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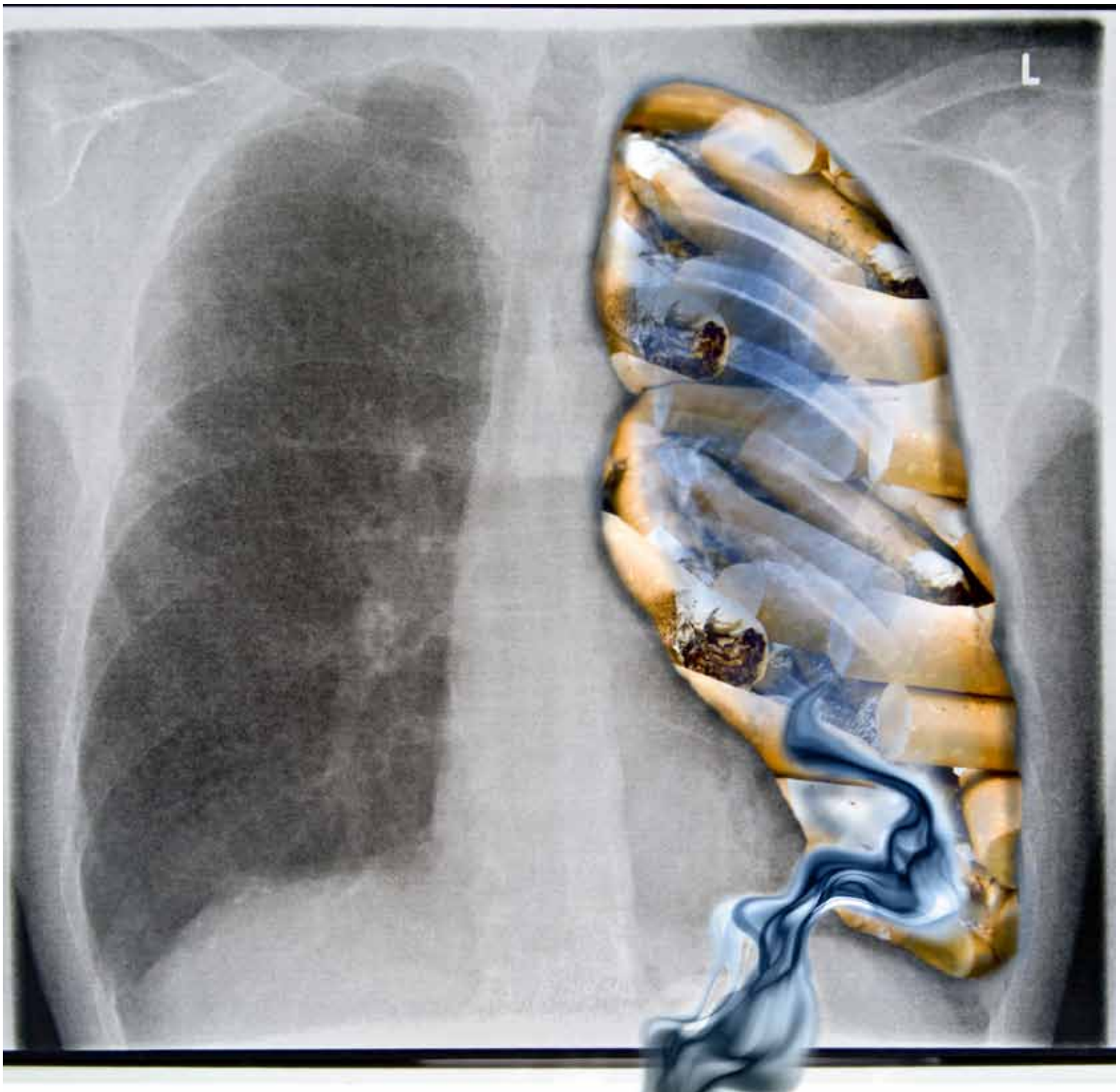

Nicotine dependence

Introduction

SMOKING is the single greatest cause of preventable illness and death in Australia. About half of all lifelong smokers die prematurely from their habit and smokers live 10 years less than non-smokers on average.[1]

Although the number of smokers is slowly falling, 18% of Australians aged 14 or over still smoked in 2010 (3.3 million people).[2] Smoking is especially common in people with mental illness, in Indigenous communities in people with substance abuse disorders and in lower socioeconomic groups.

Most smokers want to quit, and most make repeated attempts to do so. About 40% try to stop smoking at least once each year.[3] However, long-term quitting is an elusive goal for many smokers. Only 3-5% of unaided quit attempts are successful 6-12 months later.[4] Most smokers need assistance to quit and GPs are well placed to assist them.

Quitting is an urgent health priority for all smokers. After the age of 35 years, three months of life is lost for each year of continued smoking.[1] The risk of most smoking-related diseases also diminishes rapidly after quitting.

Smoking is no longer seen as a habit or lifestyle choice of the weak-willed. The new paradigm of smoking defines it as a powerful drug dependence with a strong genetic basis. Smokers deserve an empathic, non-judgemental and supportive approach.

This article presents an update on nicotine dependence. It discusses the role of nicotine metabolism, the importance of nicotine dependence and the overlooked issue of drug interactions with smoking. The latest evidence-based strategies for GPs to help smokers quit are provided with a comprehensive update of pharmacotherapy.

