Smoking cessation pharmacotherapy: an update for health professionals

The Royal Australian College of General Practitioners

Smoking cessation pharmacotherapy: an update for health professionals is intended to serve as a reference and a resource for health professionals providing advice for smoking cessation and should be treated as an addendum to the *Smoking cessation guidelines for Australian general practice* 2004 edition. It should be noted that while the guidelines include a range of therapies, neither The Royal Australian College of General Practitioners (RACGP) nor the endorsing organisations hold a commercial interest in any product being appraised. Treatment should be based on the selection of the best pharmacotherapy option available to a patient, taking into account their individual circumstances. Any part of the publication may be reproduced without seeking copyright permission from the RACGP provided there is appropriate acknowledgment.

Suggested citation

Zwar N, Richmond R, Borland R, Peters M, Stillman S, Litt J, Bell J, Caldwell B. Smoking cessation pharmacotherapy: an update for health professionals. Melbourne: The Royal Australian College of General Practitioners, 2007.

© The Royal Australian College of General Practitioners 2007
Reviewed and updated April 2009

ISBN 978-0-86906-288-3

The development of this update has been sponsored by Pfizer Pty Limited. The RACGP has independently created these guidelines and holds editorial rights over them.

Although every effort has been made to ensure that drug doses and other information are presented accurately in this publication, the ultimate responsibility rests with the prescribing clinician. For detailed prescribing information on the use of any pharmacotherapy, please consult the prescribing information issued by the manufacturer.

Contents

Content advisory group

Professor Nicholas Zwar (Chair)
School of Public Health and Community Medicine, University of New South Wales

Professor Robyn Richmond
School of Public Health and Community Medicine, University of New South Wales

Dr Ron Borland
The Cancer Council Victoria

Dr John Litt
Department of General Practice, Flinders University, South Australia

Associate Professor Matthew Peters
Respiratory Medicine, Concord Hospital and Action on Smoking and Health, New South Wales

Ms Suzanne Stillman
Quit Victoria, The Cancer Council Victoria

Mr John Bell
Pharmaceutical Society of Australia, New South Wales

Ms Belinda Caldwell
Australian Practice Nurses Association, Victoria

Acknowledgments

We are grateful for comments from:

- Dr Neal L Benowitz, Division of Clinical Pharmacology and Experimental Therapeutics, San Francisco General Hospital Medical Center, Departments of Medicine, Psychiatry, and Biopharmaceutical Sciences, University of California, San Francisco, California, USA
- Professor Michael C Fiore, Director, Center for Tobacco Research and Intervention, University of Wisconsin Medical School, Madison, Wisconsin, USA
- Dr Hayden McRobbie, Research Fellow, Clinical Trials Research Unit, University of Auckland, Auckland, New Zealand

Declaration of competing interests

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

Associate Professor Matthew Peters is a member of the varenicline advisory board and has received honoraria for speaking at meetings for Pfizer Pty Limited.

Dr John Litt has provided smoking cessation advice and training for Pfizer Pty Limited and is a member of the varenicline advisory board for Pfizer Pty Limited.

Endorsements

The Royal Australian College of General Practitioners

The Pharmacy Guild of Australia

Australian Practice Nurses Association

QUIT Group

Action on Smoking and Health

The Cancer Council Australia

Pharmaceutical Society of Australia

The Thoracic Society of Australia and New Zealand

Introduction

While the rate of smoking in Australia has declined over recent decades, smoking remains the risk factor with the highest levels of disease and death.[1]

Smoking cessation advice and support from health professionals are key aspects of a comprehensive approach to tobacco control. Since the publication of the *Smoking cessation guidelines for Australian general practice* in June 2004, there have been important developments in the understanding of nicotine addiction and the pharmacotherapies available to assist cessation, including a new first line medicine for the treatment of nicotine dependence and a broader indication for the use of nicotine replacement therapy (NRT).

This update aims to inform a range of health professionals – doctors, nurses, pharmacists, dentists, Quitline counsellors and other health professionals – to enable them to provide up-to-date advice to patients on medicines to assist smoking cessation.

Tobacco smoking: the scope of the problem

Tobacco smoking is a worldwide threat to human health. The World Health Organization estimates that around five million people die prematurely from tobacco related disease each year, and that this number will increase to 10 million by 2020. Seventy percent of these deaths will occur among people in the developing world.[2]

Australia is part of the Framework Convention on Tobacco Control, a worldwide effort to control the effects of tobacco smoking on human health.[2] With the advent of national tobacco control policies and programs, the prevalence of smoking in Australia is among the lowest of any nation.[3] Nevertheless, smoking still causes a higher burden of disease than any other behavioural risk factor, representing 9.5% of the total burden in men and 6% in women.[4] More than one in six Australians continue to smoke every day, and tobacco smoking is responsible for the deaths of about 16 000 Australians each year.[5]

Smoking is a known cause of many serious diseases including cancer, heart disease, stroke and chronic obstructive pulmonary disease. Smoking also has adverse effects in pregnancy both for the mother and the developing foetus, and exposure to environmental tobacco smoke damages the health of children and adults[6,7] (*Figure 1*).

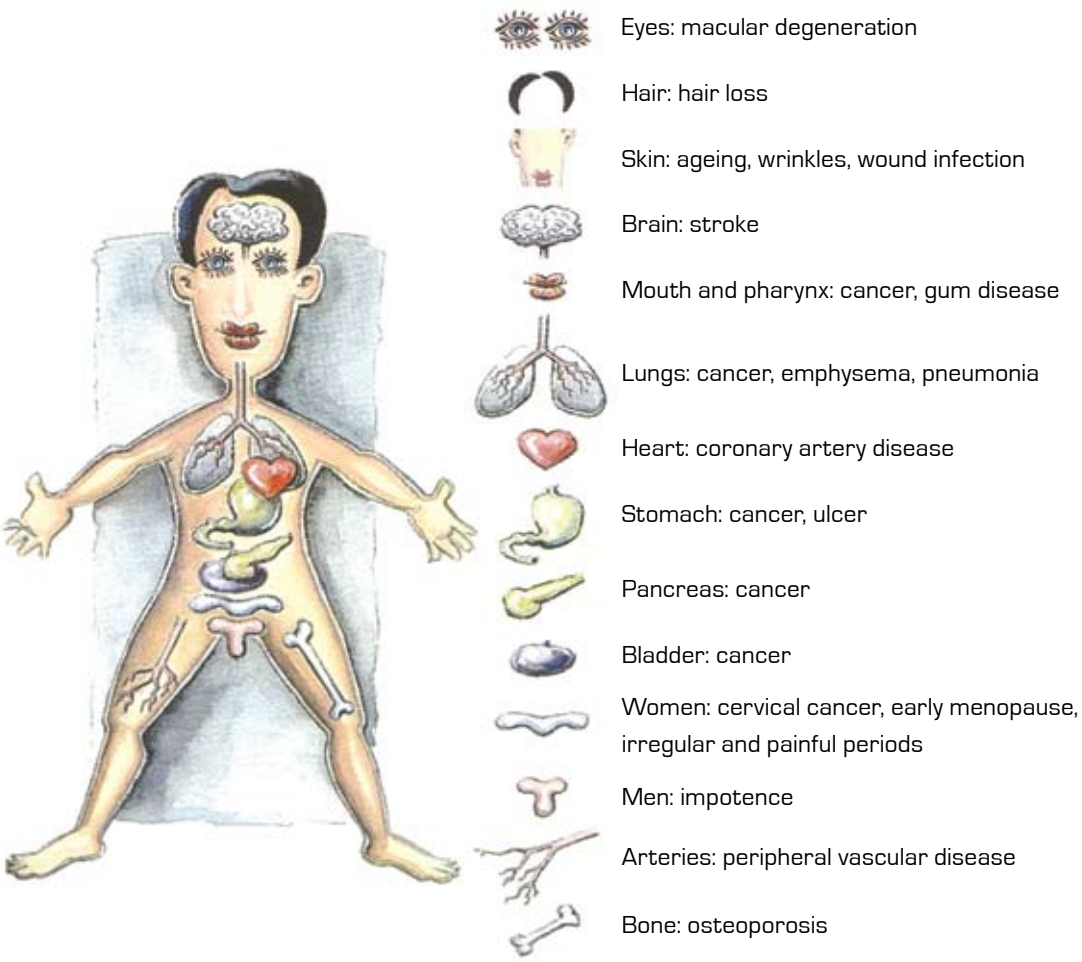


Figure 1. Health effects of smoking (from the Smokescreen Program)[7,8]

According to the 2004 National Drug Strategy Household Survey[9] conducted between June and November 2004:

- 19% of Australians aged 14 years and over were daily or weekly smokers (20.6% of men and 17.5% of women)
- the prevalence of daily smoking was 17.4% (18.6% of men and 16.3% of women)
- the prevalence by state is similar, with the exception of the Northern Territory, which has the highest rate (27.3% daily smokers)
- the highest rate of smoking is in the 20–29 years age group (23.5%)
- the prevalence is higher among people from lower socioeconomic groups
- some Australians have higher prevalence rates, eg. Aboriginal people and Torres Strait Islanders (56% of men and 52% of women) and people of southeast Asian background (Vietnam, Lao and Cambodia) (around 50% in men, but low in women)
- the rate of smoking in adolescents has fallen to 10.7% daily smoking in people aged 14–19 years.

The survey also identified other groups with smoking rates higher than those of the general population, including:

- people with a mental illness (70–90%)
- people with substance use disorders (74–100%)
- pregnant women (15–26% of all women and 72% of indigenous women smoke during pregnancy).

Effectiveness of treating tobacco use and dependence

The benefits of quitting smoking are now established. Successfully quitting smoking can result in an increase in life expectancy of up to 10 years,[10] and there is now substantial evidence that advice from general practitioners[11,12] and other health professionals[6] helps smokers quit. While spending more time (longer than 10 minutes) advising smokers to quit yields higher abstinence rates than minimal advice,[6] offering brief advice (as little as three minutes) has been shown to have clear benefits (*Figure 2*).[13]

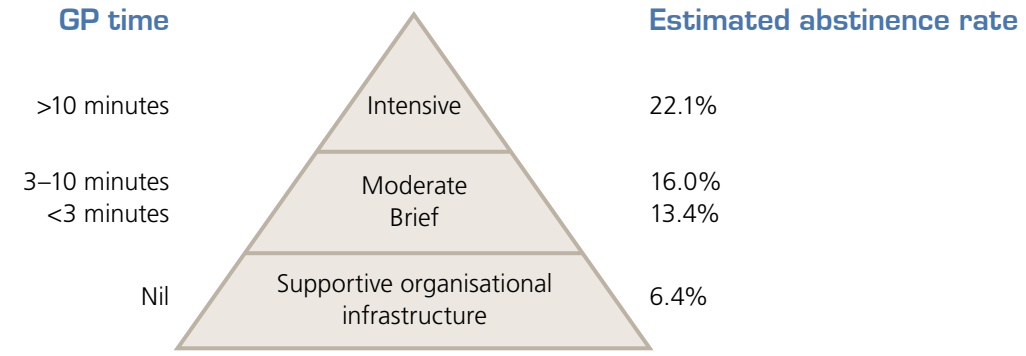


Figure 2. Reality pyramid: levels of intervention (adapted from Litt J et al)[13]

Smoking cessation is both clinically and cost effective compared with other medical and disease preventive measures such as the treatment of hypertension and hypercholesterolaemia, and preventive screening interventions such as mammography and cervical smears. Research has shown that the cost of smoking cessation interventions per life year gained ranged from $500 to $2000, while the median cost per life year gained for other medical interventions was $40 000.[7] Along with childhood immunisation and aspirin use with high risk adults, overall efforts to reduce tobacco smoking are among the most beneficial preventive interventions on human health.[6,14,15]

All health professionals should systematically identify smokers, assess their smoking status and offer them advice to stop smoking at every opportunity.[11,16] Where appropriate, smokers should be referred to more intensive help (eg. Quitline).

Brief interventions for smoking cessation in primary care involve opportunistic advice, encouragement and referral. Interventions should include one or more of the following:[7,17]

- simple advice to stop smoking
- an assessment of the smoker's commitment to stop
- an offer of pharmacotherapy and counselling where appropriate
- self help material and referral to more intensive support (eg. Quitline).

'People smoke for nicotine but die of smoke'

Michael Russell, pioneer in nicotine addiction research

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 after smoking a modern cigarette. Dependence would not occur without nicotine – but nicotine is not responsible for the harmful effects of smoking.[7,18]

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. But although most smokers possess some understanding of the health effects of tobacco use, recent research in Australia indicates that the majority of smokers do not take into account a thorough understanding of these effects when making daily decisions about their smoking.[19,20]

The huge surface area of the lungs means that nicotine is rapidly absorbed into the pulmonary venous circulation. Nicotine is active within the 'brain reward system' of the central nervous system within seconds of inhalation.[20,21] This 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.

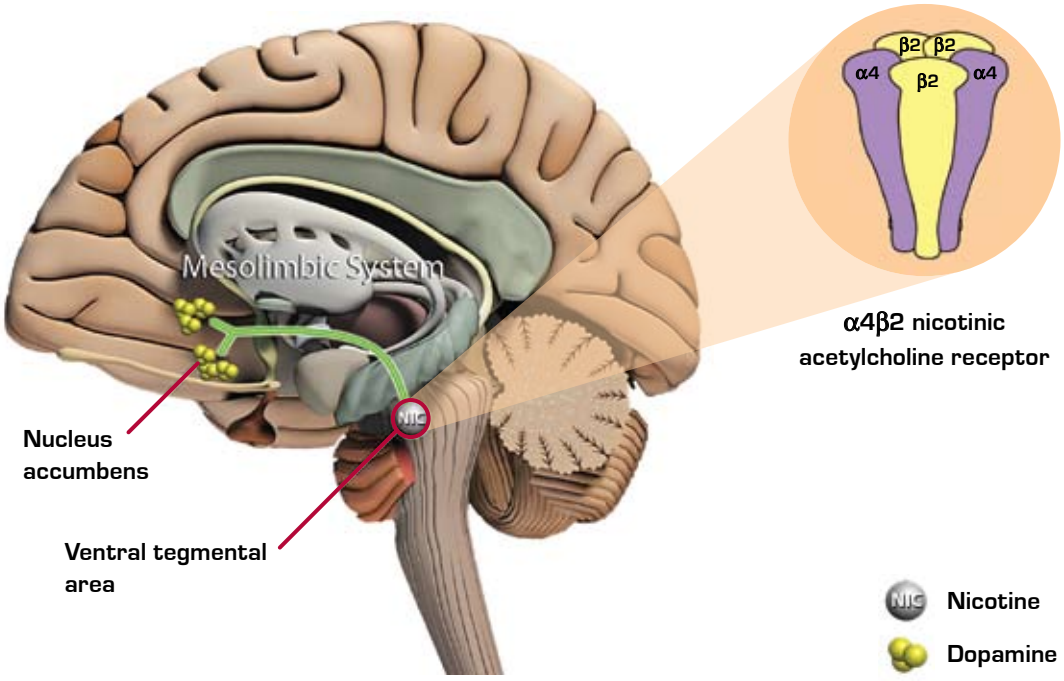


Figure 3. The primary role of the α4β2 nicotinic acetylcholine receptor in the dependence producing effects of nicotine, measured by increased dopamine release in the key brain site for motivation and reward, the nucleus accumbens[23]

Within this system, nicotine interacts most critically with specific $\alpha 4\beta 2$ nicotinic acetylcholine (ACh) receptors. This interaction triggers the release of dopamine and the brief but intense activation of the brain reward system. Dopamine levels then decline slowly, with a half life of about 90 minutes. The eventual deactivation of this same reward system leads to sensations of withdrawal or cravings, which may be relieved by smoking another cigarette[22,23] (*Figure 3*).

A long term smoker cycles continuously between pleasure and withdrawal, with the negative effects of nicotine withdrawal being the major factors in a person's decision to continue smoking.

Genetic factors may play a role in determining whether this cycle of dependence develops in a long term smoker. Some characteristics of a nondependent smoker include smoking fewer than seven cigarettes per day, a long interval before the first cigarette of the day, and periods of cessation and recommencement of smoking not associated with withdrawal symptoms.

Assessment of nicotine dependence

Most smokers become nicotine dependent. Assessment of nicotine dependence can help predict whether a smoker is likely to experience nicotine withdrawal upon stopping smoking.

Nicotine withdrawal symptoms commonly include craving, as well as onset of any of the following shortly after stopping:[7]

- depressed mood
- insomnia
- irritability, frustration, anger
- anxiety
- difficulty in concentration
- restlessness
- decreased heart rate
- 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.[24]

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 and withdrawal symptoms when you have tried to quit?

Smoking within 30 minutes of waking, smoking more than 15 cigarettes per day and a history of withdrawal symptoms in previous attempts to quit are all indicators of nicotine dependence (see *Quit smoking brief intervention*).[7]

The 5As structure for smoking cessation

Tobacco dependence is a chronic condition that typically requires repeated cessation treatment and ongoing care.[6] A minority of smokers achieve long term abstinence on the first attempt to quit; the majority cycle through multiple attempts with relapse and remission before achieving long term or permanent abstinence. Twenty or more attempts over a period of years is not unusual.

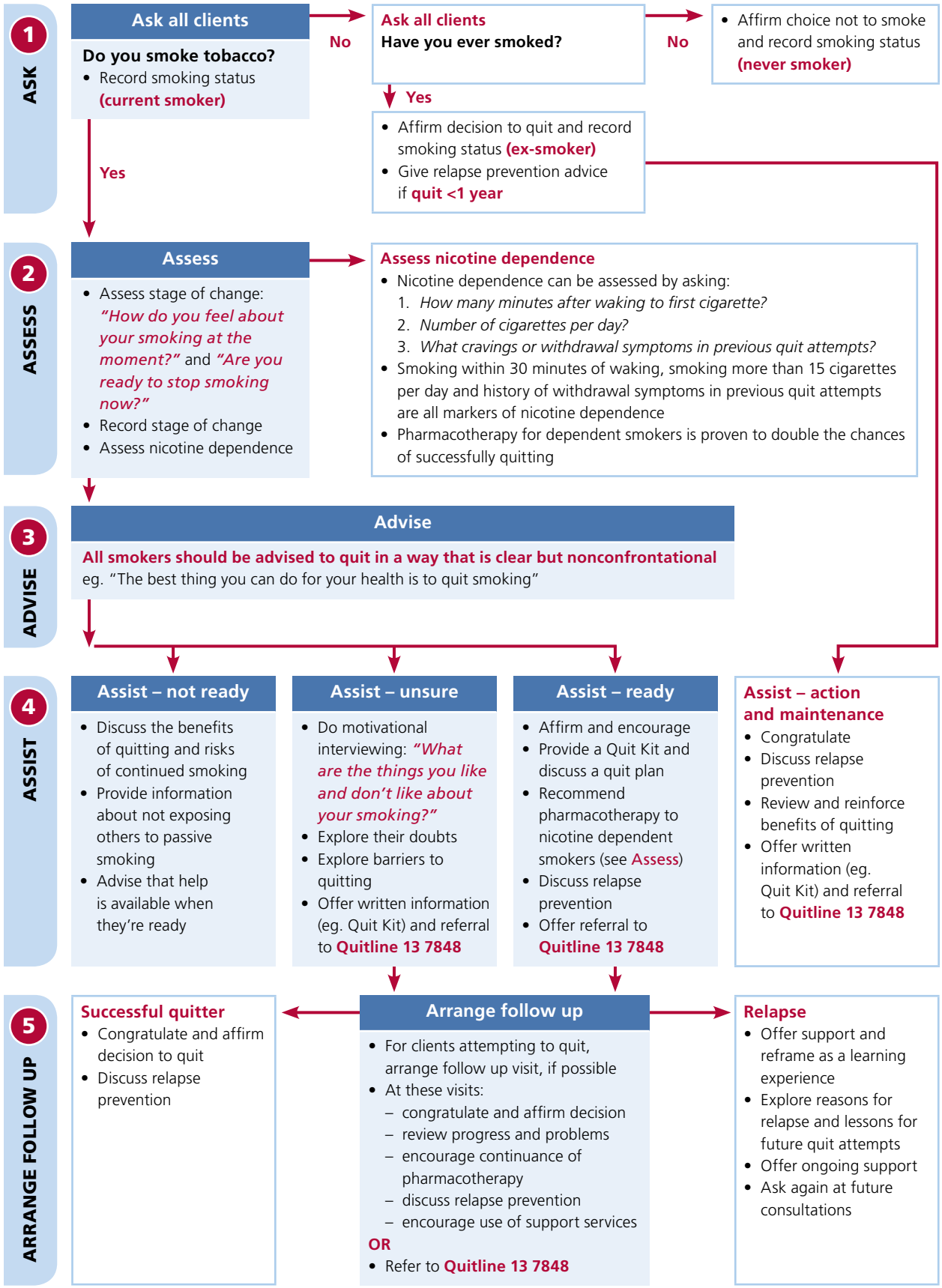
It is important to take every opportunity in a health care setting to identify all smokers, document their smoking status and offer treatment, which may involve counselling by a health professional, referral and pharmacotherapy.

Evidence is now accumulating to show that increasing the number of attempts to quit is the most important strategy for improving cessation rates in the population, and health professionals have a role in prompting and encouraging attempts to quit.[7,25] The 5As approach provides a structure for identifying all smokers and offering support to help them quit (*Quit smoking brief intervention*).[7]

The process of quitting smoking ('stage of readiness to change')[26] – involving a series of stages from thinking about quitting to making a quit attempt – is a useful framework to identify and provide the appropriate support for a smoker's level of interest in quitting. This approach has been widely used in guidelines for the management of other risk factors.[27] However, 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.[28] This means there is benefit in encouraging all smokers to consider quitting whenever the opportunity arises.

The evidence is also compelling that both advice based help and pharmacotherapy can increase the rate of success of quit attempts, and when both are used the benefits are additive.[29,30]

Quit smoking brief intervention



A number of medicines have been shown to assist smoking cessation in meta-analyses of randomised clinical trials.[29–32]

No form of pharmacotherapy is a substitute for motivation. A range of nicotine replacement products are available from pharmacies (and supermarkets in some cases) in addition to two prescription only medicines currently registered in Australia.

Nicotine replacement therapy (NRT) can be used effectively without the intervention of a health care professional; the two prescription only medicines should be given in combination with counselling support from a health professional or a support service.

Both prescription medicines have shown efficacy in clinical trials in smokers who have regular counselling support. While both advice based help and pharmacotherapy have been shown to increase the rate of success of attempts to quit, when used together the benefits are additive.[29,30]

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, varenicline and bupropion.

From currently available evidence, varenicline is the most effective form of pharmacotherapy.[33,34] This conclusion is based on a small number of studies, and further research is awaited in different patient populations. Varenicline has been shown to be more effective than bupropion in a number of studies. In the one prospective study comparing varenicline with NRT, continuous abstinence was significantly higher with varenicline at the end of the treatment period but the difference no longer significant by week 52.[35] Further research is needed to confirm if varenicline is more effective than NRT, including studies comparing to high dose NRT and combination therapy.

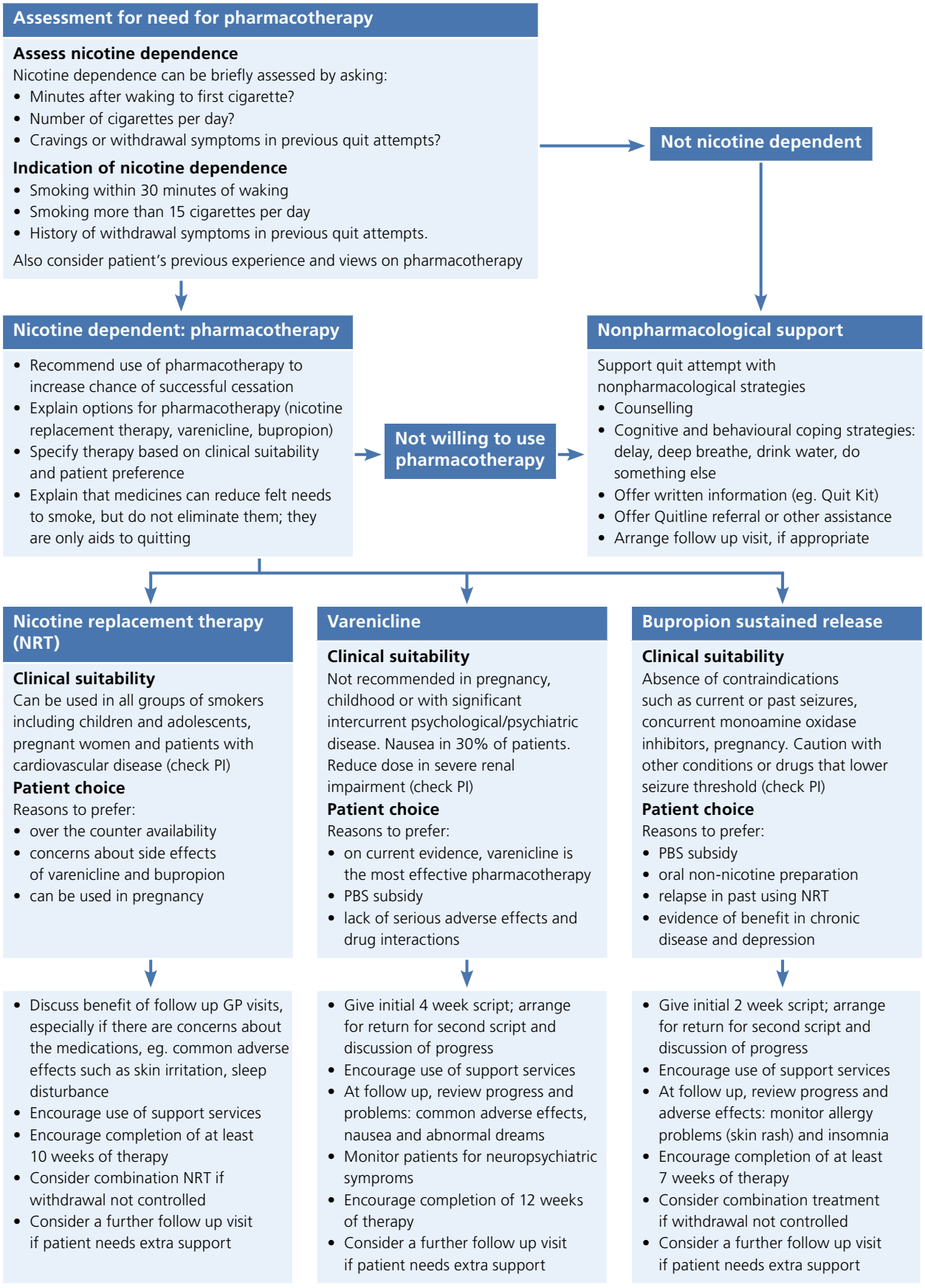
However, context and patient preference are important in choosing the pharmacotherapy that is most likely to assist the smoker in an attempt to quit: some smokers may prefer a nonprescription medicine such as NRT that they can commence immediately, while others may prefer a non-nicotine option subsidised by the Pharmaceutical Benefits Scheme (PBS) (see *Treatment algorithm*). The PBS requirement for subsidy is that these medicines are provided only in combination with counselling.

Nicotine replacement therapy

Nicotine replacement therapy is available over the counter in pharmacies, and some forms are available in supermarkets. 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. None of the available forms of NRT – transdermal patch, inhaler, lozenge, sublingual tablet and gum – offer the same rapid nicotine delivery of a cigarette.

Some oral forms of NRT are available in two strengths: 2 mg and 4 mg. The 4 mg version is recommended for more dependent smokers. The 2004 guidelines recommend that pharmacotherapy with NRT should be offered to all smokers who are motivated to quit.[7] Regular use of NRT beyond 12 months is not generally recommended. 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.[36]

Treatment algorithm



There have been some recent changes to the indications listed for NRT products:[37,38]

- more than one form of NRT can be used concurrently
  - in Australia, NRT patch and 2 mg gum are licensed for smokers who have relapsed in the past or who experience cravings using only one form of NRT
- NRT can be used by pregnant and lactating smokers
- all forms of NRT can be used by patients with cardiovascular disease
- all forms of NRT can be used by smokers aged 12–17 years
- some forms of NRT are now available in supermarkets; the other NRT products are available over the counter in pharmacies.

Although quitting smoking completely remains the best goal, there is a strong argument for the use of nicotine assisted reduction to help patients quit. New research suggests that reducing smoking with NRT as a first step can increase the number of smokers who quit altogether.[37]

The available evidence shows that:

- all forms of NRT are equally effective in aiding long term cessation
- NRT helps smokers unwilling or unable to stop smoking to reduce their cigarette consumption ('cut down then stop')
- there are no real risks of use; using NRT to quit is always safer than continuing to smoke
  - exceptions are pregnant women, for whom there may be a risk to the fetus, and people with acute cardiovascular disease.

There has been little research on the success of combinations of different types of NRT.

Varenicline (Champix®)

Varenicline is a new class of drug for first line pharmacotherapy. 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 α4β2 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 α4β2 receptor sufficiently to cause the pleasure and reward response (*Figure 4*).

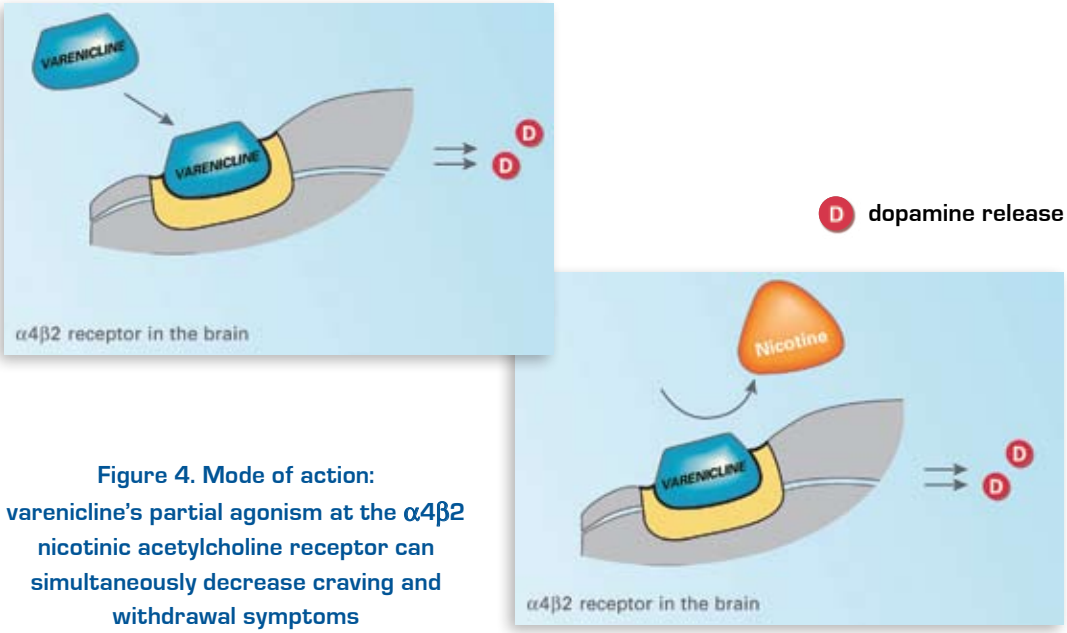


Figure 4. Mode of action: varenicline's partial agonism at the α4β2 nicotinic acetylcholine receptor can simultaneously decrease craving and withdrawal symptoms

In two clinical studies with identical study designs, varenicline in combination with counselling produced a continuous abstinence rate from week 9 through to 1 year of 21.9% (8.4% in placebo group [p <0.001] and 16.1% in bupropion group [p = 0.057]) and 23% (10.3% in placebo group [p <0.001] and 14.6% in bupropion group [p = 0.004]) respectively.[39,40] The abstinence rate for varenicline was significantly better than both bupropion and placebo long term. In an open label radomised trial comparing varenicline with nicotine patch continuous abstinence was significantly higher for varenicline (55.9%) than nicotine patch (43.2%) in the last 4 weeks of the treatment period, but by week 52 the difference was no longer significant (26.1% for varenicline vs 20.3% for nicotine patch.[35]

Cahill and colleagues conducted a systematic review of the 10 published RCTs comparing varenicline with either placebo (8 studies) or NRT (2 studies).[41] Three of the varenicline/placebo trials also included a bupropion arm. Varenicline more than doubled the chances of quitting at 6 months or longer, with a relative risk (RR) compared with placebo of 2.38 (95% CI 2.00, 2.84). It also outperformed bupropion (RR 1.52 [95% CI 1.22, 1.88]) and nicotine replacement (RR 1.31 [95% CI 1.01, 1.71]). 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 one year from the start of treatment. However, the difference in continuous abstinence for weeks 13–52 between intervention and control groups was small.[42] The benefit appears to be maintained only for the period of use of varenicline.

Nausea is the most common adverse effect of varenicline and was reported in the studies in 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. Dose adjustment is required for severe renal impairment; dosing should begin at 0.5 mg once per day for the first 3 days, and then be increased to 1 mg once per day. No dose adjustment is needed for patients with hepatic impairment.

There is a lack of evidence of the efficacy and safety of varenicline in patients with significant psychiatric problems, and therefore use in such patients is not recommended. There have been reports of depressed mood, agitation, hallucinations, changes in behaviour, suicidal ideation and suicides in patients attempting to quit smoking using varenicline. Smoking cessation itself can be associated with exacerbation of underlying psychiatric disease. Although a casual association of these symptoms with varenicline has not been demonstrated, prescribers should ask patients to report any mood or behaviour changes. Patients should be advised to stop taking varenicline at the first sign of any of these symptoms.

Varenicline is available in Australia on the PBS as short term adjunctive therapy for nicotine dependence. The first script is a starter pack lasting 4 weeks, followed by a maintenance batch for the remainder of the 12 week course.[43] The patient should set a quit date 1–2 weeks after commencing varenicline. The medicine can be taken whole with water and food to help reduce nausea.

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	1 mg twice per day

Bupropion sustained release (Zyban®)

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

Since 2001, bupropion sustained release 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 doubles the cessation rate compared with placebo: 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.[6,44] It has been shown to be effective in a range of patient populations including smokers with depression, cardiac disease and respiratory diseases including chronic obstructive pulmonary disease.[45] It has also been shown to improve short term abstinence rates for people with schizophrenia.[46]

Bupropion is contraindicated in patients with a history of seizures, eating disorders and patients taking monoamine oxidase inhibitors. It should be used with caution in people taking medications that can lower seizure threshold, such as antidepressants and oral hypoglycaemic agents.[47,48]

Seizures are the most clinically important adverse effect (0.1% risk). Common adverse effects are insomnia, headache, dry mouth, nausea, dizziness and anxiety.[6,30]

Bupropion is available as a starter pack of 30 tablets and a continuation pack of 90 tablets. The dose of bupropion sustained release 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. Bupropion can be used in combination with NRT, but blood pressure should be monitored.

Clinical trials have shown that bupropion is not as effective as varenicline, and it is likely to be the treatment of choice only in cases where varenicline is not appropriate (patient choice or as a result of severe side effects) or for smokers with depression or schizophrenia.

Second line pharmacotherapy options

Nortriptyline

The tricyclic antidepressant nortriptyline has been shown to approximately double cessation rates compared to placebo (OR=2.34).[30,31,49] A recent 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.[50] The efficacy of nortriptyline does not appear to be affected by a past history of depression; it is, however, limited in its application by its potential for serious side effects. These include dry mouth, constipation, nausea, sedation and headaches, and a risk of arrhythmia in patients with cardiovascular disease. It 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 per day for 12 weeks. Further information about dose titration can be obtained from the *New Zealand smoking cessation guidelines*.[38]

Possible future options

There are a number of tobacco cessation therapies and nicotine vaccines in development.[51–53] The selective type 1 cannabinoid receptor antagonist rimonabant[54] and the nicotine receptor partial agonist cystine[55] have demonstrated some efficacy in studies, but as yet there is insufficient evidence for their use in tobacco cessation. Further data and research are needed before any of these methods of treatment for tobacco dependency can be recommended.

There are several population groups for whom there are particular implications regarding nicotine dependence and the effects of smoking, and 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.[7,39] In addition, all smokers should be offered pharmacotherapy with the following guidance (*Table 1*).

Table 1. First line pharmacotherapy in special populations

Special group	Varenicline	Bupropion	Nicotine replacement therapy
Pregnant and lactating women	ND	ND	✔[a]
Children and adolescents (12–18 years)	ND	ND	✔
People with smoking related diseases	ND	✔	✔
• Cardiovascular disease	ND	✔	✔
• Chronic obstructive pulmonary disease	ND	✔	✔
• Diabetes	ND	ND	✔[b]
• Severe renal impairment	✔[c]		✔[d]
• Moderate to severe hepatic impairment	✔		✔[d]
People with mental illness	ND	✔	✔
• Depression	ND	✔	✔
• Schizophrenia	ND	✔[e]	✔
People with substance use disorders	ND	✔[f]	✔
Contraindications (apart from hypersensitivity to active ingredient)		Yes[g]	

✔ = suitable ND = lack of safety data

a = intermittent dosing products preferable
b = but closely monitor blood sugar levels
c = dosing adjustment required
d = with caution
e = with close follow up
f = caution with alcohol abuse
g = seizures, anorexia, bulimia, central nervous system tumours, monoamine oxidase inhibitor treatment within 14 days

Supporting quality use of smoking cessation pharmacotherapies

Even motivated smokers relapse. Most relapses occur in the first few weeks of an attempt to quit. It often takes a number of attempts to quit smoking successfully,[26] and smokers should be encouraged to keep trying to quit even if they have returned to smoking.

All available first line medicines for stopping smoking (NRT, varenicline and bupropion) have been shown to double the chance of quitting, but only if they are used correctly and for the right length of time. Optimum use of these medicines involves prescribing them in conjunction with patient counselling and support. Integrating behavioural therapy (face-to-face, internet and telephone counselling and coaching) increases the quit rate significantly. Many different health professionals (physicians, nurses, dentists, psychologists, pharmacists) are effective in increasing abstinence rates.[6,7]

Besides the support offered to smokers by health professionals, other support options include:

- individual face-to-face support (doctor or other health professional with special training to help people to quit smoking)[8]
- telephone advice (Quitline)
  - the national Quitline number is 13 QUIT (13 7848) and calls are charged at the cost of a local call (about 25c, mobile phones extra). All Quitline services in Australia have agreed to national minimum standards of service delivery
  - research based proactive counselling service
  - fax referral to Quitline (smokers can be referred to the Quitline for extended support using the fax referral sheet)[7]
  - Quitline adviser, course leader or coach
  - self help books (eg. www.quitbecauseyoucan.org.au)
- support programs offered by pharmaceutical companies such as:
  - www.click2quit.com.au (NRT, GlaxoSmithKline Consumer Healthcare)
  - ActiveStop, www.nicorette.com.au (NRT, Johnson & Johnson Pacific)
  - Champix 'My Time to Quit' program (varenicline, Pfizer)
  - www.mytimetoquit.com.au

Internet resources

RACGP publications (including *Smoking cessation guidelines for Australian general practice*)

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

Action on Smoking and Health (ASH) Australia

www.ashaust.org.au

Tobacco dependence is a chronic condition which leads to disease and death for smokers, and substantial costs for the public health system.

There are now three first line medical options available in Australia to assist smokers to quit:

- nicotine replacement therapy
- varenicline
- bupropion.

These pharmacotherapies have been shown to be effective in increasing long term abstinence. Other agents for tobacco dependence treatment are in development, further increasing the potential options for smokers who want to quit smoking.

It is important for health professionals to maximise the opportunities for smoking cessation by encouraging all smokers to quit and by supporting all patients attempting to quit. Supporting a quit attempt involves recommending pharmacotherapy that suits the individual smoker, and ensuring all smokers have access to appropriate counselling and support.

References

1. Australian Bureau of Statistics. National Health Survey: summary of results Australia 2004–05. Canberra: ABS, 2006. Report No.: 4364.0.
2. World Health Organization. WHO framework convention on tobacco control. Geneva: WHO, 2005. Available at: www.who.int/tobacco/framework/WHO_FCTC_english.pdf.
3. Shafey O, Dolwick S, Guindon GE, editors. Tobacco control country profiles 2003. Atlanta, GA: American Cancer Society, 2003. Available at www.cancer.org/downloads/TOB/Australia.pdf.
4. Australian Institute of Health and Welfare. Australia's health 2006. Canberra: AIHW, 2006. Report No.: AIHW Cat. No. AUS 73.
5. Begg S, Vos T, Barker B, Stevenson C, Stanley L, Lopez AD. The burden of disease and injury in Australia 2003. Canberra: AIHW, 2007. Report No.: AIHW Cat. No. PHE 82. Available at: www.aihw.gov.au/publications/hwe/bodaiia03/bodaiia03.pdf.
6. Fiore MC, Bailey WC, Cohen SJ, Dorfman SF, Goldstein MG, Gritz ER et al. Treating tobacco use and dependence: clinical practice guideline. Rockville, MD: United States Department of Health and Human Services, 2000.
7. Zwar N, Richmond R, Borland R, Stillman S, Cunningham M, Litt J. Smoking cessation guidelines for Australian general practice: practice handbook 2004 edition. Canberra: Australian Government Department of Health and Ageing, 2004.
8. Richmond R, Webster I, Elkins L, Mendelsohn C, Rollnick S. Smokescreen for the 1990s: A stop smoking programme for general practitioners to use with smokers. 2nd edition. Sydney: NSW Department of Health,1991.
9. Australian Institute of Health and Welfare. 2004 National Drug Strategy Household Survey: detailed findings. Canberra: AIHW, 2005. Report No.: AIHW Cat. No. PHE 66. (Drug Statistics Series No. 16). Available at: www.aihw.gov.au/publications/phe/ndshsdf04/ndshsdf04-c00.pdf.
10. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ 2004;328:1519.
11. Lancaster T, Stead LF. Physician advice for smoking cessation. Cochrane Database Syst Rev 2004;4:CD000165.
12. Richmond RL, Makinson RJ, Kehoe LA, Giugni AA, Webster IW. One-year evaluation of three smoking cessation interventions administered by general practitioners. Addict Behav 1993;18:187–99.

13. Litt J, Ling M-Y, McAvoy B. How to help your patients quit: practice based strategies for smoking cessation. Asia Pacific Family Medicine 2003;2:175–9.
14. Cromwell J, Bartosch WJ, Fiore MC, Hasselblad V, Baker T. Cost-effectiveness of the clinical practice recommendations in the AHCPR guideline for smoking cessation. J Am Med Assoc 1997;278:759–66.
15. Maciosek MV, Coffield AB, Edwards NM, Flottemesch TJ, Goodman MJ, Solberg LI. Priorities among effective clinical preventive services: results of a systematic review and analysis. Am J Prev Med 2006;31(1):52–61.
16. Parrott S, Godfrey C, Raw M, West R, McNeill A. Guidance for commissioners on the cost-effectiveness of smoking cessation interventions. Thorax 1998;53:S1–38.
17. National Institute for Health and Clinical Excellence. Brief interventions and referral for smoking cessation in primary care and other settings. London: NICE, March 2006. Report No.: N1014.
18. Winstanley M, Woodward S. Tobacco in Australia: Facts and Issues. Carlton South (Australia): Quit Victoria, 1995. Available at: www.quit.org.au/quit/fandi/welcome.htm. [Accessed September 2007].
19. Brennan E, Durkin S. Perceptions about the health effects of smoking and passive smoking among Victorian adults, 2003–2006. Melbourne: Centre for Behavioural Research in Cancer, The Cancer Council Victoria, August 2007. Report No.: CBRC Research Paper Series No. 27.
20. Hughes JR. Effects of abstinence from tobacco: etiology, animal models, epidemiology, and significance: a subjective review. Nicotine Tob Res 2007;9:329–39.
21. Tomkins DM, Sellers EM. Addiction and the brain: the role of neurotransmitters in the cause and treatment of drug dependence. CMAJ 2001;164:817–21.
22. Keating GM, Siddiqui MA. Varenicline: a review of its use as an aid to smoking cessation therapy. CNS Drugs 2006;20:945–60.
23. