 min	*0*
Do you find it difficult to refrain from smoking in places where it is forbidden?	*Yes*	*1*
	No	*0*
Which cigarette would you hate most to give up?	*The first one in the morning*	*1*
	Any other	*0*
How many cigarettes per day do you smoke?	*≤10*	*0*
	11–20	*1*
	21–31	*2*
	≥31	*3*
Do you smoke more frequently during the first hours after waking than during the rest of the day?	*Yes*	*1*
	No	*0*
Do you smoke if you are so ill that you are in bed most of the day?	*Yes*	*1*
	No	*0*

One more recently published scale for assessing dependence is the Cigarette Dependence Scale [16].

Step 5: ARRANGE (arrange a follow-up contact)

Follow-up is important in maintaining motivation and in providing continuing support. For some smokers, referral to a specialist smoking cessation clinic will be appropriate.

Follow-up visits should occur soon after the initiation of the smoking cessation intervention near the quit date, preferably during the 1st week, with a second visit within the 1st month. More frequent contact or visits (ideally once weekly) are needed to assess the responsiveness to pharmacological treatment, to consider the use of more intensive treatment or to monitor possible side-effects of medications. Telephone contact may also be helpful. At each follow-up, contact success should be congratulated, and problems and difficulties should be identified to help facilitate the patient's attempt. Further follow-up contacts are also essential for support to prevent relapses. Ideally, cessation should be validated in 1 month, and then again in 3, 6 and 12 months.

Baseline and follow-up assessments during a smoking cessation programme

Nicotine dependence

Tobacco dependence is an important factor that has to be assessed at the initiation of a smoking cessation programme. The Fagerström questionnaire for Nicotine Dependence (FTND) is a widely used and researched short (six items) questionnaire (table 1) [14]. The information can be obtained in an interview or the smokers can fill in the questionnaire themselves. The score ranges 0–10 and the average of representative samples of smokers is usually in the range of 3–4 points. The two most important questions to answer are time to first cigarette in the morning and number of cigarettes. Just these two questions give almost as much information as the whole questionnaire. Recently, it has been suggested that the best indicator of dependence is time to first cigarette [15]. Another strong, but relatively infrequent, indicator of dependence is nocturnal smoking. These smokers usually score very highly on the FTND.

CO measurements

Expired air carbon monoxide (CO) measurements using a portable analyser can be seen as an indicator of total smoke intake [17]. The CO concentration in the body can easily be obtained by having the smoker exhale into a CO analyser. The measurement unit of CO is in parts per million (ppm) and can easily be converted to COHb. Measuring CO in smokers also has a great motivational value. The smoker blows into the machine where they immediately and invariably see a high-value reading (normally >10 ppm; 2–5% COHb) that can be compared with the normal value of <5 ppm. The abnormal CO value detected can be used to inform the smoker of the mechanisms by which smoking, and particularly CO, contributes to cardiovascular disease. CO is recommended for the validation of smoking cessation. CO has a half-life of approximately 4 hours. One or certainly 2 days after the last cigarette, CO is normal. This rapid normalisation is very rewarding for the subject to see. After normalisation of the CO assessment, it can be used for control purposes, which usually is a good support during the follow-up.

Smoking cessation clinics

Over the last few years, the long-realised importance of smoking cessation in treatment and in improving prognosis among patients has been translated into the provision of well-organised smoking cessation clinics that offer more intensive interventions to smoker patients who want to quit. Many of these services are hospital based in order to provide help to patients with smoking-related diseases. Specific recommendations for hospital-based smoking cessation services have been published by the Tobacco Committee of the British Thoracic Society [18]. These services should have close links with the community cessation services. Essential communication skills in individual smoking cessation, performed by clinicians at a level of clinic-based smoking cessation programmes, have been well described in a recent review paper [19].

The experience from one smoking cessation clinic, organised by the respiratory department in a general hospital [20], suggests that an intensive programme with individual counselling support performed by the respiratory physicians, in combination with medication treatment, was more effective than cognitive behavioural treatment carried out by specialists. It is essential that respiratory physicians play a leading role in smoking cessation initiatives and further organisation of smoking cessation clinics, as stopping smoking is the major treatment intervention in many respiratory diseases. The consistent identification, documentation and suggestion of treatment to every smoker who is seen in a healthcare setting is mandatory in order to fight a real-world epidemic such as smoking.

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Nicotine replacement in smoking cessation

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Statement of interest

K. Fagerström has received speaking fees, been reimbursed to attend symposia and consulted for most of the pharmaceutical companies with an interest in tobacco-dependence treatments. K. Fagerström owns stock in a small company (NicoNovum AB, Helsingborg, Sweden), which develops nicotine replacement products. K. Fagerström chairs an advisory board for Swedish Match, which oversees its Food and Drug administration application for registering snus as a smoking cessation treatment.

The rationale for nicotine replacement is that when the smoker stops smoking cigarettes, the administration of nicotine in a different modality will decrease withdrawal symptoms during the initial phase of smoking abstinence. Pharmacological dependence on cigarettes is then transferred to the nicotine replacement product, enabling the subject to focus on the behavioural aspects of coping with the urges from a strongly ingrained habit. Usually, pharmacological dependence is not fully maintained because of a lower level of nicotine in these products compared to cigarettes. After a variable period of 2–6 months, the nicotine supplementation can be gradually tapered off. In essence, nicotine dependence is transferred, tapered and eliminated. Different types of nicotine replacement modalities are presented here.

Transdermal systems

There are three main nicotine patches on the market. The main difference between the patches is their drug release kinetics.

Twenty-four-hour patches (Niquitin®; GlaxoSmithKline, Brentford, UK; and Nicotinell®; Novartis, Horesham, UK) produce a more even and sustained blood level of nicotine throughout the entire day and night, whereas the 16-hour patch (Nicorette®; Pfizer Ltd, Tadworth, UK) provides nicotine replacement only during waking hours. The two patches designed for 24-hour application contain and deliver higher total amounts of nicotine than the 16-hour patches. Peak plasma nicotine concentrations, which are normally reached within 4–9 hours after patch application, vary between 13 and 23 ng per mL. Trough levels normally range 2–11 ng per mL.

Acute systems

Nicotine gum

After a single dose of nicotine gum, the increment in plasma nicotine levels is ~4–5 mg per mL for the 2 mg strength and 6–7 mg for the 4 mg strength. After a single dose, the time to maximum concentration is achieved after ~30 minutes. In clinical trials, nicotine concentrations have been shown to equate to about one-third of smoking nicotine levels with the 2 mg strength and two-thirds with the 4 mg strength. In reality, gum use is usually between 5–10 pieces per day, and the plasma nicotine concentrations, therefore, rarely exceed 10 ng per mL for the 2 mg strength and 15 ng per mL for the 4 mg strength.

Nicotine nasal spray

One dose of nicotine nasal spray consists of 1 mg of nicotine, 0.5 mg to each nostril. The spray is the fastest acting of the nicotine replacement products. It takes <10 minutes to reach maximum plasma concentration and the increment of a dose is about 3–5 ng per mL. If used regularly, 1, 2 or 3 times per hour, the plasma nicotine concentrations after 12 hours are 6, 13 and 18 ng per mL, respectively. Although the spray is faster than gum, it is still slower than nicotine uptake from a cigarette.

Oral inhaler

The oral inhaler, a mouthpiece 90 mm long and 10 mm wide, contains a porous plug that is saturated with 10 mg nicotine plus 10% menthol to mask the taste of nicotine and reduce irritation. It is a flexible *ad libitum* dosing form, but offers more habit replacement than any of the other nicotine replacement products.

When room temperature air is sucked through the porous plug, the nicotine concentration is 2 μmol per L. A puff of 50 mL (similar to an ordinary puff on a cigarette) releases ~0.1 μmol, whereas a cigarette would give about 1 mmol. With higher ambient temperature, the concentrations of nicotine increase, but will not reach the yield of a cigarette. In other words, the oral inhaler is a relatively weak nicotine-dosing system, which requires the subject to work hard to obtain reinforcing levels of nicotine. Moreover, in a study where nicotine was radioactively labelled, it was found that only very minute amounts are inhaled into the lungs. Most of the nicotine was deposited buccally or in the upper respiratory tract. With ordinary use, the inhaler gives about the same nicotine concentrations as 2 mg gum.

Sublingual tablet

The sublingual tablet contains 2 mg nicotine. The tablet should be kept under the tongue and be allowed to dissolve for ~20 min. The sublingual tablet is bioequivalent to nicotine gum 2 mg. It is recommended that highly dependent smokers use two tablets.

Lozenge

Like nicotine gum, nicotine from lozenges is absorbed slowly through the buccal mucosa and delivered into the systemic circulation. The amount of nicotine absorbed per lozenge appears to be somewhat higher than that delivered by gum. Single-dose studies have demonstrated 8–10% higher maximum concentration values and 25–27% higher area under the curve values from 2- and 4-mg lozenges (Niquitin) compared to gums at both 2- and 4-mg dose levels, respectively, which is probably due to the residual nicotine retained in the gum. There is also a 1-mg lozenge (Nicotinell) available for lighter smokers in some countries. The indication for the lozenge allocates smokers to the 2- or 4-mg dose based on whether the first cigarette of the day is smoked within 30 minutes after awakening or not.

Figure 1 shows plasma nicotine levels for smoking compared with some of the systems described above.

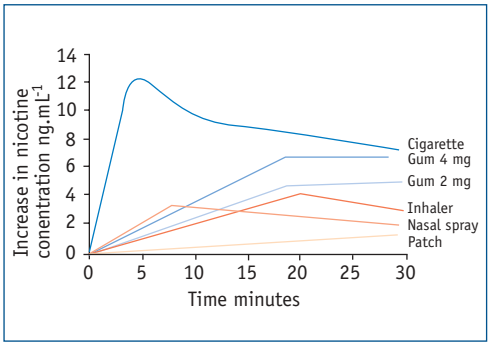

Figure 1
Plasma nicotine concentrations for smoking and nicotine replacement therapy. Modified with permission from BALFOUR *and* FAGERSTRÖM.

Combination of products

Under-dosing is very common with nicotine replacement products. Many smokers, particularly highly dependent smokers with a higher intake of nicotine, experience great difficulties in fully substituting their habit with current nicotine replacement products. Therefore, some researchers have evaluated combining products.

The rationale for a concurrent combination of

Suggested further reading

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Shiffman S, Fant R, Gitchell J, Cone E, Henningfield J, Fagerström KO. Nicotine delivery systems: how far has technology come? Am J Drug Deliv 2003; 1: 113–124.
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nicotine medications is that the provision of nicotine using different forms and modes of delivery can provide improved symptom relief and possibly enhanced cessation outcomes than either product used alone, by more adequately providing both higher daily levels of nicotine and the on-demand doses so readily provided by cigarettes. The nicotine patch, which delivers nicotine in a passive form, produces relatively steady levels of drug in the body. A patch provides a general reduction of withdrawal symptoms and craving after application. However, this steady-state nicotine dosing does not allow users to respond to "breakthrough" cravings with acute nicotine doses. These cravings, while usually brief, can be quite intense and are probably significant contributors to relapse. Most studies testing the efficacy of combined nicotine replacement found it to be more effective than single product use.

In summary, all current nicotine replacement products have a similar efficacy. Choice of product is, therefore, largely a matter of preference.

Safety

The safety of nicotine replacement medications when used alone has been well demonstrated in numerous clinical trials. In general, nicotine-delivering medications provide lower doses than those obtained by cigarette smoking, and the rate of nicotine infusion to arterial blood is substantially slower for nicotine medications than that achieved from inhaled cigarette smoke. Despite the fact that nicotine can produce adverse effects, severe acute adverse effects rarely occur when people are smoking or using nicotine replacement products, since tobacco users quickly learn not to exceed nicotine concentrations that are at the threshold for producing effects such as nausea or light headedness.

When smoking tobacco is the alternative, there are no contraindications for nicotine replacement.

The use of antidepressants in smoking cessation

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Bupropion
Bupropion (Zyban) is an older antidepressant drug, an amino-ketone agent, with an inhibitory effect on noradrenaline and dopamine re-uptake, although it may also have a direct effect on neuronal nicotinic receptors. A large number of studies have been performed on this drug. Bupropion is as efficacious as nicotine replacement therapy and generally well tolerated in smoking cessation. It is regarded a first-line medication. The most common adverse events from bupropion are insomnia and dry mouth. Aggravation of hypertension is also reported, as well as allergic rash. The most serious adverse event is seizures.

Nortriptyline
Nortriptyline is a classical tricyclic antidepressant and has been shown to be effective in smoking cessation. It is not clear if the effect of this agent on smoking cessation is drug specific or a class effect. As the potential side-effects of nortriptyline are more troublesome and serious compared with bupropion, nortriptyline is relatively seldom used for smoking cessation.

Other antidepressants
Several other antidepressants have not been found to be effective in smoking cessation, i.e. doxepin, fluoxetine, sertraline, moclobemide and venlafaxine. It also means that the selective serotonin reuptake inhibitor has no proven role in smoking cessation.