

# Supporting smoking cessation: a guide for health professionals







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#### Statements of competing interests

Dr Ron Borland has developed QuitCoach and onQ smoking cessation programs, although he has no commercial interest in them.

Associate Professor John Litt has provided smoking cessation advice and training at meetings supported by Pfizer Pty Ltd and is a member of the varenicline advisory board for Pfizer Pty Ltd.

Associate Professor Matthew Peters has received honoraria from Pfizer Pty Ltd for contribution to the varenicline advisory board and for CME lectures at meetings supported by Pfizer Pty Ltd.

Professor Nicholas Zwar has provided expert advice on smoking cessation education programs to Pfizer Pty Ltd and GlaxoSmithKline Australia Pty Ltd and has received support to attend smoking cessation conferences.

## Endorsements

Action on Smoking and Health Australia

Cancer Council Australia

Pharmaceutical Society of Australia

The Royal Australian and New Zealand College of Psychiatrists

The Royal Australian College of General Practitioners

SANE Australia

The Australian Lung Foundation

The National Heart Foundation of Australia

## Evidence for recommendations

#### Explanation of levels of evidence

**Level I** Evidence obtained from systematic review of relevant

randomised controlled trials

**Level II** Evidence obtained from one or more well designed, randomised

controlled trials

**Level III** Evidence obtained from well designed, non-randomised

controlled trials, or from well designed cohort or case control

studies

**Level IV** Evidence obtained from case series, either post-test or pre-test

and post-test

**Level V** Opinions of respected authorities based on clinical experience,

descriptive studies, reports of expert committees

No evidence No evidence was found relevant to general practice on the issue

being considered.

Source: National Health and Medical Research Council (NHMRC). A guide to the development, evaluation and implementation of clinical practice guidelines. Canberra: NHMRC, 1999.

#### Strength of recommendation

**A** There is good evidence to support the recommendation

- **B** There is fair evidence to support the recommendation
- **C** There is poor evidence regarding the inclusion, or exclusion of the recommendation, but recommendations may be made on other grounds

Source: United States Preventive Services Task Force. Guide to clinical preventive services. 2nd edn. Baltimore: Williams and Wilkins, 1996.

Readers should note some important changes from earlier guidelines.

- The emphasis on 'Stages of Change' model as an approach to smoking cessation has been changed because the evidence does not support the restriction of quitting advice and encouragement only to those smokers perceived to be in a stage of readiness.
- A key message is that all people who smoke, regardless of whether they express a desire to stop or not, should be advised to stop smoking.
- New data have been included about varenicline and cardiovascular disease.
- Changes to the approved use of nicotine replacement therapy in Australia are included.
- A section dealing with smoking cessation methods, which have not yet been researched but may prove useful, is included.
- The guide covers smoking cessation in high prevalence populations and in populations with special needs.

A summary of the evidence and recommendations is listed in *Appendix 1*.

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### Introduction

Australia has made major progress in tobacco control with population prevalence of smoking falling substantially since the 1960s. In recent years smoking rates have continued to fall, including in the indigenous population for the first time – where rates have been unacceptably high.<sup>1,2</sup> However, despite the decline in prevalence, smoking remains the behavioural risk factor responsible for the highest levels of preventable disease and premature death.<sup>3</sup> The task of further reducing the number of Australians who are using tobacco requires a collaborative effort between government, health authorities, health professionals and the community at large.

The former chief adviser to the Australian Government on tobacco control, Professor David Hill, has likened tobacco control efforts to keeping a spring compressed – take the pressure off and rates of tobacco use, and the harm that follows, will rebound. Tobacco control involves preventing uptake and supporting cessation. Health professionals play a key role in both, but have a particular responsibility to assist all smokers to stop. <sup>4,5</sup> Reducing parental smoking rates is the intervention with the clearest effect on youth smoking uptake.

Two publications, *Smoking cessation guidelines for Australian general practice* (2004)<sup>6</sup> and *Smoking cessation pharmacotherapy: an update for health professionals* (2009),<sup>7</sup> provided a framework for assisting quitting, and informed health professionals of developments in the understanding of nicotine addiction and the pharmacotherapies available to assist smoking cessation. These publications were based on a literature review undertaken for the National Tobacco Strategy,<sup>8</sup> experience with cessation programs in Australia – in particular the Smokescreen Program<sup>9</sup> – and international experience with smoking cessation guidelines in other countries.<sup>10–13</sup>

Since these publications, there have been important developments in both the science and practice of cessation support. These include advances in our understanding of the neurobiology of nicotine addiction, further research on the use of varenicline and substantial changes in the approved use of nicotine replacement therapy (NRT). Another important development for smoking cessation in Australia has been the listing of nicotine patches on the Pharmaceutical Benefits Scheme, initially for Aboriginal and Torres Strait Islander people in 2008, and for the general community since February 2011.

Supporting smoking cessation: a guide for health professionals aims to be a practical, succinct and evidence based resource that can be used by a wide range of health professionals working in a variety of contexts. As with the previous publications, it is based on research evidence and is informed by guidelines from other countries with similar population profiles. It seeks to link smoking cessation advice by health professionals to the materials and support services provided through the telephone quitlines operating in each state and territory. It also seeks to build on the momentum for cessation gained by public health interventions such as tax increases, restrictions on smoking in public places, changes to tobacco display and packaging and the social marketing of smoking cessation.

## Tobacco smoking: the scope of the problem

Tobacco smoking is a worldwide threat to human life. The World Health Organization (WHO) estimates that around 5.4 million people died prematurely in 2008 from tobacco related diseases and, on current trends, this number will increase to 8 million deaths each year before 2030. Eighty percent of these deaths will occur among people in the developing world. Fortunately, in Australia the prevalence of tobacco smoking has decreased. The proportion of people aged 14 years and over smoking tobacco daily in 2010 was 15.1%, down 16.6% from 3 years previously. While rates remain much higher in the indigenous population than in the rest of the Australian population, the first statistically significant decline in smoking rates for Indigenous Australians was seen between 2002 and 2008, from 53% to about 50% respectively.

Australia is a signatory to the WHO Framework Convention on Tobacco Control, a worldwide effort to control the effects of tobacco smoking on human health.<sup>15</sup> The framework is the world's first public health treaty and commits governments to enacting a minimum set of policies, which are proved to curb tobacco use. These include bans on tobacco advertising, promotion and sponsorship, clear warning labels, smoke free policies, higher prices and taxes on tobacco products and access to, and availability of, smoking cessation services. It also encourages international cooperation in dealing with cigarette smuggling and cross border advertising.

As a result of changes in public policy and changing community attitudes to tobacco, the status of tobacco smoking is gradually shifting from a socially acceptable behaviour to an antisocial one.<sup>16</sup> With the advent of national tobacco control policies and programs, the prevalence of smoking in Australia is among the lowest of any nation.<sup>17</sup> While Australia's level of smoking continues to fall and is the third lowest for OECD (Organisation for Economic Cooperation and Development) countries,<sup>18</sup> Indigenous Australians are still more than twice as likely as non-Indigenous Australians to be current daily smokers.<sup>2</sup>

The importance of smoking cessation was reinforced in the report of the National Preventative Health Taskforce, which stated that the evidence for interventions to reduce smoking is strong and has accumulated over many years. The report made several key recommendations on improving advice from health professionals, including ensuring all smokers in contact with health services are routinely asked about their smoking status and supported to quit.<sup>19</sup>

#### National Preventative Health Taskforce. Key action area 6: Tobacco control<sup>19</sup>

Ensure all smokers in contact with health services are encouraged and supported to quit, with particular efforts to reach pregnant women and those with chronic health problems.

Ensure all state or territory funded healthcare services (general, maternity and psychiatric) are smoke free and protecting staff, patients and visitors from exposure to secondhand smoke, both indoors and on facility grounds.

Nevertheless, smoking still causes a higher burden of disease than any other behavioural risk factor, representing 9.6% of the total burden in men and 5.8% in women.<sup>20</sup> Tobacco smoking is responsible for the deaths of about 15 500 Australians each year (*Table 1*).<sup>21</sup>

Specific cause	Number of deaths	Percentage of all tobacco caused deaths (rounded)*
Lung cancer	6309	41
COPD	4175	27
CHD	1962	13
Stroke	577	4
Oesophageal cancer	572	4
Other	1916	12
Total	15 511	

Reprinted with permission: Scollo MM, Winstanley MH, editors. Tobacco in Australia: Facts and Issues. 3rd edn. Melbourne: Cancer Council Victoria; 2008. Available from www.tobaccoinaustralia.org.au

Interventions to assist cessation are in the context of a changing environment: the low community tolerance for tobacco smoking is one sign of a continuing 'denormalisation' of tobacco use in Australia.<sup>22</sup>

Tobacco smoking harms almost every organ of the body, causing a wide range of diseases and harming the health of smokers (*Table 2*).<sup>23</sup>

Smoking is strongly related to many chronic diseases including coronary heart disease, stroke, chronic obstructive pulmonary disease, asthma, rheumatoid arthritis and osteoporosis, and is responsible for 20% of all cancer deaths in Australia. Smoking also has adverse effects in pregnancy, both for the mother and the developing fetus, and exposure to secondhand tobacco smoke has been shown to damage the health of children and adults. The only proven strategy for reducing the risk of tobacco related diseases and death is to avoid taking up smoking and, failing that, to quit as early as possible in adult life. Quitting smoking has immediate, as well as long term benefits, reducing the risks for diseases caused by smoking and improving health in general.

Eyes	Stomach		
Macular degeneration	Cancer, ulcer		
Hair	Pancreas		
Hair loss	Cancer		
Skin	Bladder		
Ageing, wrinkles, wound infection	Cancer		
Brain	Women		
Stroke	Cervical cancer, early menopause, irregular and painful periods		
Mouth and pharynx	Men		
Cancer, gum disease	Impotence		
Lungs	Arteries		
Cancer, emphysema, pneumonia	Peripheral vascular disease		
Heart	Bones		
Coronary artery disease	Osteoporosis		

# Key findings from the 2010 National Drug Strategy Household Survey report<sup>1</sup>

- 15.1% of people in Australia, aged 14 years or older, were daily smokers. This declined from 16.6% in 2007, and from 24.3% in 1991
- One-quarter of the population were ex-smokers and more than half had never smoked
- Tobacco smoking (smoked in the previous 12 months) remains higher among certain populations, such as those with the lowest socioeconomic status (24.6%) and those living in remote areas (28.9%)
- Indigenous Australians were 2.2 times as likely as non-Indigenous Australians to smoke tobacco
- Compared with non-smokers (ex-smokers and those who never smoked), smokers were more likely to rate their health as being fair or poor, were more likely to have asthma, were twice as likely to have been diagnosed or treated for a mental illness and were more likely to report high or very high levels of psychological distress in the preceding 4 week period
- A higher proportion of smokers reported being diagnosed, or treated for a mental illness in 2010 (from 17.2% in 2007 to 19.4%)
- Almost 40% of smokers had reduced the amount they smoked in a day, and 29% had tried unsuccessfully to give up smoking
- The proportion of people nominating cost as a factor for wanting to quit smoking increased significantly from 35.8% in 2007 to 44.1% in 2010.

#### Effectiveness of treating tobacco dependence

The benefits of quitting smoking are well established. Successfully quitting smoking can result in an increase in life expectancy of up to 10 years, if it occurs early enough.<sup>25</sup> There is also substantial evidence that advice from health professionals including doctors, nurses, pharmacists, psychologists, dentists, social workers and smoking cessation specialists helps smokers to quit.<sup>26–29</sup> While spending more time (longer than 10 minutes) advising smokers to quit yields higher abstinence rates than minimal advice,<sup>10</sup> offering brief advice (as little as 3 minutes) has been shown to have clear benefits.<sup>26,30,31</sup> Providing brief advice to most smokers is more effective and efficient than spending a longer time with a few patients.<sup>30,32</sup>

Smoking cessation is both cost and clinically effective compared with other medical and disease preventive measures, such as the treatment of hypertension and hypercholesterolaemia.<sup>33–36</sup> Research shows that the cost per life year saved by smoking cessation interventions makes it one of the most cost-effective healthcare interventions.<sup>37,38</sup> Along with childhood immunisation and aspirin use with high risk adults, overall efforts to reduce tobacco smoking are among the most beneficial preventive interventions for human health.<sup>37,39,40</sup>

Advice based help and pharmacotherapy can both increase the rate of success of quit attempts, and when they are used the benefits are cumulative. <sup>10</sup> Smokers should be offered cessation treatment, either counselling (individual or group) or medication, or both, which is individualised and customised to their own personal situation and experience.

## The role of health professionals

Smoking cessation advice and support from health professionals are key aspects of a comprehensive approach to tobacco control. Health professionals can make an important contribution to tobacco control in Australia and to the health of the community by providing opportunities for smokers to quit. An encouraging environment can be provided in health settings (primary and community care, hospitals, dental, eye care and pharmacies)<sup>5,7,26–29,41</sup> and in non-health settings (workplaces, prisons, schools, state housing, social welfare services).<sup>42,43</sup> All types of health professionals can play an important role – WHO states that involvement in offering smokers advice and assistance with quitting should be based on factors such as access, rather than professional discipline.<sup>12</sup>

Health professionals play an important role in educating and motivating smokers as well as assessing their dependence on nicotine and providing assistance to quit. All health professionals should systematically identify smokers, assess their smoking status and offer them advice and cessation treatment at every opportunity. Here a client presents with a problem caused or exacerbated by smoking, it is of vital importance for health professionals to raise the issue of smoking cessation.

There is a range of evidence based strategies that can improve the implementation of effective smoking cessation intervention in the practice setting. <sup>45–48</sup> Providing a systematic approach to smoking cessation is associated with higher levels of success. <sup>10</sup> Routine enquiry through waiting room surveys <sup>47,49</sup> or use of additional practice staff to provide counselling, is associated with higher quit rates. <sup>29</sup> Where health professionals are not able to offer support or treatment within their own practices, they should refer smokers for help elsewhere – for example, to Quitline and local programs that may be available in each state such as the Fresh Start course by Quit Victoria. <sup>50</sup>

Brief interventions for smoking cessation involve opportunistic advice, encouragement and referral. Interventions should include one or more of the following:<sup>6,10,51</sup>

- · brief advice to stop smoking
- · an assessment of the smoker's interest in quitting
- an offer of pharmacotherapy and counselling where appropriate
- providing self help material
- referral to more intensive support such as Quitline (see *Appendix 2*) and other local programs that may be available in each state.

#### Beliefs that can be barriers to optimal smoking cessation advice

Asking about smoking and offering advice and assistance are key roles for health professionals. Barriers raised by health professionals to engaging in greater efforts to provide smoking cessation advice include:

- a perception that it is ineffective
- lack of time
- lack of smoking cessation skills
- reluctance to raise the issue due to perceived patient sensitivity about smoking
- perceived lack of patient motivation. 52,53

Table 3 presents evidence in relation to these barriers.

Belief	Evidence
Assistance with smoking cessation is not part of my role	Most patients think smoking cessation assistance is part of your clinical role <sup>44,54</sup>
I have counselled all my smokers	Only 45–71% of smokers are counselled <sup>55,56</sup>
Smokers aren't interested in quitting	Nearly all smokers are interested in quitting although some are temporarily put off by past failures. More than 40% of smokers make quit attempts each year and more think about it <sup>57</sup>
I routinely refer patients for smoking cessation assistance	Referrals to Quitline are low (10-25%) <sup>58</sup>
I'm not effective	Clinicians can achieve substantial quit rates over 6–12 months, 12–25% abstinence, which have important public health benefits <sup>26,44,50</sup>
Smokers will be offended by enquiry	Visit satisfaction is higher when smoking is addressed appropriately <sup>56,59</sup>
I don't have time to counsel smokers	Effective counselling can take as little as a minute <sup>10</sup>

#### Evidence

Smoking cessation advice from health professionals is effective in increasing quit rates. The major effect is to help motivate a quit attempt. **Level I**. All health professionals can be effective in providing smoking cessation advice. **Level I** 

#### Recommendation

All smokers should be offered brief advice to quit. Strength A

## The 5As structure for smoking cessation

Tobacco dependence is a chronic condition that typically requires repeated cessation treatment and ongoing care. <sup>10,60</sup> A minority of smokers achieve long term abstinence on the first attempt to quit, while the majority cycle through multiple attempts with relapse and remission before achieving long term, or permanent abstinence. Multiple attempts over a period of years are not unusual.

It is important to take every opportunity to identify all smokers, document their smoking status and offer treatment, which may involve counselling by a health professional, referral to more intensive support and pharmacotherapy.

Research shows that the most common method used by most people who have successfully stopped smoking is unassisted cessation (either stopping abruptly or cutting down on their own),<sup>61</sup> although now more than half of all smokers making quit attempts are using some form of help, mainly medications.<sup>62</sup> If smokers want to try to quit unassisted they should be encouraged to do so, but told that support is available should they want it. Many smokers need encouragement, assistance and guidance to quit successfully. Smokers who are more nicotine dependent are more likely to seek treatment.<sup>63</sup>

There are two ways to increase the number of people successfully quitting: improve the success rate and/or increase the number of attempts. Given the costs and limited achievement in improving success rates, increasing the number of attempts to quit remains the most important strategy for improving cessation rates in the population. Health professionals are the key to increasing the frequency of quit attempts by encouraging smokers to keep trying. Smokers should be aware that it is normal to make multiple attempts, and that many of those who have succeeded in quitting have had this same experience. Health professionals can increase the chances of success by encouraging use of the most effective strategies.

#### Ask, assess, advise, assist and arrange follow up

The 5As approach (five components of effective tobacco cessation counselling) originally proposed by the US Clinical Practice Guideline, <sup>10</sup> provides health professionals with an evidence based framework for structuring smoking cessation by identifying all smokers and offering support to help them quit. <sup>6,7</sup> The approach is adopted in guidelines from The Netherlands and WHO, <sup>11,12</sup> and adopted in modified forms in other international guidelines. <sup>13,51</sup>

The 5As structure allows health professionals to provide the appropriate support for each smoker's level of interest in quitting (*Figure 1*). Where possible, health professionals should maintain long term and ongoing relationships with smokers, in order to foster the person's motivation and confidence to attempt smoking cessation. It is important for health professionals to ask all patients/clients if they use tobacco, assess their willingness to make a quit attempt, advise on the importance of quitting and offer assistance in the form of help from the health professional or referral.

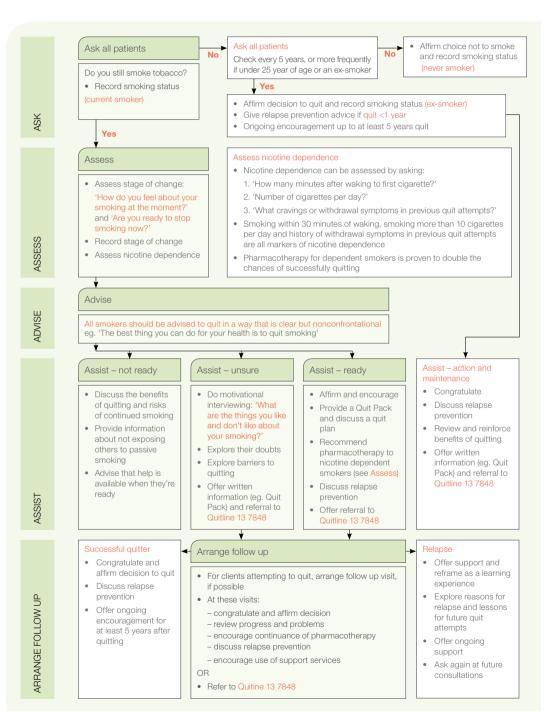
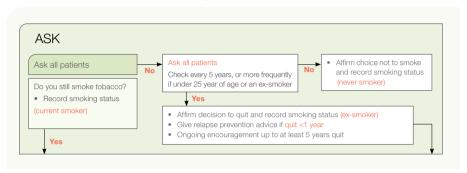


Figure 1. The 5As structure for health professionals for smoking cessation

#### 1. Ask all patients about smoking



Health professionals should ask all their patients/clients whether they smoke and their smoking status should be recorded. Implementing recording systems that document tobacco use almost doubles the rate at which clinicians intervene with smokers and results in higher rates of smoking cessation.<sup>10</sup>

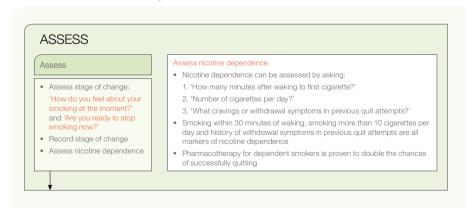
#### Evidence

Instituting a system designed to identify and document tobacco use almost doubles the rate of health professional intervention and results in higher rates of cessation. Level II

#### Recommendation

A system for identifying all smokers and documenting tobacco use should be used in every practice or healthcare service. Strength A

#### 2. Assess readiness to quit



#### Assessment of readiness to quit

Prochaska and DiClemente's Stages of Change Model<sup>66</sup> acknowledges that the smoker's level of motivation is an important issue in cessation and advice can be tailored on the basis of a smokers' readiness to quit.<sup>6</sup>

## The role of Stages of Change Model to assisting smoking cessation

- The model serves as a reminder that people at all stages can be offered assistance
- Smokers do not necessarily progress through each of the stages of change before attempting to quit, but the model can help clinicians tailor advice in a way that is most applicable to the smoker at that encounter
- Smokers are in different stages of readiness when the clinician sees them at different times, so readiness needs to be re-evaluated at every opportunity.
   The extent of the assessment will depend on the clinical context
- Stages of change can be influenced by the nature of the communication and the relationship between health professional and smoker.<sup>67</sup>

Though there is a lack of evidence for greater effectiveness of stage based approaches, 68 this model provides a useful framework to help clinicians identify smokers and provide tailored support for a smoker's level of interest in quitting in a way that is time efficient and likely to be well received. 9,69

There is some evidence that the likelihood of success in an attempt to quit is unrelated to the smoker's expressed interest in quitting in the period leading up to the attempt – unplanned attempts to quit are as likely (or even more likely) to be as successful as planned attempts.<sup>70,71</sup> Thus, there is benefit in encouraging all smokers to consider quitting whenever the opportunity arises.<sup>10</sup>

#### Evidence

Factors consistently associated with higher abstinence rates are high motivation, readiness to quit, moderate to high self-efficacy and supportive social networks. **Level III** 

#### Recommendation

Assessment of readiness to quit is a valuable step in planning treatment. **Strength C** 

#### Assessment of nicotine dependence

Most smokers become nicotine dependent – dependence can happen quickly and, in some cases, even after a few cigarettes. As nicotine addiction is under-recognised by clinicians, routine assessment of nicotine dependence can help predict whether a smoker is likely to experience nicotine withdrawal upon stopping smoking, 72,73 and the intensity and type of support that may be required to assist quitting.

Nicotine withdrawal symptoms commonly include craving, as well as onset of any of the following shortly after stopping:

- depressed mood
- insomnia
- irritability, frustration, anger
- anxiety
- · difficulty in concentration
- restlessness
- mouth ulcers
- constipation
- increased appetite or weight gain.

Characteristics of smokers with nicotine dependence include smoking soon after waking, smoking when ill, difficulty stopping smoking, finding the first cigarette of the day the most difficult to give up, and smoking more in the morning than in the afternoon.<sup>72,74,75</sup>

A quick assessment of nicotine dependence can be made by asking the smoker:

- 'How soon after waking do you have your first cigarette?'
- 'How many cigarettes do you smoke each day?'
- 'Have you had cravings for a cigarette, or urges to smoke and withdrawal symptoms when you have tried to quit?'

Smoking within 30 minutes of waking, smoking more than 10 cigarettes per day (although some dependent smokers may not be daily smokers) and a history of withdrawal symptoms in previous attempts to quit are all indicators of nicotine dependence. Time to first cigarette has been shown to be a reliable indicator of nicotine dependence.

#### 3. Advise all smokers to quit



Brief, repeated, consistent, positive reminders to quit and reinforcing recent quit efforts by a number of health professionals can increase success rates. When the practice is routinely applied to a large proportion of clients who smoke, a larger impact on population smoking rates can be achieved. Establishing rapport and asking permission minimises any risk of harming the patient-health professional relationship. In fact, asking if smokers would like to have help to quit can be appreciated and can strengthen the relationship. Where possible, it helps to personalise the advice and the benefits of quitting. Patients express greater visit satisfaction when smoking cessation is addressed. Patients express greater to raising the topic is to acknowledge that the smoker is aware of the risks, and ask if he or she is ready to discuss options.

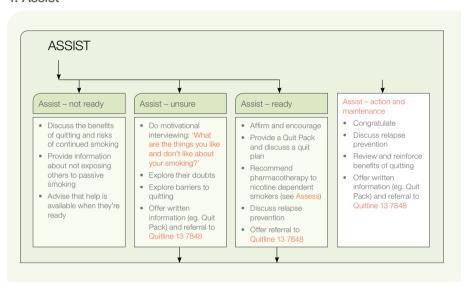
#### Evidence

Brief smoking cessation advice from health professionals delivered opportunistically during routine consultations has a modest effect size, but substantial potential public health benefit. **Level I** 

#### Recommendation

Offer brief cessation advice in routine consultations and appointments whenever possible (at least annually). **Strength A** 

#### 4. Assist



The decision on whether and what assistance to provide to smokers and recent quitters depends on their needs, preferences and suitability for available support, and the capacity of the health professional and their service. A package of assistance can be put together, which may involve the health professional and their service, or referral or a combination of these options. When necessary, clients should be referred to a health professional with a smoking cessation practice, or to a tobacco treatment specialist where medication can be prescribed where indicated.

Assistance from the health professional may involve motivational interviewing. This is a counselling technique based on a therapeutic partnership that acknowledges and explores a client's ambivalence about a behaviour. Motivational interviewing is a counselling philosophy that values patient autonomy and mutual respect and the use of open-ended questions, affirmations, reflection and summarising.<sup>78</sup>

#### Motivational interviewing

This type of counselling requires more time available than brief interventions. It is a proven counselling technique to help explore a client's ambivalence about their behaviour (eg. smoking).<sup>79</sup>

Motivational interviewing is a directive, non-confrontational, client centred counselling strategy aimed at increasing a person's motivation to change. It is a counselling style based on collaboration rather than confrontation, evocation rather than education and autonomy instead of authority – as opposed to a set of techniques.

#### Barriers to quitting

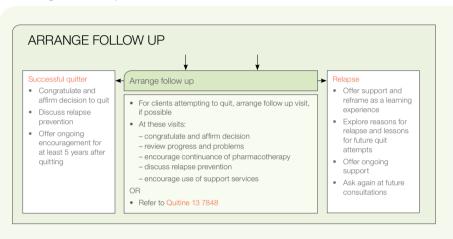
It is important for health professionals to be aware of the potential difficulties smokers face when attempting to quit and, where possible, to address the barriers at the time of the quit attempt. This could include providing treatment for withdrawal symptoms or mental health issues, or recommending physical activity and a healthy diet to minimise weight gain. Situations likely to lead to unsuccessful attempts at quitting include: 16,53

- · lack of knowledge of the benefits of quitting
- high dependence on nicotine and heavy smoking (more than 20 cigarettes per day, time to first cigarette)
- enjoyment of nicotine or smoking behaviour
- psychological or emotional concerns (stress, depression, anxiety, psychiatric disorders)
- fear of weight gain
- substance use (alcohol and other drugs)
- living with other smokers
- peer pressure, social smoking
- circumstances that result in the smoker giving quitting a low priority such as poverty, social isolation and how 'normal' smoking is regarded in the smoker's social circles.

Belief	Strategy to counteract the belief <sup>80–82</sup>
I can quit at any time/l'm not addicted	Ask about previous quit attempts and success rates
Use of cessation assistance is a sign of weakness/help is not necessary	Reframe assistance Highlight unassisted quit rate is 3–5%
Too addicted/too hard to quit	Ask about previous quit attempts  Explore pharmacotherapy used and offer options, eg. combination therapy
Too late to quit/I might not benefit so why bother	Benefits accrue at all ages, and are greater if earlier: at age 30 years, similar life expectancy to non-smoker. Provide evidence/feedback, eg. spirometry, absolute risk score
My health has not been affected by smoking/you have to die of something/l know a heavy smoker who has lived a long time	Provide evidence/feedback, eg. spirometry, absolute risk score  Reframe, eg. chronic obstructive pulmonary disease (COPD) = smoker's lung
Not enough willpower/no point in trying unless you want to/to quit successfully you really have to want to, then you will just do it	Explore motivation and confidence. Explore and encourage use of effective strategies, eg. Quitline, pharmacotherapy

Smokers should be reassured that it may take many attempts at quitting (more than 8–14 times) before successfully stopping, but that this should not stop them attempting. They can also learn something from each attempt to help overcome tobacco dependence.

#### 5. Arrange follow up



Follow up visits to discuss progress and to provide support have been shown to increase the likelihood of successful long term abstinence.<sup>44,83</sup>

Relapse prevention includes awareness of coping strategies for high risk situations such as stress, negative emotional states, alcohol and other social cues to smoke. It is important to frame each lapse (a single smoke), or full relapse to smoking as a learning experience and encourage the smoker to try again with support in the future.

All interventions by a health professional, or by a team of health professionals, should be recorded so that progress in quitting can be monitored and adjustments made where and when necessary to current medications, cessation pharmacotherapy and intensive counselling.

#### Evidence

Follow up is effective in increasing guit rates. Level I

#### Recommendation

All smokers attempting to quit should be offered follow up. Strength A

## Nicotine addiction

Almost 25 years ago, the US Surgeon General's report, The *Health Consequences of Nicotine Addiction*, concluded that nicotine was the drug in tobacco that caused addiction.<sup>23</sup> Many international medical authorities, including WHO, have confirmed the findings that tobacco products are highly addictive.<sup>84</sup> Of all people who commence tobacco use, almost one third (32%) become addicted smokers.<sup>16</sup> Dependence on nicotine develops quickly. Studies show that non-daily tobacco use triggers the emergence of nicotine dependence – in the second Development and Assessment of Nicotine Dependence in Youth study, where subjects had smoked at least one cigarette, 62% smoked at least once per month, 53% experienced dependence symptoms and 40% experienced escalation to daily smoking.<sup>85</sup> Dependence would not occur without nicotine, but nicotine is not responsible for the harmful effects of smoking, which are caused mainly by tar, oxidising chemicals, carbon monoxide and other constituents of tobacco or tobacco smoke.<sup>16,23,84</sup>

Dependence on smoking is a complex process. It requires a close link in time between the context in which smoking occurs, its rituals, the sensory stimuli of touch, taste and smell, and the extremely rapid delivery of nicotine to the brain that occurs when smoking a modern cigarette. Evidence suggests that psychosocial, biological and genetic factors all play a role in nicotine addiction.<sup>23,84,89</sup>

Greater understanding of the neurobiology of nicotine dependence is improving the use of existing cessation therapies and is helping to develop new compounds to aid smoking cessation. When cigarette smoke is inhaled, the large surface area of the lungs means that nicotine is rapidly absorbed into the pulmonary venous circulation and travels quickly to the brain through the bloodstream.  $^{86}$  Nicotine is active within the brain reward system within seconds of inhalation.  $^{87}$  The addictive components of tobacco products affect multiple types of nicotine receptors in the brain including, but not confined to, the  $\alpha 4\beta 2$  nicotinic acetylcholine receptor. Activation of this and other receptors triggers the release of dopamine and other neurotransmitters. This reward system is the common pathway for the experience of pleasure from many different social, physical and chemical stimulants, including other drugs of addiction such as cocaine and opiates. As well as the activation of the reward system, the negative effects of nicotine withdrawal are important factors in the continuation of smoking.

Genetic factors play a role in the differing patterns of smoking behaviour and smoking cessation. The degree of susceptibility to developing tobacco addiction – as well as the ease or difficulty of quitting and sustaining abstinence – has been reported from twin and adoption studies. This research shows a high degree of heritability of cigarette smoking (50–70%). 88,89 The finding points to an understanding of why smokers vary widely in their relationship to tobacco and their ability to quit. However, a useful way to target treatment based on genetics has not yet been shown. The studies also indicate that there may be some smokers who never fully overcome their addiction, or who can never quit all nicotine use. 84

The most immediate benefit of research into the genetics of smoking is the development of effective drugs to assist smokers to stop smoking. It might also allow better matching of smokers to cessation treatments.<sup>90</sup>

## Pharmacotherapy for smoking cessation

Three forms of medicine (nicotine replacement therapy, varenicline and bupropion) are licensed and available in Australia to assist smoking cessation. These medicines have been shown to assist smoking cessation in meta-analyses of randomised clinical trials.<sup>91–94</sup>

Pharmacotherapy is recommended for all dependent smokers who express an interest in quitting, except where contraindicated. 6,10 Smokers who want to try unassisted quitting should be encouraged to do so. However, best results are achieved when medicines are used in combination with counselling and support, 61,63 although there is some evidence that nicotine replacement therapy (NRT) can increase quit rates with or without counselling. 93 The choice of pharmacotherapy is based on clinical suitability and patient choice (Figure 2).

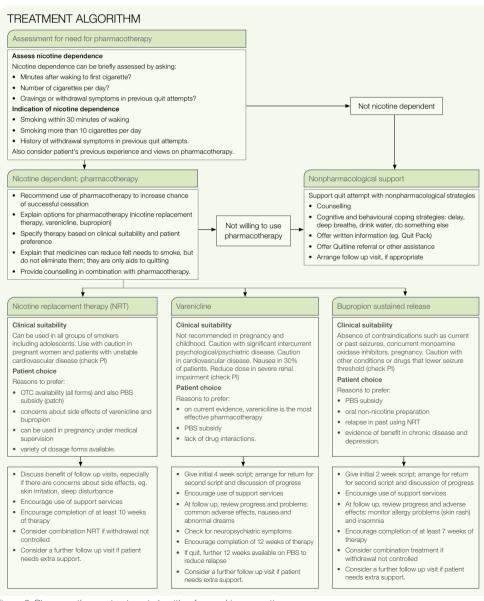


Figure 2. Pharmacotherapy treatment algorithm for smoking cessation

#### First line pharmacotherapy options

First line options are medicines that have been shown to be effective and are licensed for smoking cessation. In Australia these are NRT (brands include Chemist's Own Nicotine, Nicabate CQ®, Nicorette®, Nicotinell®, QuitX® and others), varenicline (brand name Champix®) and sustained release preparations of bupropion hydrochloride (brand names Buproprion-RL™, Clorprax®, Prexaton and Zyban SR®).

From current available evidence, varenicline is the most effective form of single pharmacotherapy for smoking cessation, but this is based on a limited number of comparison studies. However, there have been concerns raised about the neuropsychiatric adverse effects and the risk of cardiovascular events with varenicline. It has been shown that varenicline is more effective than bupropion in a number of studies. In the one prospective study comparing varenicline with NRT (21 mg/day), continuous abstinence was modestly higher with varenicline at the end of the treatment period (RR 1.29) but the difference was no longer significant by 6 months. Further research is needed to determine whether varenicline is more effective than NRT, including the need for studies comparing varenicline to high dose NRT, combination NRT and other regimes such as pre-cessation NRT.

However, clinical assessment, context and patient preference are important in choosing the pharmacotherapy that is most likely to assist the smoker in an attempt to quit. Consideration should be given to factors such as the potential for adverse effects, possible drug interactions, previous experience with pharmacotherapy convenience and cost. <sup>98</sup> Some smokers may prefer to use one or more forms of NRT, while others may prefer the non-nicotine options. An advantage of NRT is that it can be purchased without a prescription. One form of NRT (patch) is now subsidised by the Pharmaceutical Benefits Scheme (PBS) if provided in combination with counselling.

#### Evidence

Pharmacotherapy with nicotine replacement therapy, varenicline or bupropion is an effective aid to assisting motivated smokers to quit. **Level I** 

#### Recommendation

In the absence of contraindications, pharmacotherapy should be offered to all motivated smokers who have evidence of nicotine dependence. Choice of pharmacotherapy is based on clinical suitability and patient choice. **Strength A** 

#### Nicotine replacement therapy

#### Key points

- Using NRT to guit is always safer than continuing to smoke
- All forms of NRT (at equivalent doses) are similarly effective in aiding long term cessation
- All forms of NRT can increase the rate of quitting by 50–70%
- Higher dose forms of NRT (4 mg) are more effective than lower dose forms (2 mg) for more addicted smokers
- More than one form of NRT can be used concurrently with increased success rates and no safety risks
- NRT can be given several weeks prior to smoking cessation to help smokers prepare for quitting
- NRT can be used by people with cardiovascular disease. Caution is advised for people in hospital for acute cardiovascular events, but if the alternative is active smoking, NRT can be used under medical supervision
- NRT can be used by smokers aged 12–17 years
- NRT may be appropriate in pregnant smokers if they have been unsuccessful in stopping smoking without NRT
- Intermittent, short acting dosage forms (oral) are preferred in pregnancy to long acting dosage forms (patches).

Nicotine is the substance in tobacco that causes addiction – it makes people dependent on cigarettes, but it is the other chemicals in combusted tobacco that cause cancer, accelerate heart disease and affect other areas of health. The aim of NRT is to reduce withdrawal symptoms by providing some of the nicotine that would normally be obtained from cigarettes, without providing the harmful components of tobacco smoke. NRT is available over the counter in pharmacies, and some forms are available in supermarkets in Australia. Nicotine patches (15 mg and 21 mg) are subsidised on the PBS. None of the available forms of NRT (transdermal patch, gum, inhaler, lozenge and sublingual tablet) offer the same rapid nicotine delivery of a cigarette.

Some oral forms of NRT are available in two strengths: 2 mg and 4 mg (gum and lozenge) and 1.5 mg and 4 mg (mini lozenge) (*Table 4*). The 4 mg version is recommended for more dependent smokers (20 or more cigarettes per day). 93

Regular use of NRT beyond 12 months is not generally recommended. However, long term use of some forms of NRT has been reported and has not caused ill health effects – it may help some people remain abstinent<sup>97</sup> and is safer than smoking.

	Patient group	Dose	Duration (weeks)	Contraindications (adapted from MIMS online 2011)
Patch	>10 cigarettes per day and weight >45 kg	21 mg/24 hr or 15 mg/16 hr	>8	(Unscheduled) non-smokers children under 12 years; hypersensitivity to nicotine of any component of the patch diseases of the skin that ma complicate patch therapy
	<10 cigarettes per day or weight <45 kg or cardiovascular disease	14 mg/24 hr or 10 mg/16 hr	>8	
Gum	10-20 cigarettes per day	2 mg 8-12 per day	>8	(Unscheduled) non-tobacco users; known hypersensitivit to nicotine or any componer of the gum; children (<12 years)
	>20 cigarettes per day	4 mg 6–10 per day	>8	
Inhaler	>10 cigarettes per day	6–12 cartridges per day	>8	(S2) Non-tobacco users; hypersensitivity to nicotine or menthol; children (<12 years)
Lozenge	First cigarette >30 minutes after waking	1.5 mg or 2 mg 1 lozenge every 1–2 hr	>8	(Unscheduled) non-smokers hypersensitivity to nicotine or any component of the lozenge; children (<12 years) phenylketonuria
	First cigarette <30 minutes after waking	4 mg 1 lozenge every 1–2 hr	>8	
Sublingual tablet	Low dependence	2 mg every 1–2 hr	>8	(Unscheduled) non-tobacco users; known hypersensitivi
	High dependence	Two 2 mg every 1–2 hr	>8	to nicotine or any componen of the tablet; children (<12 years)

#### Higher dose and combination NRT

Combining two forms of NRT (patch plus oral form, such as lozenge or gum) has been shown to be more efficacious than a single form of nicotine replacement. The patch provides a steady background nicotine level and the oral forms provide relief for breakthrough cravings as needed. Health professionals should encourage smokers to use combined NRT if they are unable to quit using one NRT product alone, or experience cravings using only one form of NRT. 93,99 In Australia, the combination of NRT patch and 2 mg gum, 2 mg lozenge or 1.5 mg mini lozenge is licensed for smokers who have relapsed in the past or who experience cravings using only one form of NRT. 5 ome experts now recommend combination therapy for all dependent smokers using NRT, rather than monotherapy.

#### Pre-cessation nicotine patch

There is evidence to support use of nicotine replacement prior to smoking cessation. A meta-analysis found that the nicotine patch used prior to quit day increased success rates compared to standard therapy.<sup>101</sup> The Therapeutic Goods Administration (TGA) approved approach involves using a 21 mg/24 hour patch (Nicabate® only brand currently approved) for 2 weeks before quitting, then continuing to use nicotine patch in the usual way for the quit attempt and adding oral NRT if needed.

#### Reduce to quit

There is also evidence for use of NRT to help smokers who are not willing to quit abruptly to reduce their tobacco and then progress to quitting.<sup>102</sup> The TGA approved approach (cut down then stop or reduce to quit) involves smokers using NRT to reduce the number of cigarettes they smoke before stopping completely within 6 months. However, a meta-analysis has found that reducing cigarettes smoked before quit day versus quitting abruptly, with no prior reduction, produced comparable quit rates.<sup>103</sup> Health professionals should offer smokers the choice to quit in either of these ways. Further research is needed to investigate those categories of smokers who benefit the most from each method.

#### Safety

Using therapeutic nicotine is always safer than continuing to smoke. All forms of NRT can be used by patients with stable cardiovascular disease, but should be used with caution in people with recent myocardial infarction, unstable angina, severe arrhythmias and recent cerebrovascular events.

NRT can be used by smokers who are pregnant, but alternative non-drug cessation strategies should be used first. Intermittent NRT dosage (oral forms) is preferred to deliver a lower daily dose of nicotine and to avoid continuous nicotine exposure. There is currently insufficient evidence to determine whether or not nicotine replacement therapy is effective or safe when used in pregnancy for smoking cessation.<sup>104</sup> However, it is likely to be effective given the strength of data in non-pregnant smokers. Nicotine passes from the mother to child through breast milk, depending on the concentration of nicotine in the maternal blood, but the nicotine in breast milk is unlikely to be dangerous.<sup>105</sup> Women who smoke should be encouraged to continue breastfeeding and provided with strategies to minimise the potential harm to their child associated with the secondhand smoke.

Because of the uncertainty of the safety of NRT used during pregnancy, pregnant women wishing to use NRT to quit should be supervised by a medical practitioner, or other suitably qualified professional.

#### Side effects

Minor side effects are common with NRT use. 100 Common adverse effects with NRT depend on the delivery system. For the patch, they include skin erythema, skin irritation and sleep disturbance (abnormal dreams). For gum, lozenge and sublingual tablet minor side effects include dyspepsia and nausea, and for the inhaler – mouth and throat irritation may occur. 53

#### Availability of nicotine patches on the PBS

Nicotine patches (15 mg over 16 hours and 21 mg over 24 hours) are listed on the PBS for use as an aid to quitting for people who participate in a support and counselling program. A maximum of one PBS subsidised 12 week course of nicotine patches (one original script plus two repeats) is subsidised per year. An authority prescription is required and the support program being used needs to be specified, eg. the GP's practice, the Quitline or other suitable programs.

Lower strength patches and other nicotine products are not subsidised. The subsidised patches are not available at the same time as other PBS subsidised smoking cessation therapies (varenicline and bupropion), but if a person is unsuccessful quitting using the nicotine patches, then they are able to access PBS subsidised medicines during that same 12 month period. Only certain brands – one 15 mg/24 hour patch (Nicorette) and two 21 mg/24 hour patches (Nicotinell Step 1 and Nicabate P) – are listed.

#### Aboriginal and Torres Strait Islander people

People who identify as Aboriginal or Torres Strait Islander qualify for PBS authority listing that provides up to two courses per year of nicotine patches, each a maximum of 12 weeks. Under this listing, participation in a support and counselling program is recommended but not mandatory. Access to nicotine patches for Aboriginal and Torres Strait Islander people can be facilitated through the Closing the Gap PBS copayment measure (see *page 43*).

Health professionals should check for updated PBS listings at www.pbs.gov.au.

#### Evidence

Nicotine transdermal patch, nicotine gum and nicotine inhaler all increase quit rates by 50-70% at 5-12 months compared with placebo, and regardless of the setting. **Level I** 

There is no evidence of increased risk for use of NRT in people with stable cardiovascular disease. **Level II** 

There is no evidence of an association between use of nicotine patch and acute cardiac events. **Level II** 

There is currently a lack of evidence on the safety of NRT in pregnancy but international guidelines recommend use of NRT in certain circumstances. **Level V** 

In more dependent smokers combinations of different forms of NRT (eg. patch plus gum) are more effective than one form alone. **Level II** 

#### Recommendations

NRT should be recommended to nicotine dependent smokers. There is no significant difference in effectiveness of different forms of NRT in achieving cessation so choice of product depends on clinical and personal considerations. **Strength A** 

NRT is safe to use in patients with stable cardiovascular disease.

#### Strength A

NRT should be used with caution in patients who have had a recent myocardial infarction, unstable angina, severe arrhythmias or recent cerebrovascular events. **Strength C** 

Use of NRT should be considered when a pregnant woman is otherwise unable to quit. Intermittent NRT is preferred to patches (lower total daily nicotine dose). **Strength C** 

Combination NRT should be offered if patients are unable to remain abstinent or continue to experience withdrawal symptoms using one type of therapy. **Strength A** 

#### **Varenicline**

#### Key points

- Varenicline is a nicotine partial agonist drug for smoking cessation
- It can more than double the chances of long term quitting
- It has been found to be more effective than bupropion, but there is a lack of studies directly comparing it to NRT
- Smokers using varenicline should be advised to report unusual mood changes, depression, behaviour disturbance and suicidal thoughts and if these occur to stop using the medicine
- The risk of cardiovascular events should be discussed with smokers and weighed up against the known benefits of the drug on smoking cessation
- There is no evidence of the efficacy of combining varenicline with any other smoking cessation pharmacotherapy
- The target quit day is in the second week of treatment, but patients should continue to use varenicline as the rate of successful cessation rises during the standard 12 week treatment period
- Longer term use (a second 12 week course) slightly reduces relapse for up to one year in people who have successfully quit at the end of week 12.

Varenicline is a nicotinic acetylcholine-receptor partial agonist. It was developed specifically for smoking cessation by targeting the nicotinic acetylcholine (ACh) receptor in the reward centres in the brain. Varenicline binds with high affinity at the  $\alpha 4\beta 2$  nicotinic ACh receptor, where it acts as a partial agonist to alleviate symptoms of craving and withdrawal. At the same time, if a cigarette is smoked, the drug prevents inhaled nicotine from activating the  $\alpha 4\beta 2$  receptor sufficiently to cause the pleasure and reward response. This mechanism may explain why quitting can occur later in a course of treatment with varenicline.

#### **Efficacy**

Varenicline at standard dose can increase the chances of successful long term smoking cessation between two and threefold compared with pharmacologically unassisted quit attempts.  $^{91,95}$  In two randomised, double blind clinical trials with identical study designs, varenicline was compared to both bupropion and to placebo.  $^{106,107}$  All three groups received brief behavioural counselling. When the results of these studies were combined in a meta-analysis, the abstinence rate for varenicline was significantly better at 1 year than bupropion (odds ratio [OR] 1.58; 95% confidence interval [CI]: 1.22–2.05), and placebo (OR 2.96; 95% CI: 2.12–4.12,  $p \le 0.0001$ ).

Two open label randomised trials have compared varenicline with nicotine patch, <sup>94,108</sup> although the more recent study was too small to contribute usefully to a pooled estimate in the Cochrane review. <sup>91,109</sup> At 52 weeks, the earlier study reported a larger benefit for varenicline over nicotine patch that almost reached statistical significance (RR 1.29; 95% Cl: 0.99–1.67) for biochemically confirmed continuous abstinence. <sup>94</sup> In the trials, varenicline was shown to significantly reduce craving and other withdrawal symptoms.

Prolonged use of varenicline has also been shown to reduce relapse. In subjects who stopped smoking at the end of 12 weeks of treatment, an additional 12 weeks of treatment was more beneficial than placebo in maintaining abstinence to the end of treatment and to 1 year from the start of treatment. However, the difference in continuous abstinence for weeks 13–52 between intervention and control groups was small.<sup>110</sup> The benefit appears to be maintained only for the period of use of varenicline.

#### Safety

The effectiveness and safety of varenicline has not been studied in patients with psychiatric conditions. Postmarketing, there have been reports of mood changes, depression, behaviour disturbance and suicidal ideation possibly associated with varenicline. Accordingly, prescribers have been advised to monitor patients for emergence of these problems. However, a meta-analysis has found that such reports are so far not substantiated as being due to the drug. Another study of drug adverse events reports in the USA found an increased risk of depression and suicidal behaviours related to varenicline compared to NRT, However, submission of adverse events reports can be influenced by publicity and does not necessarily prove causality. It is important that prescribers ask patients to report any mood or behaviour changes. Smokers should be advised to stop taking varenicline at the first sign of any of these symptoms. Although a causal relationship of these symptoms with varenicline has not been demonstrated, prescribers should weigh up possible risks of varenicline against the benefits of smoking cessation.

A meta-analysis of 14 placebo controlled trials in a total of 8216 people, with and without cardiovascular disease, reported an association between use of varenicline and an increased risk of cardiovascular events (non-fatal myocardial infarction, need for coronary revascularisation and new diagnosis of peripheral vascular disease or admission for a procedure to treat peripheral vascular disease), OR 1.72; 95% CI: 1.09–2.71. From the meta-analysis, based on one study in patients with cardiovascular disease and data reported in the others, it is possible that use of varenicline is associated with an increase risk in selected non-fatal cardiovascular events. The US Food and Drug Administration (FDA) guidance in relation to this finding is that the absolute risk with varenicline, in relation to its efficacy, is small but that health professionals should discuss the risk of cardiovascular events with their clients and carefully balance the risks associated with varenicline use against the known benefits of the drug on smoking cessation. In Australia, the TGA has not, to date, added a caution for use of varenicline in patients with cardiovascular disease.

#### Side effects

Nausea is the most common adverse effect of varenicline and was reported in studies of almost 30% of smokers, although less than 3% discontinued treatment due to nausea. Abnormal dreams were also more common in the varenicline group (13.1%) than either the bupropion (5.9%) or placebo groups (3.5%). No clinically meaningful drug interactions have been identified.

Varenicline is excreted almost entirely by the kidneys. For people with creatinine clearance < 30 mL/min, the recommended daily dosage is 1 mg/day (0.5 mg/day for 3 days then increasing to 1 mg/day). Avoid varenicline in end stage renal failure in favour of other approaches to smoking cessation. Dose adjustment is not routinely required in elderly people or in people with hepatic impairment.<sup>113</sup>

#### Availability of varenicline on the PBS

Varenicline is available in Australia on the PBS as short term adjunctive therapy for nicotine dependence. It can be prescribed for up to 24 weeks of continuous therapy for smoking cessation for smokers who are enrolled in a support and counselling program and who are abstinent at 12 weeks.

The first script is a starter pack lasting 4 weeks (including dose titration), followed by a maintenance batch for 8 weeks of treatment.

A third authority prescription is required for a final 12 weeks of treatment, for those who respond to the first 12 weeks (*Table 5*). The medicine can be taken whole with water and food to help reduce nausea.

Health professionals should check for updated PBS listings at www.pbs.gov.au.

#### Table 5. 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. The exact date can be determined on the basis of perceived effects of the drug, but should not exceed 2 weeks. 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 8 week course
- A final 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.

### Evidence

Varenicline is an efficacious smoking cessation treatment. Level I

### Recommendation

### **Bupropion**

### Key points

- Bupropion is a non-nicotine oral therapy, originally developed as an antidepressant
- It significantly increases cessation rate compared with placebo
- It has been shown to be effective for smokers with depression, cardiac disease and respiratory diseases, including COPD
- It has been shown to improve short term abstinence rates for people with schizophrenia
- Bupropion has been shown to be not as effective as varenicline for smoking cessation
- There is limited evidence of the safety or efficacy of combining bupropion with NRT and no evidence on its combination with varenicline.

Originally developed as an antidepressant, bupropion is a non-nicotine oral therapy that reduces the urge to smoke and reduces symptoms from nicotine withdrawal.

### Efficacy

Bupropion significantly increases the long term cessation rate compared with placebo RR 1.69; 95% CI: 1.53–1.85)<sup>92</sup> over 12 months. Data from two randomised controlled trials showed 9% and 19% of smokers had not smoked for the 12 months following placebo and bupropion therapy, respectively.<sup>99,114</sup> It has been shown to be effective in a range of patient populations including smokers with depression, cardiac disease and respiratory diseases including COPD.<sup>115</sup> It has also been shown to improve short term abstinence rates for people with schizophrenia.<sup>116</sup>

Clinical trials have shown that bupropion is not as effective as varenicline. However, bupropion is a useful option in cases where varenicline is not appropriate (patient choice, or as a result of side effects). There is also more evidence for the use of bupropion than varenicline in smokers with depression or schizophrenia. There is insufficient evidence that adding bupropion to NRT provides an additional long term benefit.<sup>92</sup>

### Safety

Bupropion is contraindicated in patients with a history of seizures, eating disorders and those taking monoamine oxidase inhibitors. The current recommendation is that it should be used with caution in people taking medications that can lower seizure threshold, such as antidepressants and oral hypoglycaemic agents.<sup>91</sup>

Alternative medication should be considered in these situations.

### Side effects

Seizures are the most clinically important adverse effect (0.1% risk) and fatalities have been reported. Common adverse effects are insomnia, headache, dry mouth, nausea, dizziness and anxiety.<sup>115</sup> Bupropion can be used in combination with NRT, but blood pressure should be monitored.<sup>115</sup>

### Availability of sustained release bupropion on the PBS

Since 2001, sustained release bupropion has been available in Australia as a PBS authority item once per year. It is a short term adjunctive therapy for nicotine dependence in conjunction with counselling with the goal of maintaining abstinence.

Bupropion is available as a starter pack of 30 tablets and a continuation pack of 90 tablets. The dose of bupropion is 150 mg once per day for the first 3 days and then increased to 150 mg twice per day. The patient should stop smoking in the second week of treatment.

Health professionals should check for updated PBS listings at www.pbs.gov.au.

### Evidence

Bupropion sustained release is an efficacious smoking cessation treatment.

### Level I

Combination treatment with bupropion and nicotine replacement therapy is effective. **Level II** 

#### Recommendations

Bupropion sustained release should be recommended to smokers who have been assessed as clinically suitable for this medication and provided in combination with counselling. **Strength A** 

Combination treatment with bupropion and nicotine patch can be considered where a smoker has not been successful on an adequate trial of one of these therapies. Blood pressure should be monitored during treatment. **Strength C** 

## Other pharmacotherapy options

### **Nortriptyline**

The tricyclic antidepressant, nortriptyline, has been shown to approximately double cessation rates compared to placebo (OR: 2.3). 92,117 A systematic review shows that the use of nortriptyline for smoking cessation resulted in higher prolonged abstinence rates after at least 6 months, compared to placebo treatment. 118 The efficacy of nortriptyline does not appear to be affected by a past history of depression, but it is limited in its application by its potential for side effects including dry mouth, constipation, nausea, sedation and headaches, and a risk of arrhythmia in patients with cardiovascular disease. Nortriptyline can be dangerous in overdose.

Nortriptyline is not registered for smoking cessation in Australia.

The dose of nortriptyline used for smoking cessation is approximately 75 mg/day for 12 weeks. Further information about dose titration can be obtained from New Zealand Smoking Cessation Guidelines.<sup>13</sup>

### Evidence

Nortriptyline is an efficacious smoking cessation treatment in people with and without a history of depression. **Level II** 

### Recommendation

Nortriptyline should only be considered as a second line agent due to its adverse effects profile. **Strength B** 

### **Future options**

A number of novel tobacco cessation therapies are in development.<sup>119,120</sup> Cytisine, a naturally occurring substance chemically related to varenicline, has been used for smoking cessation for decades in parts of Eastern Europe, but robust evidence of its effectiveness is lacking and there is limited evidence of its role in smoking cessation relative to other options.<sup>91</sup> A trial investigating this question is currently underway in New Zealand – a recent study has shown that cytisine is more effective than placebo for smoking cessation.<sup>121</sup>

Also in development are antinicotine vaccines. The rationale for immunisation against nicotine is to induce antibodies that bind nicotine in the blood, thereby preventing it from crossing the blood brain barrier. It is postulated that with less nicotine reaching the brain immediately after smoking, the vicious cycle between smoking and nicotine related gratification will be broken. Phase II studies have evaluated three different vaccines, NicVAX®, Nicotine-Qbeta™ and TA-NIC. While some results from these small studies are promising, the NicVAX data are disappointing. The vaccines need to be administered regularly to maintain effects – they will not provide long term protection with a single course of treatment. Larger ongoing studies of a longer acting vaccine are needed before this approach can be evaluated. <sup>122,123</sup>

Given that the current available first line medications are all efficacious, and non-drug factors make a substantial contribution to the likelihood of quitting successfully, 100 choice should be based on clinical suitability and patient preference (see *Figure 2. Pharmacotherapy treatment algorithm for tobacco smoking cessation*).

# Other forms of treatment and support for smoking cessation

Although many smokers are likely to attempt quitting unassisted, this approach has a low likelihood of succeeding (3–6% success rate) on any given attempt. The most successful quit approach for those who are nicotine dependent is counselling and support combined with first line pharmacotherapy and follow up. Health professionals should offer to assist their patients/ clients with a quit attempt, using pharmacotherapy and counselling, either within the health service or by referring them for intensive support to a telephone Quitline (13 7848), or to a tobacco treatment specialist.

Health professionals should be aware of extravagant claims of success for interventions that have not been subjected to rigorous testing and for which there is no clinical evidence to support.

The following smoking cessation interventions have been proven to be effective.

### Brief motivational advice from health professionals

There is strong evidence that advice from health professionals (doctors, nurses, nurse practitioners, medical assistants, dentists, hygienists, respiratory therapists, mental health counsellors, pharmacists) is effective in encouraging smoking cessation. Health professionals can make a difference with even a minimal (less than 3 minutes) intervention RR 1.66; 95% CI: 1.42–1.94). More intense interventions can result in better outcomes, but may not be practical in many clinical contexts. (See page 7, The role of health professionals.)

Every smoker should be offered at least a brief intervention for smoking cessation, which should include one or more of the following:<sup>127</sup>

- simple opportunistic advice to consider quitting
- an assessment of the smoker's commitment to quit
- offer of pharmacotherapy and/or behavioural support
- self help material
- referral to more intensive, proactive support such as Quitline (13 7848), a tobacco treatment specialist or cessation programs.

### Evidence

Brief smoking cessation advice from health professionals delivered opportunistically during routine consultations has a modest effect size, but substantial potential public health benefit. **Level I** 

#### Recommendation

Offer brief cessation advice in routine consultations whenever possible (at least annually). **Strength A** 

### **Group or individual counselling**

There is clear evidence that both individual (RR 1.39; 95% CI: 1.24–1.57)<sup>128</sup> and group counselling (RR 1.98; 95% CI: 1.60–2.46)<sup>129</sup> increases quit rates over that of minimal support.

Individual counselling typically involves weekly face-to-face meetings between a smoker and a counsellor trained in smoking cessation over a period of at least 4 weeks after the quit date and is normally combined with pharmacotherapy. Group behaviour therapy involves scheduled meetings (typically 4–8) where smokers receive information, advice and encouragement and some form of behavioural intervention. 127

Counselling should include practical advice consisting of problem solving and skills training, and social support as part of the treatment. Group techniques, which focus on skills training and provide mutual support, can also be effective for those who find this method appropriate.<sup>53</sup>

In some states, quitlines keep registers of local support programs led by approved providers.

### Telephone counselling and quitlines

Telephone counselling provides advice, encouragement and support by specialist counsellors to smokers who want to quit, or who have recently quit. Counsellors can call the client (a proactive service) usually several times over the period leading up to, and the month following, their quit attempt or the client can call the service (a reactive service). There is stronger evidence that the proactive form of support is more effective, 130–133 in part because most smokers do not make the call to Quitline often enough to get the full benefit, yet they readily accept and appreciate proactive calls. Telephone counselling, also known as Quitline, is provided through state or national services available in many countries (eg. Australia, New Zealand, United Kingdom, United States). A review in New Zealand of the cost effectiveness of a variety of interventions found quitlines, particularly when they include the use of pharmacotherapy, to be among the highest rated. 34

Adding Quitline counselling to pharmacotherapy and minimal intervention increases abstinence rates (RR 1.29; 95% CI: 1.20–1.38).<sup>130</sup>

### Evidence

Telephone callback counselling services are effective in assisting cessation for smokers who are ready to quit. **Level II** 

### Recommendation

Referral to such services should be considered for this group of smokers.  $\textbf{Strength} \ \textbf{A}$ 

### Quitline services in Australia

Quitline (13 7848) (13 QUIT) exists in all Australian states and territories. Quitline can provide a free Quit pack and telephone counselling assistance. Quitline can also assist in linking callers into community programs. Counsellors can help callers find a course and email the link to them.

Calls are charged at the cost of a local call (about 25 cents, mobile telephone extra) from both rural and metropolitan areas.

All Quitline services in Australia have agreed to national minimum standards of service delivery.

- In most states and territories, smokers are offered free proactive telephone
  counselling. Proactive or callback counselling protocols usually allow up to two
  sessions pre-quit and four post-quit over the first month, with two in the first
  week, but vary from state to state
- Fax referral to Quitline (smokers can be referred by all health professionals to the Quitline for extended support using the fax referral sheet). Services provide feedback to health professionals regarding patients referred to a Quitline (see Appendix 2 for fax referral form)
- Processes for online referral to Quitline through patient management software are likely to become available
- Quitline adviser, course leader or coach
- Adolescent protocols
- Indigenous counsellors or indigenous liaison people are available at Quitline Australia wide
- Self help books (eg. www.quitbecauseyoucan.org.au).

### Services for those from culturally and linguistically diverse backgrounds:

- In some states, bilingual educators conduct information sessions in a number of community languages. Visit www.quit.org.au.
- Community language specific Quitline telephone numbers available (see below)

### Web-based material:

- iCanQuit: www.iCanQuit.com.au
- Quit Coach: www.quitcoach.org.au.

### Self help materials

Self help interventions for smoking cessation in the form of structured programs in written (books, brochures, manuals) or electronic (CDs, online) formats provide support and advice for smokers without the help of health professionals, counsellors or group support. On their own, these materials show only marginal effect compared to no intervention, and there is no evidence that they have an additional benefit when used with other interventions, such as advice from a health professional or NRT.<sup>131</sup> There is evidence that materials

tailored for individual smokers in different tobacco dependent populations are more effective than untailored materials.<sup>10,133</sup>

Two studies have found that text message mobile phone support programs are effective in the short term (6 weeks)<sup>134</sup> and long term.<sup>135</sup> Combined internet/mobile telephone programs can be effective for up to 12 months for assisting smokers to quit.<sup>136,137</sup>

Online smoking cessation interventions are low cost and have the potential to reach a large number of smokers. <sup>138,139</sup> A major advantage of the internet over printed material is its interactivity and the ability to tailor information to individual needs, but relatively few sites make use of this possibility (for a good example of a site designed to tailor information to individual needs, see the Quit Coach at www.quitcoach.org.au). <sup>16</sup> Web based programs are a promising delivery system for assisting smokers to quit, but further research is needed to identify their most effective use.

### Ineffective and unproven approaches to smoking cessation

There are several quitting methods, which are in widespread use, but have not yet been shown in well designed trials to be effective for quitting other than a placebo effect – or more than counselling and support provided at the same time.<sup>16</sup>

There are some approaches that have the potential to assist with maintaining long term smoking cessation, but they have not yet been adequately investigated for cessation. These approaches include physical activity, the Alan Carr method and electronic nicotine delivery systems (ENDS), also called electronic cigarettes or e-cigarettes.

### Hypnotherapy (without counselling)

Hypnotherapy is widely promoted as an effective way to stop smoking. It is said to assist smoking cessation by weakening the desire to smoke, or strengthening the will to stop. Despite being in use for some decades, there are only a few well designed studies to evaluate its use. A Cochrane meta-analysis has concluded that, although it is possible that hypnotherapy could be as effective as counselling treatment on quit rates, there is not enough high quality evidence at this time to be certain. 40

### Acupuncture

People sometimes have acupuncture for quitting smoking with the aim of reducing withdrawal symptoms. Related therapies include acupressure, laser therapy and electrical stimulation. At present, there is no consistent evidence that acupuncture, or any related therapy, is better than doing nothing. Well designed trials of acupuncture, acupressure and laser stimulation are needed before these treatments can be recommended as effective in smoking cessation.<sup>141</sup>

### Evidence

There is no significant effect of acupuncture or hypnotherapy in smoking cessation. Level I

### Recommendation

On the evidence available acupuncture and hypnotherapy are not recommended as aids to smoking cessation. **Strength A** 

### Naltrexone

At present there is inconclusive evidence that the long acting, opioid antagonist naltrexone can increase the likelihood of smoking cessation. It is promoted to help reduce nicotine addiction by blocking some of the rewarding effects of smoking. Data from larger trials are needed to confirm naltrexone's efficacy for smoking cessation.

### Aversive or rapid smoking

There is limited evidence to suggest that rapid (or aversive) smoking may be effective. However, this technique should not be attempted without appropriate training.

### Biomedical feedback

Demonstration of the effects of smoking, with the exception of spirometry,<sup>144</sup> has not been shown to increase quit rates. Strategies used include carbon monoxide results, vascular ultrasounds and genetic susceptibility.<sup>145</sup>

### Physical activity

There are two major aspects to quitting tobacco use: overcoming nicotine addiction and changing lifestyle. It is well known that increased physical activity has many benefits for a healthy life. Exercise has been investigated as a way of helping with symptoms of nicotine withdrawal and cravings during attempts to quit. Exercise may also help by increasing self esteem and might help to manage the weight gain that often follows quitting. However, there is currently no evidence to show higher abstinence rates long term with exercise alone. 146

Well designed studies with larger sample sizes and sufficiently intense interventions are underway to test whether physical activity could be recommended as an adjunct to cessation. However, increased activity should not be discouraged as part of a support program as it brings other health advantages.

### Allen Carr method

Although it has considerable popular support, there is no high quality, empirical evidence that the Allen Carr method is effective.<sup>13</sup>

### St John's wort

The herbal antidepressant St John's wort (*Hypericum perforatum*) herb extract has not been shown to aid in smoking cessation. There is as yet no convincing evidence that St John's wort, alone or with individual motivational and behavioural support, is likely to be effective as an aid in smoking cessation.<sup>149</sup>

### Other nicotine related agents

NicoBloc® and Nicobrevin are nicotine related agents, which are occasionally recommended by some healthcare professionals. These are available in some pharmacies, 150 despite a lack of any empirical evidence of effectiveness. 13,151

While available in many countries, electronic cigarettes (e-cigarettes), which deliver nicotine by inhalation, are not regulated. Before these products can be recommended for consumers, research must be conducted on the safety and efficacy for smoking cessation.<sup>152</sup>

# Smoking reduction rather than smoking cessation

Some smokers are unable or unwilling to completely quit smoking. It has been proposed that reducing the number of cigarettes smoked per day has long term benefits. However, it is not clear whether this strategy decreases the risk for tobacco related diseases. Research has shown that smoking reduction by 50% significantly reduces the risk of lung cancer in heavy smokers (15 or more cigarettes each day). But studies have not shown a decrease of risk of fatal or non-fatal myocardial infarction, hospitalisation for COPD or all cause mortality compared with heavy smokers who do not change smoking habits. Health professionals should always encourage smoking cessation as the proven method of reducing harm from smoking.

There is insufficient evidence about long term benefit to support the use of interventions intended to help smokers reduce, but not quit smoking. Some people who do not wish to quit can be helped to cut down the number of cigarettes smoked by using nicotine gum or nicotine inhaler. Because the long term health benefit of a reduction in smoking rate is unclear, this use of NRT is more appropriate before quitting. <sup>157</sup> Smokers who use NRT for smoking reduction are approximately twice as likely to progress to quitting than those who do not. <sup>157</sup>

## Relapse

Relapse is common. Most smokers make repeated quit attempts before finally achieving long term abstinence. Relapse is associated with the severity of withdrawal symptoms and the association of factors, such as stress and weight gain, with the process of quitting tobacco. There is no intervention that is proven to prevent relapse, but advice and pharmacotherapy are recommended to treat symptoms of withdrawal, stress and weight gain. 159

# Smoking cessation in high prevalence populations

Although the proportion of people aged 14 years of age and over smoking tobacco daily has continued to decline from 16.6% in 2007, to 15.1% in 2010, the smoking rate is lower in more affluent, better educated segments of the community while the number of smokers in disadvantaged groups remains disproportionately high. The proportion of Australians who smoke is inversely related to the socioeconomic status of where they live – in 2010, 24.6% of people in areas with the lowest socioeconomic status smoked compared with 12.5% in areas with the highest socioeconomic status.<sup>1</sup>

In many countries, including Australia, social inequalities in tobacco use contribute to inequalities in health.<sup>51</sup> There is a clear relationship between smoking and socioeconomic status, with disadvantaged groups in the population being more likely to start smoking and to remain long term smokers. In particular, three sociodemographic variables are closely connected with the likelihood of smoking: education, family income and Index of Relative Socioeconomic Disadvantage.<sup>18,160</sup> The most recent National Health Survey 2004–2005 indicates that smokers tend to report other lifestyle risk factors such as higher levels of alcohol consumption, lower daily fruit and vegetable intake and lower levels of exercise.<sup>24</sup> There is extensive evidence that tobacco use contributes to poverty and inequality, encouraging smokers to quit has the potential to improve health and also to alleviate poverty.

The same guidelines for quitting smoking apply to all groups – every opportunity should be taken to offer all smokers advice and support to stop smoking.<sup>7</sup> Counselling and behavioural interventions may be modified to be appropriate for the individual smoker. Quitlines and other service providers have been trained for clients from many high prevalence groups, including Aboriginal and Torres Strait Islander people. All smokers should be offered pharmacotherapy, unless contraindicated.

### Aboriginal and Torres Strait Islander people

Half of the Aboriginal and Torres Strait Islander population are current daily smokers, a prevalence rate more than double that of the non-indigenous Australian population. Since the 1994 National Health Survey, smoking rates have decreased for the total Australian population, but they have remained stable over this period for the indigenous population, falling slightly for the first time over the period 2002–2008. If the smoking rate among Indigenous Australians can be reduced to that of the non-indigenous population, the overall indigenous burden of disease should fall by around 6.5%, and provide improved life outcomes for around 420 Aboriginal and Torres Strait Islander people each year.

Compared with other Australians, Aboriginal and Torres Strait Islander people experience socioeconomic disadvantage across a range of indicators including education, employment, income and housing. Because of the strong association between low socioeconomic status, poor health and increased exposure to health risk factors, smoking is a major contributor to the 17 year life expectancy gap between Indigenous and non-Indigenous Australians.

Aboriginal and Torres Strait Islander people experience higher mortality from a number of smoking related diseases (including cardiovascular diseases, a number of cancers and respiratory disease) compared to the general Australian population.<sup>162</sup>

Though various smoking cessation methods have been shown to be effective across different racial and ethnic groups in other countries,99 there has been a lack of research and evaluation of tobacco interventions in the Indigenous Australian population. Smoking cessation methods identified as being effective, such as brief advice and pharmacotherapy, should be provided for all smokers. Effective smoking cessation methods should be modified or tailored to meet the needs of Aboriginal and Torres Strait Islander people. This approach can involve working in collaboration with Aboriginal Health Workers. Appropriate cessation services for Aboriginal and Torres Strait Islander people can be found at the Centre for Excellence in Indigenous Tobacco Control (CEITC) at www.ceitc.org.au/quitting\_resources. Specific barriers to smoking cessation treatment for Aboriginal and Torres Strait Islander people, such as the social context that normalises smoking, are being addressed by healthcare workers in many Aboriginal communities. There is also evidence of less knowledge about the harmful effects of tobacco smoking among Aboriginal and Torres Strait Islander people, as well as evidence that this population uses medicines at a lower rate than other Australians – despite initiatives in place to improve access to treatment. Other factors such as a lack of availability and access to culturally appropriate health services, language barriers and high rates of smoking among Aboriginal health workers are a significant barrier to the success of smoking cessation strategies for indigenous communities.163

People who identify as Aboriginal or Torres Strait Islander qualify for the PBS Authority listing for NRT, which provides up to two courses per year of nicotine patches, each of a maximum of 12 weeks. Under this listing, participation in a support and counselling program is recommended but not mandatory.

### Closing the Gap PBS copayment measure

The Closing the Gap (CTG) measure is part of the Australian Government's Indigenous Chronic Disease Package, established to improve access to medicines by reducing the cost of accessing PBS medicines for eligible Aboriginal and Torres Strait Islander people who are living with or are at risk of chronic disease.

Under this measure, eligible patients must be registered at a rural or urban indigenous health service, or a general practice that participates in the Indigenous Health Incentive (IHI) under the Practice Incentives Program (PIP) in order to receive a CTG annotated PBS prescription.

Depending on the indigenous patient's concessional status, when a CTG annotated prescription is dispensed at a pharmacy, the patient pays a lower, or nil, copayment for all PBS medicines. A concessional patient's copayment reduces to nil and a general patient's copayment reduces to that of a concessional patient. Some suppliers of PBS medicines impose a brand premium on some brands of medicine, which the patient must pay. Brands that carry a manufacturer's surcharge are indicated by a 'B' on the PBS Schedule.

For further information email PBS-Indigenous@health.gov.au or visit www.health.gov.au/tackling-chronic-disease.

### Culturally and linguistically diverse groups

Prevalence of tobacco use in culturally and linguistically diverse groups in Australia varies from one community to another. Smoking is more common in men from Vietnamese and Chinese backgrounds and men and women from Middle Eastern backgrounds. People born in Oceania (New Zealand, Melanesia, Micronesia and Polynesia), Southern and Eastern Europe, and North West Europe were the most likely to report high rates of current smoking (24%, 23% and 22% respectively). However, average smoking rates in some of these communities are lower than for the rest of the Australian population. Tobacco is more commonly used via waterpipes in the Middle Eastern and African communities and by chewing it in the Burmese community rather than smoking cigarettes.

Some smokers in culturally and linguistically diverse groups in Australia face extra barriers to quitting, including a lack of awareness of the health consequences of smoking and secondhand smoke, lack of tobacco control regulations and norms in their culture of origin and difficulties accessing health information because of low literacy in English. These problems are most common among recently arrived groups and refugees.

Health professionals should offer advice, support and pharmacotherapy for all smokers. Support for cessation for these groups should use culturally appropriate resource materials.

The telephone Quitline service provides printed resources in 13 languages other than English, and callers can ask to have their call returned with an interpreter, in a range of languages other than English. Bilingual educators from Quit Victoria conduct information sessions in a number of community languages (www.quit. org.au) and the NSW Multicultural Health Communication Service provides information and services to help health professionals communicate with non-English speaking communities (www.mhcs.health.nsw.gov.au).

### Community language Quitline telephone numbers

Arabic	1300	7848	03
Chinese (Cantonese and Mandarin)	1300	7848	36
Italian	1300	7848	61
Vietnamese	1300	7848	65
Korean	1300	7848	23
Greek	1300	7848	59
Spanish	1300	7848	25

# Smoking cessation in populations with special needs

There are several population groups for whom there are particular implications regarding nicotine dependence and the effects of smoking, as well as the use of medicines for smoking cessation. Many of these groups (children and adolescents, pregnant and lactating women, people with mental illnesses, people with substance use disorders and people with smoking related diseases) have not been studied in clinical trials of pharmacotherapy for smoking cessation. However, the same guidelines for quitting smoking apply to all groups – every opportunity should be taken to offer all smokers advice and support to stop smoking. Counselling and behavioural interventions may be modified to be appropriate for the individual smoker.<sup>6</sup> In addition, all smokers should be offered pharmacotherapy and referred for intensive treatment to the telephone Quitline (13 7848), other cessation programs or local face-to-face services where available.

Aboriginal and Torres Strait Island people are particularly vulnerable to tobacco use and consequent disease caused by tobacco use. This group is highly represented in many categories of those with special needs: pregnant women, adolescents, prisoners, people with substance use problems and people with smoking related diseases such as diabetes.

### Pregnant and lactating women

As well as the serious long term health consequences for the mother, cigarette smoking by pregnant women causes a range of adverse fetal outcomes including stillbirth, spontaneous abortion, reduced fetal growth, premature birth, low birth weight (a key indicator of infant health), placental abruption, sudden infant death, cleft palate, cleft lip and childhood cancers. Approximately 17% of women in Australia smoke during pregnancy 164 and 20% of women who are pregnant or breastfeeding continue to smoke.

Pregnant women who are most disadvantaged are more than four times more likely to smoke than women who are least disadvantaged (28% compared to 6%) and Aboriginal or Torres Strait Islander women are more than three times more likely to smoke during pregnancy than non-indigenous women (53% compared with 16%).<sup>16</sup>

Although 20–30% of women quit when they become pregnant, about 70% of these women relapse either during pregnancy, or after the baby is born. This is an important group of smokers to identify as they have made a quit attempt and are motivated. Smoking cessation interventions have been shown to be effective during pregnancy – overall by approximately 6%.<sup>166</sup> Relapse in the postpartum period is high although there is evidence that this rate could be reduced by smoking cessation interventions at this time, but the difference is not significant at longer follow up.<sup>166</sup> Health professionals should inform pregnant women and new mothers of the dangers of passive smoking to newborn babies and young children.

The only safe level of smoking in pregnancy is not smoking at all because:

- any level of nicotine or tobacco smoke exposure increases the risk of adverse effects<sup>23,167–169</sup>
- the greatest gain in health benefits comes from quitting rather than cutting down.<sup>14,23,170</sup>

While not smoking at all in pregnancy has the greatest benefits to both the fetus and mother, quitting at any point throughout pregnancy has benefits. Therefore, health professionals should offer cessation interventions to pregnant smokers as soon as possible in the pregnancy, throughout the pregnancy, and beyond. Because of the uncertainty of the safety of NRT used during pregnancy, pregnant women wishing to use NRT to quit should be supervised by a medical practitioner, or other suitably qualified heath professional.

Many pregnant women do not disclose their smoking status to a health professional – some guidelines recommend multiple choice question formats to improve disclosure. Health professionals should encourage pregnant smokers to attempt cessation using counselling, advice and support interventions before using pharmacological approaches as the efficacy and safety of these approaches during pregnancy are not well documented. Pharmacotherapy should be considered for pregnant women only if the increased likelihood of quitting outweighs the harmful effects on the fetus of nicotine replacement therapy and possible continued smoking. Pregnant women should be encouraged to use Quitline. If these quit attempts are unsuccessful, and the woman is motivated to quit, NRT could be considered.

There is limited evidence of the effectiveness of NRT in helping pregnant women stop smoking. The main benefits of using NRT are the removal of the other toxins contained in tobacco smoke and the lower dose of nicotine delivered by NRT than tobacco smoke. NRT can be used by pregnant and breastfeeding mothers, but the risks and benefits should be explained carefully to the woman and the clinician supervising the pregnancy should be consulted. 6,16

In general, intermittent (oral) NRT should be used during pregnancy to deliver a lower total daily nicotine dose.<sup>13</sup> If patches are used by pregnant women, they should be removed before going to bed to protect the fetus from continuous exposure to nicotine. While nicotine passes from mother to child in breast milk, it is unlikely to be dangerous.<sup>105</sup> Women who continue to smoke after the birth should be encouraged to breastfeed their babies. Women who are unable to quit smoking completely can be given strategies to minimise exposure to the baby of secondhand smoke.

Neither of the two prescription medicines for smoking cessation in Australia, varenicline and bupropion, has been shown to be effective or safe for smoking cessation treatment in pregnant and breastfeeding smokers and they are not recommended. If a woman becomes pregnant while taking either agent, treatment should be ceased, and, if she agrees, reporting her pregnancy outcome to health authorities and the manufacturer may over time help better understand any risk.

All woman of child bearing age should be encouraged to stop smoking. Smoking cessation policy hopes to minimise the effects of smoking among all women – long term reduction in nicotine exposure during pregnancy can be achieved only by encouraging adolescent girls and young women not to start smoking.<sup>23</sup> It is also important to advise partners of pregnant women not to smoke around them and to encourage them to quit, as this can improve quit rates.

### Recommended smoking cessation treatment

- Pregnant women should be encouraged to stop smoking completely
- They should be offered intense support and proactive telephone counselling
- Self help material can supplement advice and support
- If these interventions are not successful, health professionals should consider NRT, after clear explanation of the risks involved
- Because of the uncertainty of the safety of NRT used during pregnancy, pregnant women wishing to quit using NRT should be monitored by a suitably qualified health professional
- Those who do quit should be supported to stay non-smokers long term.

### Evidence

There is currently a lack of evidence on the safety of pharmacotherapy in pregnancy, but international guidelines recommend use of NRT in certain circumstances. **Level V** 

### Recommendation

Use of NRT should be considered when a pregnant woman is otherwise unable to quit. Intermittent NRT is preferred to patches (lower total daily nicotine dose). **Strength C** 

### Adolescents and young people

It is estimated that more than 80% of smokers become addicted to nicotine as teenagers. Adolescence is the primary time when cigarette smoking is initiated and transition from experimentation to dependence occurs. In Australia in 2010, 3.8% of teenagers (12–17 year olds) smoked tobacco and 2.5% smoked daily.¹ Although men were generally more likely to be daily smokers than women, in the 12–17 years age group, young women were more likely to be daily smokers (3.2%) than young men (1.8%). However, young Australians aged 12–17 years were the age group least likely to smoke daily (2.5%).¹ One third of teenagers who become regular smokers will eventually die prematurely from smoking related diseases.¹¹¹

The reasons young people commence smoking are varied and relate to social and parental norms, advertising, peer influence, parental smoking, weight control and curiosity. Recruitment and retention of adolescents in formal smoking cessation programs are difficult and are a major determinant of intervention targeting young people. Computer and internet cessation programs are potential vehicles for programs aimed at young people, but as yet there is no clear evidence on efficacy.

Many adolescent anti-tobacco programs focus on preventing teenagers from starting to smoke, rather than quitting. These programs are largely ineffective. Likewise, there is insufficient evidence to show that smoking cessation programs to help teenagers who already smoke to quit are effective. There are also few studies with evidence about the effectiveness of pharmacological interventions for adolescent smokers.

Some quitting medications can be used by younger smokers. NRT can be offered if the smoker is nicotine dependent and ready to quit. Although NRT has been shown to be safe in adolescents, there is little evidence that these medications and bupropion or varenicline are effective in promoting long term quitting in adolescent smokers. The majority of studies included an intensive counselling component (6 or more sessions).<sup>10</sup>

### Recommended smoking cessation treatment

- Counselling is considered to be vital in this age group
- Health professionals should ask about smoking and provide a strong antismoking message
- NRT is recommended to adolescents only with precautions. The health professional should assess the nicotine dependence, motivation to quit and willingness to accept counselling before recommending NRT
- Bupropion and varenicline are not approved for use by smokers under 18 years of age.

### People with mental illness

Smoking in people with mental health problems is common. The smoking rate of the Australian population is just over 15%,¹ but for people with a mental health problem the rate is about 32%.²¹ In some cases, such as for people with schizophrenia, the rate is up to 62%.¹¹³ Although there is a belief that nicotine may modify some negative psychotic symptoms, such as lack of motivation and energy, and may decrease positive psychotic symptoms, such as auditory hallucinations, the belief is not supported by clinical evidence¹¹⁴4.¹¹¹⁵ and nicotine has proved ineffective as an adjunctive treatment for mental disorders.¹¹⁵

People with mental illness such as schizophrenia, depression, bipolar disorder and anxiety often experience physical, financial and social disadvantages because of their illness.<sup>177,178</sup> Many people with mental illness who smoke wish

to quit. Actively encouraging and assisting smoking reduction and cessation are important to improve their quality of life. Tobacco smoking can also interfere with the medications taken for schizophrenia and depression, and the doses of some medications may need to be increased or decreased.

Treating tobacco dependence is a worthwhile intervention for people with severe mental illness and may be just as effective as for the general population. In people with stable psychiatric conditions it should not worsen mental health.<sup>178,179</sup>

Health professionals should offer people with a mental illness smoking cessation interventions that have been shown to be effective in the general population.<sup>7</sup> Mental illness is not a contraindication to stopping smoking but the illness and its treatment need to be monitored carefully during smoking cessation.<sup>180–182</sup>

### Recommended smoking cessation treatment

- Intensive smoking cessation counselling and close follow up are important in this group
- NRT is safe and effective for people with a mental illness
- Consultation with a psychiatrist may be considered for advice on use of medicines for smoking cessation in people with significant mental illness
- Bupropion may not be suitable for people with a history of seizures, people with a history of anorexia or bulimia and people using other antidepressants. Caution is needed if there is concomitant use of bupropion with drugs such as tricyclic antidepressants and selective serotonin reuptake inhibitors. These drugs should be initiated at the lower end of the dosage range while a smoker is taking bupropion. In the more common situation that bupropion is initiated for a person already taking such antidepressants then the dose of tricyclic, or selective serotonin reuptake inhibitor, may need to be decreased. Bupropion should not be used in patients taking monoamine oxidase inhibitors (MAOIs) including moclobemide. A 14 day washout is recommended between completing MAOIs and starting bupropion. Consultation with a psychiatrist may be considered for advice on coprescribing bupropion with other antidepressants
- There is limited evidence of the safety and efficacy of varenicline in people with significant psychiatric illness. Varenicline helps with withdrawal symptoms and takes away the pleasure of smoking. There have been reports of depressed mood, suicidal ideation and changes in emotion and behaviour using this product; so far these reports have not been substantiated.<sup>86</sup> There is recent evidence from a study of drug adverse events that these effects are more common with varenicline than NRT.<sup>111</sup> Prescribers should ask patients to report any mood or behaviour changes. Smokers should be advised to stop taking varenicline at the first sign of any of these symptoms. The findings from a small pilot study show that when used with appropriate clinical monitoring, varenicline can help smoking cessation in people with schizophrenia.<sup>180</sup>

### People with substance use problems

Tobacco smoking is common in people with other drug use such as alcohol, cannabis and opiate dependence. Cannabis and tobacco are often used together as a way of smoking cannabis. As rates of cigarette smoking decline, it is now more common for cannabis dependence to lead to tobacco dependence than was previously the case. Smoking cessation has not been a major part of clinical interventions with these people as the attention is usually focussed on the alcohol or illicit drug use. There is good evidence that smoking cessation can enhance short term abstinence, rather than compromise the outcome of drug and alcohol treatments. States of cigarette smoking decline, it is now more common for cannabis and tobacco are often used to sea alcohol, and should be common for cannabis and tobacco are often used to sea alcohol, and should be common for cannabis and tobacco are often used to sea alcohol, as a state of cigarette smoking decline, it is now more common for cannabis and tobacco dependence than was previously the case. The case of cigarette smoking decline, it is now more common for cannabis and tobacco dependence than was previously the case. The case of cigarette smoking decline, it is now more common for cannabis and tobacco dependence than was previously the case. The case of cigarette smoking decline, it is now more common for cannabis and tobacco dependence to lead to tobacco dependence than was previously the case. The case of cigarette smoking decline, it is now more common for cannabis and tobacco dependence to lead to tobacco dependence than was previously the case. The case of cigarette smoking decline, it is now more common for cannabis and tobacco dependence to lead to tobacco dependence to lead to tobacco dependence than was previously to the case. The case of cigarette smoking decline, it is now more common for cannabis and tobacco dependence to lead to tobacco dependence to lead t

There is evidence that people with alcohol dependence can have similar success rates in smoking cessation to the general population, 185 although binge drinking is a risk factor for relapse. 186 There is also evidence that continued smoking adversely affects treatment for cannabis dependence. Success in smoking cessation for people with opiate dependence is lower than the general population. Monitoring and support are needed for smoking cessation in people with substance use problems who may benefit from the involvement of other health professionals, such as a drug and alcohol counsellor or intensive counselling from Quitline.

### Recommended smoking cessation treatment

- Health professionals should offer encouragement, motivation, advice and counselling to these people
- NRT is effective for quit attempts
- Bupropion should be monitored carefully when used concurrently with alcohol use
- Varenicline<sup>10</sup> there have been some reports of depressed mood, suicidal ideation and changes in emotion and behaviour using this product but so far these reports have not been substantiated.<sup>91</sup> Prescribers should ask patients to report any mood or behaviour changes. Smokers should be advised to stop taking varenicline at the first sign of any of these symptoms.

### **Prisoners**

The prevalence of smoking in the prison population is far higher than among the general population, and tobacco use is accepted as the norm in prison life. There is a strong association between smoking tobacco and social disadvantage and those from low socioeconomic groups are over represented in the prison system, for example, indigenous people, drug users, the less educated and those suffering mental illness. Each of these factors predicts higher smoking rates. <sup>16</sup>

Motivation to quit smoking is high in the prison population. In New South Wales prisons where smoking rates were 80% in 2006, 52% of inmates had attempted

to reduce or quit smoking and 58% had plans to quit.187 In some Australian states, smoking cessation groups and telephone support from Quitline have been provided in some prisons. In Victoria, NRT is available free of charge through a levy fund, which has operated in Victoria's public prisons since 1993. Some prisons also sell NRT patches through prison canteens.16 In New Zealand, smokefree prisons have been successfully implemented, including freely available NRT for prisoners and staff who smoke.

Smoking cessation programs conducted in prisons should address prison specific difficulties by including items such as a stressor pack to assist prisoners during transfer to other prisons and court appearances.<sup>42</sup> Support programs should also discuss how to prevent relapse on release from prison.

### Recommended smoking cessation treatment

- Health professionals should take every opportunity to offer advice to quit
- Provide pharmacotherapy (NRT, bupropion, varenicline)
- Proactive telephone counselling (Quitline 13 7848)
- Close follow up.

### People with smoking related diseases

There is clear evidence that people with a smoking related disease or with other risk factors for cardiovascular disease such as diabetes, lipid disorders and hypertension who continue to smoke greatly increase their risk of further illness. It is important to target this population of smokers for smoking cessation, given the role that smoking plays in exacerbating these conditions. To For example, second heart attacks are more common among cardiac patients if they continue to smoke and people with successfully treated cancers who continue to smoke are at increased risk of a second cancer. People with diabetes who smoke increase their risk of cardiovascular disease, peripheral vascular disease, progression of neuropathy and nephropathy. Smoking also increases the risk associated with hospitalisation for surgery. Quitting smoking after a heart attack or cardiac surgery can decrease a person's risk of death by at least one third.

Smoking has an ongoing impact on patients with chronic airways disease, such as COPD and asthma. There is a clear relationship between continued smoking and progression of COPD.<sup>6</sup> Smoking in those with COPD is associated with a faster decline in lung function, an increase in symptoms – as well as an increased risk for respiratory tract infection and hospitalisation.<sup>189,190</sup> In people with asthma, smoking further impairs lung function, increases symptoms and impairs the effectiveness of treatment.<sup>191,192</sup> First line management of all smokers with asthma should always be strong encouragement to quit.

Many studies have found significant associations between cigarette smoking and the development of diabetes, impaired glycaemic control and diabetic complications.<sup>23</sup> Smokers with type 2 diabetes need a larger insulin dose

to achieve metabolic control similar to that in patients who do not smoke.<sup>193</sup> Smoking is associated with increased risk of type 2 diabetes in both men and women.<sup>194–196</sup> Health professionals should be aware that smoking cessation is a crucial aspect of diabetes care for adequate glycaemic control and limiting development of complications.<sup>23</sup>

There is strong evidence that people with cardiovascular disease are highly motivated to quit smoking and success rates can be high, especially where they understand the link between their health problem and their smoking. It is recommended that smoking cessation programs are integrated into the routine chronic disease management programs for this population of smokers. High intensity behavioural interventions are effective. There is some evidence that adding NRT, bupropion or varenicline to intensive counselling is effective in this group. 197-199

### Recommended smoking cessation treatment

- Use of the medical condition as an opportunity to integrate quitting into a management program
- Intensive cognitive behavioural counselling may be worthwhile
- Varenicline or NRT
- Bupropion for cardiovascular disease and COPD
- If diabetes is well controlled with insulin or oral hypoglycaemic medicine, 150 mg once daily of bupropion can be prescribed. If the condition is poorly controlled, NRT should be considered.<sup>13</sup>

### Evidence

Continued smoking is a major factor in the recurrence or increasing severity of smoking related diseases. Overwhelming epidemiological evidence

### Recommendation

Smoking cessation should be a major focus of the management of people with smoking related diseases **Strength A** 

### Secondhand smoke

Secondhand smoke, or passive smoking, can affect the health of people who do not smoke. There is clear evidence of the harms of exposure to environmental tobacco smoke in pregnancy, to children (higher rates of respiratory and middle ear infections, meningococcal infections and asthma) and adults (increased risk of lung cancer and coronary heart disease). The evidence for the health effects of secondhand smoking has been summarised by a number of health authorities including the National Health and Medical Research Council.<sup>11,84,127,200</sup> The US Department of Health and Human Services has stated that there is no safe level of exposure to tobacco smoke. Any exposure to tobacco smoke – even an occasional cigarette or exposure to secondhand smoke – is harmful,<sup>23</sup> especially to children.<sup>201</sup>

There is a lack of evidence on the effectiveness of counselling non-smokers to limit exposure to tobacco smoke. There is evidence that providing information to parents on the harms of exposing children to environmental tobacco smoke can reduce their exposure. Due to the evidence of harms from exposure, non-smokers, especially parents of babies and young children and pregnant women, should be strongly advised to limit exposure to tobacco smoke. Smoking parents should be encouraged not to smoke in the house, or in a confined space such as a motor vehicle at any time.

### Evidence

Introducing smoking restrictions into the home can assist quitting smoking successfully. **Level IV** 

### Recommendation

People attempting to quit should be advised to ban, or restrict smoking by others in their homes. **Strength C** 

### Resources for health professionals

RACGP publications (including *Smoking cessation guidelines for Australian health professionals*) www.racgp.org.au/guidelines

www.racgp.org.au/guidelines www.racgp.org.au/guidelines/smokingcessation

Quit Victoria www.quit.org.au

Federal, state and territory initiatives (provides links to other tobacco control sites) www.quitnow.info.au

US Department of Health and Human Services Clinical Practice Guideline Treating Tobacco Use and Dependence. 2008 Update www.surgeongeneral.gov/tobacco/treating\_tobacco\_use08.pdf

New Zealand Smoking Cessation Guidelines www.health.govt.nz/publications/new-zealand-smoking-cessation-guidelines

World Health Organization GlobaLink. Global tobacco control. International Tobacco Control Network managed by the International Union against Cancer. www.globalink.org

World Health Organization site on tobacco www.who.int/tobacco/en

Treatobacco.net is produced and maintained by the Society for Research on Nicotine and Tobacco, in association with the World Bank, Centers for Disease Control and Prevention, the World Health Organization, the Cochrane Group and a panel of international experts. This site provides evidence based data and practical support for the treatment of tobacco dependence. It is aimed at health professionals and policy makers. www.treatobacco.net

Action on Smoking and Health (Australia) is a not for profit organisation, which aims to reduce the harmful effect of tobacco use by advocating a comprehensive tobacco control, strategy at national, state and local levels. www.ashaust.org.au

Resilience Education and Drug Education. This website from the Australian Government Department of Education, Employment and Workplace Relations contains a comprehensive database of resources, policies and materials for drug education.

www.redi.gov.au

SANE is an advocacy organisation to assist people with mental illness. SANE has developed a number of resources on mental illness and smoking such as the SmokeFree Zone resource pack and the Smokefree Kit for health professionals. www.sane.org

Australian Association of Smoking Cessation Professionals (AASCP) for referral to a tobacco treatment specialist. www.aascp.org.au

Support programs offered by pharmaceutical companies such as:

- www.nicabate.com.au/support-tools (NRT, GlaxoSmithKline Consumer Healthcare)
- ActiveStop: www.nicorette.com.au (NRT, Johnson & Johnson Pacific)
- My Time to Quit: www.mytimetoquit.com.au (varenicline, Pfizer).

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### Appendix 1

### Summary of evidence and recommendations

 Evidence Smoking cessation advice from health professionals is effective in increasing quit rates. The major effect is to help motivate a quit attempt. Level I

All health professionals can be effective in providing smoking cessation advice. **Level I** 

**Recommendation** All smokers should be offered brief advice to quit. **Strength A** 

2. Evidence Instituting a system designed to identify and document tobacco use almost doubles the rate of health professional intervention and results in higher rates of cessation. Level II

**Recommendation** A system for identifying all smokers and documenting tobacco use should be used in every practice or healthcare service. **Strength A** 

3. **Evidence** Factors consistently associated with higher abstinence rates are high motivation, readiness to quit, moderate to high self-efficacy and supportive social networks. **Level III** 

**Recommendation** Assessment of readiness to quit is a valuable step in planning treatment. **Strength C** 

**4. Evidence** Brief smoking cessation advice from health professionals delivered opportunistically during routine consultations has a modest effect size, but substantial potential public health benefit. **Level I** 

**Recommendation** Offer brief cessation advice in routine consultations and appointments whenever possible (at least annually). **Strength A** 

**5. Evidence** Telephone callback counselling services are effective in assisting cessation for smokers who are ready to quit. **Level II** 

**Recommendation** Referral to such services should be considered for this group of smokers. **Strength A** 

6. Evidence Follow up is effective in increasing quit rates. Level I

**Recommendation** All smokers attempting to quit should be offered follow up. **Strength A** 

7. Evidence Pharmacotherapy with nicotine replacement therapy, varenicline or bupropion is an effective aid to assisting motivated smokers to quit.
Level I

**Recommendation** In the absence of contraindications, pharmacotherapy should be offered to all motivated smokers who have evidence of nicotine

dependence. Choice of pharmacotherapy is based on clinical suitability and patient choice. **Strength A** 

**8. Evidence** Nicotine transdermal patch, nicotine gum and nicotine inhaler all increase quit rates by 50–70% at 5–12 months compared with placebo and regardless of the setting. **Level I** 

There is no evidence of increased risk for use of NRT in people with stable cardiovascular disease. Level IIThere is no evidence of an association between use of nicotine patch and acute cardiac events. **Level II** 

There is a lack of evidence on the safety of NRT in pregnancy and when breastfeeding, but international expert guidelines recommend that it should be used in certain circumstances. **Level V** 

In more dependent smokers, combinations of different forms of NRT (eg. patch plus gum) are more effective than one form alone. **Level II** 

**Recommendations** NRT should be recommended to nicotine dependent smokers. There is no significant difference in effectiveness of different forms of NRT in achieving cessation, so choice of product depends on clinical and personal considerations. **Strength A** 

NRT is safe to use in patients with stable cardiovascular disease. Strength A

NRT should be used with caution in patients who have had a recent myocardial infarction, unstable angina, severe arrhythmias or recent cerebrovascular events. **Strength C** 

Pharmacotherapy with NRT should be considered when a pregnant woman is otherwise unable to quit, and when the likelihood and benefits of cessation outweigh the risks of using NRT. **Level C** 

Combination NRT should be offered if patients are unable to remain abstinent or continue to experience withdrawal symptoms using one type of therapy. **Strength A** 

9. Evidence Varenicline is an efficacious smoking cessation treatment. Level I

**Recommendation** Varenicline should be recommended to smokers who have been assessed as clinically suitable for this medication and should be provided in combination with counselling. **Strength A** 

 Evidence Bupropion sustained release is an efficacious smoking cessation treatment. Level I

**Recommendation** Bupropion sustained release should be recommended to smokers who have been assessed as clinically suitable for this medication and provided in combination with counselling. **Strength A** 

- **11. Evidence** Nortriptyline is an efficacious smoking cessation treatment in people with and without a history of depression. **Level II** 
  - **Recommendation** Nortriptyline should only be considered as a second-line agent due to its adverse effects profile. **Strength B**
- **12. Evidence** There is no significant effect of acupuncture or hypnotherapy in smoking cessation. **Level I** 
  - **Recommendation** On the evidence available acupuncture and hypnotherapy are not recommended as aids to smoking cessation. **Strength A**
- **13. Evidence** There is currently a lack of evidence on the safety of pharmacotherapy in pregnancy, but international guidelines recommend use of NRT in certain circumstances. **Level V** 
  - **Recommendation** Use of NRT should be considered when a pregnant woman is otherwise unable to quit. Intermittent NRT is preferred to patches (lower total daily nicotine dose). **Strength C**
- **14. Evidence** Continued smoking is a major factor in the recurrence or increasing severity of smoking related diseases. Overwhelming epidemiological evidence.
  - **Recommendation** Smoking cessation should be a major focus of the management of people with smoking related diseases. **Strength A**
- **15. Evidence** Introducing smoking restrictions into the home can assist quitting smoking successfully. **Level IV** 
  - **Recommendation** People attempting to quit should be advised to ban or restrict smoking by others in their homes. **Strength C**

## Appendix 2

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### Appendix 3

### Effect of smoking abstinence on medications

Smoking tobacco can alter the metabolism of a number of medicines. This is primarily due to substances in tobacco smoke, such as hydrocarbons or tar-like products that cause induction (speeding up) of some liver enzymes (CYP 1A2, in particular). Therefore, medicines metabolised by these enzymes are broken down faster and can result in reduced concentrations in the blood (see table below). When a person stops smoking, the enzyme activity returns to normal (slows down), which may result in increased levels of these medicines in the blood. Monitoring and dosage reduction may often be required.

### Smoking affects the following medications

Medication Effect of smoking

Caffeine Increased clearance (by 56%)

Chlorpromazine Decreased serum concentrations (by 24%)
Clozapine Decreased plasma concentrations (by 28%)

Estradiol Possibly anti-estrogenic effects
Flecainide Increased clearance (by 61%)

Fluvoxamine Decreased plasma concentrations (by 47%)
Haloperidol Decreased serum concentrations (by 70%)

Heparin Increased clearance

Imipramine Decreased serum concentrations

Insulin Decreased subcutaneous absorption due to poor

peripheral blood flow

Lidocaine Decreased oral bioavailability
Olanzapine Increased clearance (by 98%)
Propranolol Increased oral clearance (by 77%)

Tacrine Decreased mean plasma concentrations (3-fold)

Theophylline Increased metabolic clearance (by 58 to 100%); within 7 days

of smoking cessation, theophylline clearance falls by 35%

Warfarin Decreased plasma concentrations (by 13%). No effect on

prothrombin time

### Stopping smoking can result in the opposite of the effects noted above.

Healthcare workers should be aware of the potential for increased blood levels of some of these medicines when smoking is stopped. Blood levels of some (eg. clozapine, theophyline) may need to be monitored.

# Smoking/smoking cessation does not affect the following medications202

- Benzodiazepines (diazepam, lorazepam, midazolam, chlordiazepoxide)
- Bupropion
- Ethinyl estradiol
- Glucocorticoids (prednisone, prednisolone, dexamethasone)
- Paracetamol
- Quinidine

# Effects of smoking/smoking cessation on the following medication is unclear

Nortriptyline