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INSIDE

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Classifying smoking

Smoking as a substance abuse disorder

IN the DSM IV-TR (Text Revision), smoking (nicotine dependence) is classified as a substance abuse disorder mediated by powerful neurochemical processes.[5] Twin studies have demonstrated that genetic factors account for 50-60% of the chance of becoming nicotine dependent after starting to smoke.

Like other drugs of abuse, nicotine activates the reward pathway in the brain, releasing dopamine that generates the pleasurable sensations associated with smoking. Dopamine levels fall within a few hours of the last cigarette, leading to withdrawal symptoms and the urge to smoke again.

Chronic nicotine exposure upregulates nicotine receptors. Over time, there are more receptors releasing dopamine, making quitting even more difficult.

Smoking is further reinforced by specific behaviours and situations that are associated with smoking, such as drinking a cup of coffee or the smell of smoke. Exposure to these smoking cues can trigger a strong craving for a cigarette.

Smokers also smoke for the other positive effects of nicotine. Nicotine can generate arousal, heightened alertness, relief of anxiety or depression, reduced hunger and control of body weight.

Smoking as a chronic disease

Smoking is also now conceptualised as a chronic medical illness requiring ongoing care.[5] Smokers typically make frequent, brief attempts to quit, interspersed with relapses and periods of cigarette reduction, often over a period of many years.

A chronic disease model is more appropriate for nicotine dependence than an acute care approach. Like patients with diabetes, smokers need to be reassessed and re-engaged at regular intervals over the long term.

The pathway to quitting can be gradual or sudden. Many smokers move through the different stages of readiness to quit, building motivation, and ultimately planning and attempting to quit. However, almost half of all quit attempts are abrupt or spontaneous and involve no planning or assistance.

Failed attempts are a normal part of the quitting process. They are valuable learning experiences, making the next attempt more likely to succeed. Smokers should be encouraged to keep trying to quit. Most smokers make repeated attempts to quit before finally achieving long-term abstinence.

The role of nicotine metabolism

The individual's rate of nicotine metabolism has an important impact on smoking behaviour and response to treatment. Most nicotine is metabolised in the liver by the cytochrome P450 2A6 enzyme. Genetic variations in the enzyme determine the rate of nicotine breakdown, which can vary by up to fourfold.[6]

Slower metabolisers have lower nicotine dependence, smoke fewer cigarettes, respond better to nicotine replacement therapies and are able to quit more easily.

Rates of nicotine breakdown also vary considerably across gender and race. For example, men metabolise nicotine more slowly than premenopausal women and Asian populations are slower metabolisers of nicotine than Caucasians.

The role of the GP

SMOKERS have lost control of their behaviour and many need assistance, especially those with higher levels of nicotine dependence.

GPs are in a prime position to help.[7] Most smokers consider their doctor to be an appropriate person to help them quit. Brief intervention by GPs can have a substantial impact on quit rates, and smoking cessation interventions are among the most beneficial preventative interventions available.

However, GPs are missing many opportunities to help smokers quit. Australian research shows that GPs identify only two-thirds of their patients who smoke and advise about half of these to quit.

The main barrier to GP intervention is a lack of time. However, there is good evidence that even very brief advice by the GP (as little as three minutes) is effective in increasing quit rates. More intensive interventions are even more effective.

GP intervention

GP intervention, as described in the Australian guidelines is based on the 5As framework (figure 1, right).[8]

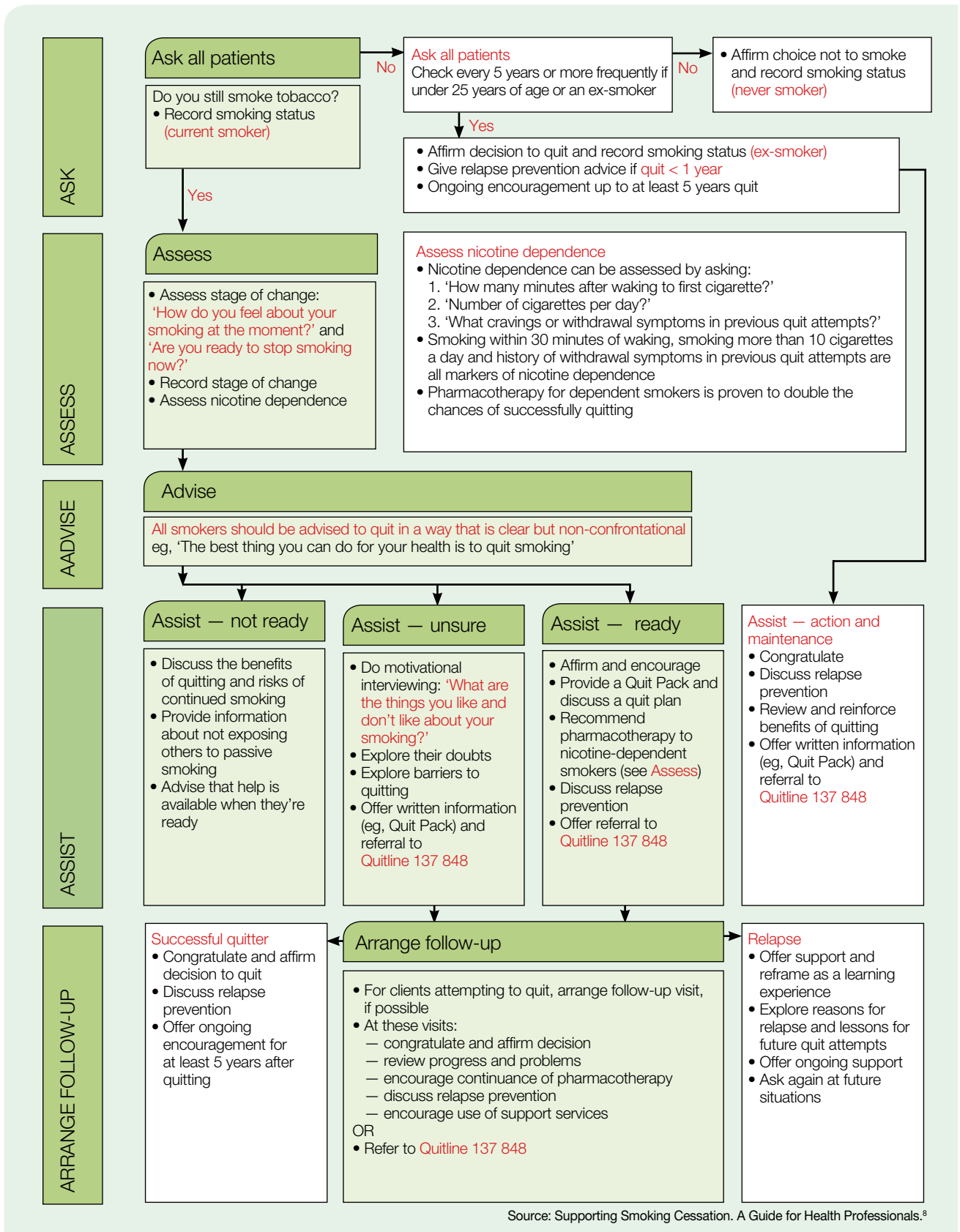
Ask
Regularly ask all smokers if they smoke and record the information in the medical record.

Assess
Assess smokers for their readiness to quit, barriers to quitting and the level of nicotine dependence.

Advise
Advise all smokers to quit in a clear, non-confrontational way.

Assist
Smokers who are ready to quit are offered advice, pharmacotherapy and support.

Arrange
Provide follow up visits for additional advice and support.



Source: Supporting Smoking Cessation. A Guide for Health Professionals.[8]

Figure 1: The five As of smoking cessation.

Assessing nicotine dependence

The level of nicotine dependence helps predict the severity of withdrawal symptoms and is a guide to the intensity of treatment required. It is also a powerful predictor of success.

The single most reliable indicator is the time to the first cigarette of the day. As most nicotine is cleared overnight (the half-life of nicotine is two hours), smokers wake in a state of nicotine deprivation. Smoking within 30 minutes of waking is a reliable sign of nicotine dependence. Smoking within five minutes of waking indicates high dependence.[8]

Cravings and withdrawal symptoms experienced in previous quit attempts are also a useful guide to nicotine dependence.

The number of daily cigarettes is a less useful guide to nicotine dependence because self-reports are often unreliable and smoking behaviour varies from one smoker to the next. Nevertheless, the level of nicotine dependence rises with higher daily consumption. Smoking more than 10 cigarettes a day is generally associated with a greater likelihood of dependence.

Barriers to quitting

SMOKERS typically have concerns or barriers that undermine successful quitting, such as weight gain, stress, withdrawal, peer pressure and a fear of failure. It is useful to explore these barriers, providing accurate information and strategies to address them.

Weight gain

Fear of weight gain is a major barrier to quitting smoking, especially for women, and this issue should be raised in the consultation.

The mean weight gain due to quitting is 4-5kg after 12 months.[9] A further 2-3 kg is typically gained over the next few years. However, 10% of men and 13% of women are at risk of major weight gain (>13kg).

Weight gain after quitting is mostly due to the loss of the appetite-suppressing effect of nicotine and the lower metabolic rate after quitting.

Smoking cessation medications can reduce weight gain during treatment by 0.5-1kg, but this small benefit is not maintained at 6-12 months.

Two recent reviews of weight gain prevention strategies concluded that interventions are of borderline clinical benefit and are not justified on current evidence. There was mixed evidence for exercise in reducing weight gain. Giving general advice about reducing kilojoules was not shown to be effective in controlling weight or in achieving abstinence and is not recommended.

A pragmatic solution is to advise patients to eat sensibly, exercise regularly and to accept some weight gain. Explain that one in four quitters will lose weight or stay the same and that the health benefits of quitting are almost always greater than the health effects of the extra weight.

Nicotine withdrawal symptoms
Irritability, frustration, anger
Increased appetite and weight gain
Difficulty concentrating
Restlessness
Depressed mood
Disturbed sleep
Mouth ulcers
Constipation

Coping with stress

Smokers often report using smoking to help them cope with stress. However, the latest research consistently shows that smoking actually increases stress levels.[10]

As nicotine levels fall between cigarettes, smokers repeatedly slip into nicotine withdrawal, resulting in frequent episodes of anxiety and restlessness. When a cigarette relieves these symptoms, it is easy to see why smokers think cigarettes reduce stress. In fact, the cigarette is simply relieving the nicotine withdrawal it has created.

Many people also feel guilty or ashamed of smoking and worry about the damage to health from smoking, and this creates additional stress. Furthermore, nicotine releases stress hormones in the body such as adrenaline that increase feelings of anxiety further.

A number of studies have found that 6-12 months after quitting, ex-smokers are more relaxed than continuing smokers.

Short-term anxiety may occur in the first few days after quitting due to withdrawal from nicotine. However, this effect can usually be well controlled by smoking cessation medication.

There are much healthier and more effective ways to relax than smoking. Alternatives include exercise, a relaxation technique, reading, music and professional counselling.

Withdrawal

Nicotine withdrawal symptoms (see box, left) and cravings are the main reason most 'cold turkey' quit attempts fail in the first few days. Withdrawal symptoms are at their peak for 48-72 hours and the worst is over by 10-14 days.[8]

Cravings can be quite severe, but only last 2-3 minutes. Cravings become weaker and less frequent over time but can last for many years.

Withdrawal symptoms can be reframed as evidence of recovery from nicotine addiction. They are signs of the body repairing itself and will gradually settle.

Patients should be reassured that smoking cessation medications provide effective relief from cravings and withdrawal symptoms. The nicotine patch, varenicline and bupropion provide steady background relief (see Pharmacotherapy, page 30). These can be combined with short-acting forms of nicotine replacement therapy (mouth spray, lozenge, gum and inhaler), which give quick relief of breakthrough cravings. The nicotine mouth spray provides the fastest craving relief.

Counselling

THE most effective way to quit smoking is with a combination of counselling and pharmacotherapy.[8] Counselling enhances motivation, teaches practical quitting skills and provides support. Pharmacotherapy is discussed in the next section.

Hypnotherapy and acupuncture are not recommended as there is no consistent evidence for their effectiveness. There is also a lack of evidence for the Allen Carr method, NicoBloc, Nicobrevin, naltrexone and St John's wort.[8]

Before quitting

Quitting smoking is like going into battle. It is advisable to see the patient once or twice before they quit, to help them prepare for the challenge. Some effective strategies to help them are as follows.

Keep a smoking diary

A smoking diary helps patients understand their habit and identifies their smoking triggers.

Plan coping strategies

Cravings for a cigarette are often triggered by specific situations, people or moods. It is important to identify these triggers or cues and to plan coping strategies for when they occur after quitting. These include distraction (thinking or doing something else), avoiding situations or people that trigger cravings, delaying a cigarette and escaping from a difficult situation.

Some coping tips for common triggers include:

- **On waking.** Have a shower as soon as you get out of bed, clean your teeth, go for a walk. Have a dose of the nicotine mouth spray, which works quickly.
- **Coffee.** Change to tea or herbal tea, have orange juice or water. Have your coffee in a different place, where you usually don't or can't smoke. Try a different brand of coffee. Use a different cup.
- **After dinner.** Clean your teeth straight away, clear the table and wash the dishes, go for a walk.
- **Phone calls.** Keep a doodle pad next to the phone. Answer with the other hand.

Discuss smoking barriers

Discuss the patient's barriers to quitting (see above).

Stop smoking in the house or car

This helps to weaken the association between smoking and the home and car before quitting.

Lifestyle changes

Suggest activities such as a new hobby or sport to fill the extra time patients will have after quitting. Consider other healthy lifestyle changes such as healthier eating or drinking less alcohol.

Exercise is recommended for all smokers trying to quit. Exercise reduces cravings and stress, reduces weight gain, helps prevent relapse and has many other health benefits.

Reduce caffeine and alcohol

Smoking accelerates the metabolism of caffeine. After quitting, blood levels rise and patients can develop caffeine toxicity, which can be confused with nicotine withdrawal. Reducing caffeine by half is recommended.[11]

Alcohol is strongly associated with smoking and a few drinks can undermine the decision to quit. It is best for patients to avoid alcohol for the first 2-3 weeks if possible and to reduce their alcohol intake subsequently.

Social support

Suggest patients tell family and friends they are quitting and ask for their support.

Set rewards

Smokers often feel deprived when they quit and setting short- and long-term rewards can help motivation. Cigarette money can be used to purchase well-deserved treats.

Set an appropriate quit day

The nicotine patch works best if started about two weeks before quit day. Varenicline and bupropion are started at least one week before quit day.

Agree on a quit day in the following two weeks. It is best to pick a day without too much pressure but one that still has activities to keep busy. A firm quit day is not essential, and some smokers chose to work towards quitting and quit when they feel ready.

Smokers can decide whether to stop abruptly on quit day or cut down gradually. Both methods are equally effective.

Advise patients to throw away all their cigarettes before bed on the day before quit day. Get rid of all ashtrays, lighters, matches and other smoking paraphernalia. Don't leave a pack around "just in case".

Quit day

See the patient on quit day to review the quitting strategy and boost motivation. Check that the medication is being taken correctly and emphasise that it should be continued for a full course.

Most relapses occur in the first week after quitting and are usually due to nicotine withdrawal. This period requires special vigilance and full doses of medication. Advise patients to take special care to avoid their personal triggers and situations that are high risk for smoking. For example, consider avoiding the pub on Friday nights if that is a powerful smoking trigger.

If the patient is using the nicotine patch, instruct them to leave it on if a lapse occurs.

After quit day

Follow-up visits to discuss progress and provide support have been shown to increase the chance of success. As the risk of relapse is greatest in the weeks after quitting, it is best to see the patient more frequently early on. Start by seeing the patient within a week of quitting. At follow-up visits:

- Give the patient genuine praise and encouragement.
- Discuss smoking triggers. Review slips in detail and plan more effective coping strategies.
- Review medication. Is it being used correctly? Are there side effects? Does the dose need to be increased?
- Review any improvements in wellbeing.
- Advise patients
  - Not to have even one puff
  - To keep busy and active
  - To take one day at a time.

Negotiate further follow-up visits as required.

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Pharmacotherapy

PHARMACOTHERAPY eases the physical discomfort of nicotine withdrawal and reduces cravings. It is recommended for all nicotine-dependent smokers who are ready to quit, unless there are contraindications.

The three first-line treatments are nicotine replacement therapy, varenicline and bupropion. All of these medications result in quit rates about double that in those who attempt without pharmacotherapy.[8]

The choice for individual patients is based on past experience, side effects, efficacy, contraindications, drug interactions (in particular with bupropion), patient preferences and cost.

Due to genetic and other variables, patients have individual responses to all of the smoking pharmacotherapies. If a medication has worked well in the past and been well tolerated, it is good practice to use it again.

Nicotine patches, varenicline and bupropion are available on the PBS with an authority prescription (table 1).

PBS requirements for prescribing are:

- Short-term, sole PBS therapy
- Patient ready to stop smoking
- Patient entered a comprehensive support and counselling program

Nicotine patches, varenicline and bupropion can be prescribed in the same 12-month period, but only one at a time. The period between commencing varenicline and bupropion must be at least six months.

Nicotine replacement therapy

Nicotine replacement therapy is the most widely used pharmacotherapy and is the only one approved in pregnancy, lactation and adolescence.[8,12] Two different forms of therapy are available:

- Long-acting form: The nicotine patch provides a steady background level of nicotine throughout the day.
- Quick-acting oral forms: Nicotine gum, lozenge, inhaler and mouth spray (the microtab has been discontinued) provide faster relief of cravings for a shorter duration.

Patient compliance and nicotine safety

Compliance with nicotine replacement therapy is generally poor. Most smokers use less than the prescribed dose of medication and do not take the full course of treatment.

A major cause of poor compliance is misinformation about nicotine replacement therapy. Many smokers believe that it is unsafe, is not effective or is addictive. Addressing these concerns with scientific information greatly increases the therapy's uptake and improves compliance.[13]

Although nicotine is the main cause of dependence on tobacco, it is not carcinogenic, does not cause respiratory disease and has only minor haemodynamic effects. However, it can delay wound healing, increase insulin resistance and is associated with harmful effects on the fetal brain and lungs. Nevertheless, nicotine replacement therapy is always safer than continuing to smoke.

Compliance with nicotine replacement therapy is generally poor.

This therapy can be used by patients with stable cardiovascular disease, but should be used with caution in people with recent MI, unstable angina, severe arrhythmias and recent cerebrovascular events.

Correct use

The oral, quick-acting forms of nicotine replacement therapy (lozenges, gum, inhalator, mouth spray) are often used incorrectly, resulting in lowered effectiveness and more side effects. It is vital to instruct patients on their correct use and to review their technique at follow-up visits (table 2).

Adequate dose

In general, patients using nicotine replacement therapy receive too little nicotine, partly due to misguided concerns about safety. The dose of nicotine needs to be titrated upwards to provide adequate relief of cravings and withdrawal symptoms for each individual.

Smokers of 10 or more cigarettes per day should normally start with a full-strength patch (21mg/24-hours or 15mg/16-hours). If cravings or withdrawal symptoms are not controlled, an oral form of nicotine replacement therapy should be added.

Smokers who smoke within 30 minutes of waking are advised to use the 4mg lozenge or gum instead of the 2mg product, regardless of their cigarette consumption.

Smokers who are more nicotine dependent or those who metabolise nicotine more quickly generally need larger doses.

Side effects

Adverse effects with nicotine replacement therapy depend on the delivery system. For the patch, they include skin irritation, disturbed sleep and abnormal dreams. For oral treatments, side effects include dyspepsia and nausea, hiccups, jaw pain (gum) and mouth and throat irritation (inhaler and mouth spray).

Combination therapy

Combining the nicotine patch with an oral form of nicotine replacement has been shown to increase quit rates by about 50% compared with using the patch alone. The patch provides a steady protection against background cravings and the oral forms give quick, flexible relief for breakthrough cravings as a result of smoking triggers, such as the smell of smoke.

Many smoking cessation experts now recommend combination therapy for all nicotine-dependent smokers using nicotine replacement, rather than monotherapy.

Multiple nicotine patches have a more modest benefit, increasing quit rates by 15% compared with single patch use.

Pre-cessation use of nicotine patch

Best practice for using nicotine patches is to start two weeks before quit day as this increases success rates over and above the traditional quit day application by 35%. Smoking while using nicotine replacement therapy is safe and is not associated with any additional adverse reactions. Patients need to be reassured about this.

Continuing nicotine patch after a lapse

Studies show that even a single episode of smoking almost inevitably leads to relapse. When a lapse occurs, about half of patch users stop using their patches within two days, usually due to misguided concerns about safety.

However, smokers who continue to use the nicotine patch after a lapse are 4-5 times more likely to be abstinent at the end of treatment. When prescribing the patch, advise patients to continue using it if a lapse occurs and emphasise that concurrent patch use and smoking is safe.

Cue-induced cravings

Most lapses are triggered by situations associated with smoking, such as exposure to alcohol, coffee or stress. Oral forms of nicotine replacement significantly reduce the intensity and the duration of

Table 1: Smoking cessation medications on the PBS

Product	Strength	Quantity	Notes	Max per year
Nicotine patch	Nicabate P; Nicotinell Step 1 21mg/24 hours	28 Rx2	12-week course PBS and DVA	PBS. One 12-week course
	Nicorette 15mg/16 hours	28 Rx2	12 week course PBS and DVA	
	Nicabate CQ, QuitX, 21mg/24 hours, Nicorette 15mg/16 hours	14 Rx2	DVA only	DVA. Two 12-week courses
	Nicabate CQ, QuitX, 14mg/24 hours, Nicorette 5mg/16 hours, Nicorette 10mg/16 hours	14 Rx0	DVA only	ATSI. Two 12-week courses
Nicotine patch (Step down course)	Nicotinell step 1 21mg/24 hours Nicotinell step 2 14mg/24 hours Nicotinell step 3 7mg/24 hours	28 Rx0 28 Rx0 28 Rx0	Step down course. Four weeks at 21mg, four weeks at 14mg and four weeks of 7mg PBS and DVA	
Varenicline	500µg × 11 tablets 1mg × 42 tablets	1 pack	Initiation pack	24 weeks
	1mg tablets	112	Continuation pack, after completing initiation pack.	
	1mg tablets	56 Rx2	Additional 12-week course for patients abstinent after the initial 12 weeks.	
Bupropion	Initial pack. 150mg tablets	30	Initiation pack	Nine weeks
	Continuation pack. 150mg tablets	90	Continuation pack, after completing the initiation pack	
Oral NRT. Lozenge, gum, mouth spray, inhalator			Not available on the PBS	

Table 2: Correct instructions for use of oral nicotine replacement therapy

Product	Instructions	Daily dose
Gum	Chew slowly until taste becomes strong then rest between gum and cheek. Chew again several times slowly when taste fades. Try not to swallow excessively. Repeat for 30 minutes or until the taste fades	2mg gum: 8-20 pieces 4mg gum: 4-10 pieces
Lozenge	Allow to dissolve in mouth (about 20-30 minutes), moving from side to side from time to time. Try not to swallow excessively. Do not chew or swallow whole	2mg and 4mg lozenges: 9-15 pieces
Mini lozenge	Allow to dissolve in mouth (about 10-13 minutes), moving from side to side from time to time. Try not to swallow excessively. Do not chew or swallow whole	1.5mg mini lozenges: 9-20 pieces 4mg mini lozenges: 9-15 pieces
Inhalator	Take shallow puffs about every two seconds or alternatively take four puffs every minute. Continue for up to 20-30 minutes	3-6 cartridges
Mouth spray	Spray into the mouth, avoiding the lips. Do not inhale while spraying. Use when cigarettes would normally be smoked or if cravings emerge. Do not swallow for a few seconds after spraying	1-2 sprays every 30-60 minutes. Maximum four sprays an hour or 64 sprays a day

cue-induced cravings and help prevent lapses. Oral therapies should be taken in anticipation of a smoking trigger if possible or otherwise when cravings are experienced.

Nicotine mouth spray

Nicotine mouth spray is the latest oral form of nicotine replacement therapy on the Australian market. In a recent phase III trial, the mouth spray more than doubled the quit rate compared with placebo at 12 months.[14]

Nicotine dispensed via mouth spray is absorbed more rapidly than other forms of nicotine replacement therapy and begins to relieve cravings after 60 seconds, significantly faster than other nicotine products.

Nicotine is sprayed from a pump pack directly into the mouth. The recommended dose is 1-2 sprays every 30-60 minutes, up to a maximum of four sprays an hour or 64 sprays a day. The spray can also be combined with a nicotine patch.

The mouth spray is well tolerated. Adverse events include irritation of the mouth and throat, salivary hypersecretion, nausea, dyspepsia, headache and hiccups.

Varenicline

Varenicline is the most effective monotherapy for smoking cessation.[15] It is uptitrated over the first week to reduce side effects. The starting dose is 0.5mg daily for three days, then 0.5mg twice daily for four days, then 1mg twice daily. Tablets should be taken with food to reduce the risk of nausea. A full course of 12 weeks is recommended.

Patients are advised to quit in the second week. However, not everyone is ready to quit then and it is acceptable for patients to continue smoking for several weeks until they are ready to quit.

A second course of varenicline significantly increases quit rates further at 12 months.

Varenicline has no known drug interactions but is contraindicated in pregnancy and lactation. The dose should be reduced in severe renal impairment.

A second course of varenicline significantly increases quit rates further at 12 months.

Adverse effects

Varenicline is well tolerated. About 30% of users experience nausea, however this is usually mild and tends to settle over time. If not, the dose can be reduced. Other side effects include headache, insomnia, disturbed dreams and drowsiness.

There have been post-marketing reports of depression, agitation, changes in behaviour and suicidal ideation with varenicline. However, smoking cessation can cause these symptoms and there is no scientific evidence of a causal relationship. Nevertheless, patients should be advised about these possible side effects and monitored for mood or behaviour changes. Advise patients to stop the medication if there is any concern and contact their doctor.

Concerns have also been raised about increased cardiovascular events from varenicline. However, subsequent reviews have failed to demonstrate any significant risk.

Bupropion

Bupropion is an antidepressant that is also an effective aid to quitting.[16] It is started with a 150mg tablet daily for three days, followed by one tablet twice daily.

The patient is advised to quit smoking in the second week and continue the medication for a full eight-week course.

Adverse events

Side-effects include insomnia, headache, dry mouth, nausea, dizziness and anxiety. As with varenicline, there have been reports of depression, suicidal and behaviour changes from bupropion, but no causal link has been confirmed.

The main risk from bupropion is a one-in-a-thousand incidence of seizures. The drug is contraindicated in patients with a raised seizure risk, such as patients with past seizures, CNS tumours, excessive alcohol or benzodiazepine use, eating disorders, past head trauma and monoamine oxidase inhibitors, as well as in pregnancy.

Bupropion should be used with caution in people taking medications that can lower seizure threshold, such as antidepressants and oral hypoglycaemic agents.

Smoking reduction with nicotine replacement therapy

Although quitting completely is the preferred option, many smokers are not ready to quit at the time of the consultation or are unable to do so. However, many of these smokers are willing to reduce their cigarette intake.

An alternative harm-reduction option for these smokers is to reduce their cigarette intake while using nicotine replacement therapy.[8,12] This strategy can lead to a long-term reduction in toxin exposure, although the health benefits are yet to be proven.

Furthermore, this intervention increases quit rates in the long term compared with giving repeated advice to quit. Studies have found a doubling of abstinence rates compared with no intervention.

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Drug interactions and smoking

CHEMICALS in tobacco smoke accelerate the metabolism of many common drugs by inducing the cytochrome P450 enzyme, CYP1A2. This can substantially lower the serum concentrations and effectiveness of these drugs in smokers.[11]

Conversely, blood levels of these medications may increase when smoking is stopped. Patients should be monitored for adverse effects, and dose reductions may be required. Immediate dose reductions should be considered for drugs with a narrow therapeutic index such as olanzapine, clozapine and warfarin to avoid drug toxicity.

Table 3: Drugs that interact with smoking. Blood levels rise after cessation of smoking[11]

Class	Medication
Antipsychotics	Olanzapine, clozapine Haloperidol, chlorpromazine, fluphenazine
Antidepressants	Duloxetine, fluvoxamine, tricyclic antidepressants, mirtazapine
Anti-anxiety agents	Alprazolam, oxazepam, diazepam
Cardiovascular drugs	Warfarin, propranolol, verapamil, flecainide
Diabetes	Insulin, metformin
Other	Naratriptan, oestradiol, ondansetron, theophylline, dextropropoxyphene

Referral options

SEVERAL referral options are available for GPs who are not able to offer treatment themselves.

Practice nurse

Many practices are training their practice nurse in smoking cessation skills. Nurses can provide counselling and support in collaboration with the GP who can prescribe medication.

Quitline

Free, proactive telephone counselling services are available in each state and provide evidence-based advice, encouragement and support. GPs can refer patients by a faxing a Quitline referral sheet or by ringing 137 848.

Tobacco treatment specialists

A network of trained, accredited tobacco treatment specialists exists across Australia. To find a tobacco treatment specialist in your area, go the website of the Australian Association of Smoking Cessation Professionals (see Online resources, page 32) and enter your location in the search box.

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E-cigarettes

SOME smokers are ordering e-cigarettes online to assist with quitting or to reduce cigarette intake. E-cigarettes are battery operated cigarette-shaped devices that contain a cartridge of liquid nicotine. The nicotine is vaporised when the patient breathes in and is rapidly delivered to the lungs as a fine mist without smoke or carbon monoxide.

There is still very little research on the safety, quality control and efficacy of e-cigarettes. Although it is highly likely that they are much less harmful to health than cigarettes, not enough is known about e-cigarettes to recommend them to patients. Smokers who are interested in quitting should be strongly directed towards evidence-based treatments.

Online resources

RACGP: Supporting Smoking Cessation. A Guide for Health Professionals (2011)
www.racgp.org.au/guidelines/smokingcessation

Australian Smoking Cessation Conference 2013
www.sydney.edu.au/bmri/ascc2013

Tobacco in Australia — facts and figures
www.tobaccoinaustralia.org.au

Australian Association of Smoking Cessation Professionals
www.aascp.org.au

Quit Now — Australian Government
www.quitnow.gov.au
Quit Victoria: www.quit.org.au
Quit South Australia: www.quitsa.org.au
Quit Tasmania: www.quittas.org.au

Cancer Institute NSW
iCanQuit
www.icanquit.com.au

OxyGen (youth website)
www.oxygen.org.au

Quit Coach
www.quitcoach.org.au

Competing interests
Dr Mendelsohn has received funding from Pfizer, GlaxoSmithKline and Johnson &Johnson (Pacific) for teaching, consulting and travel.

How to Treat Quiz

Nicotine dependence — 7 June 2013

INSTRUCTIONS
Complete this quiz online and fill in the GP evaluation form to earn 2 CPD or PDP points.
We no longer accept quizzes by post or fax.

The mark required to obtain points is 80%. Please note that some questions have more than one correct answer.

GO ONLINE TO COMPLETE THE QUIZ
www.australiandoctor.com.au/education/how-to-treat

1. Which TWO statements are correct regarding the epidemiology of smoking and nicotine dependence?
a) About 40% of smokers try to stop smoking at least once a year
b) Every year of smoking after the age of 35 years shortens the smoker's lifespan by three months
c) About 25% of lifelong smokers die prematurely, with an average lifespan five years shorter than that of non-smokers
d) In 2010, 5% of Australians aged 14 or over smoked

2. Which TWO statements are correct regarding the pathophysiology of smoking and nicotine dependence?
a) Genetic variations of cytochrome P450 2A6 can vary by up to fourfold, affecting the rate of nicotine breakdown
b) Smoking addiction is primarily driven by psychosocial habituation
c) The nicotine reward is mediated by pituitary endorphins that degrade within a few hours
d) Chronic nicotine exposure upregulates nicotine receptors that over time makes quitting more difficult

3. Which TWO statements are correct regarding nicotine replacement therapies?
a) Patients who smoke more than 10 cigarettes a day will require a full-strength nicotine patch
b) Nicotine mouth spray may more than double the quit rate of placebo at 12 months
c) Patients should avoid combining different forms of nicotine replacement
d) Smoking should stop before starting nicotine replacement to prevent overdose

4. Which THREE common medications may have an increased level in the blood after smoking cessation?
a) Metformin
b) Alprazolam
c) Olanzapine
d) Amoxycillin

5. You ask Samantha, a 34-year-old woman who smokes a pack a day, about her smoking. Which TWO statements are correct?
a) GPs are shown to identify 95% of their patients who smoke
b) Brief three-minute advice by the GP is effective in increasing quit rates
c) Most smokers do not want to quit and thus need a lot of encouragement
d) GPs advise only about 50% of the patients they have identified as smokers to quit

6. You assess Samantha's level of nicotine dependence. Which TWO statements are correct?
a) Self-reported smoking history is a reliable guide to nicotine dependence
b) The single most reliable indicator for nicotine addiction is the time to the first cigarette of the day
c) History taken about past failed attempts at quitting does not help inform future management
d) The level of nicotine dependence is a powerful predictor of success of nicotine replacement therapy

7. You discuss weight gain as a barrier to smoking cessation with Samantha. Which TWO statements are correct?
a) The mean weight gain due to quitting is 4-5kg in the first 12 months
b) 25% of smokers who quit will lose weight or stay the same
c) Smoking cessation medications can normalise weight gain from smoking cessation
d) Detailed dietary advice is effective in controlling weight after quitting

8. You discuss stress as a barrier to smoking cessation with Samantha. Which TWO statements are correct?
a) Smoking reduces stress levels
b) Smoking relieves symptoms of nicotine withdrawal as opposed to actually reducing stress
c) Nicotine releases stress hormones in the body, which increase feelings of anxiety
d) Samantha should be advised that ex-smokers have a persistent but negligible higher level of stress than continuing smokers

9. You discuss nicotine withdrawal with Samantha. Which TWO statements are correct?
a) Chewing a nicotine lozenge provides the fastest craving relief
b) Cravings become weaker and less frequent over time but can last for many years
c) Smoking cessation medications provide effective relief from cravings and withdrawal symptoms
d) Withdrawal symptoms are worst at 10-14 days, which is when lapses occur

10. You discuss the use of smoking cessation medications with Samantha. Which TWO statements are correct?
a) A second course of varenicline significantly increases quit rates at 12 months
b) Varenicline is safe in pregnancy and lactation
c) Bupropion has no known drug interactions and may be used with antidepressants and oral hypoglycaemic agents
d) Bupropion has a one-in-a-thousand incidence of seizures

CPD QUIZ UPDATE

The RACGP requires that a brief GP evaluation form be completed with every quiz to obtain category 2 CPD or PDP points for the 2011-13 triennium. You can complete this online along with the quiz at **www.australiandoctor.com.au.** Because this is a requirement, we are no longer able to accept the quiz by post or fax. However, we have included the quiz questions here for those who like to prepare the answers before completing the quiz online.

Australian Doctor Education

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NEXT WEEK There are many causes of painful mouth, with the most common being from dental or periodontal disease. Left untreated, painful mouth may compromise eating and swallowing. Next week's How to Treat details these causes and how a GP might manage these conditions. The author is **Associate Professor Geoffrey Quail**, clinical associate professor, department of surgery, Monash Medical Centre, Melbourne, Victoria.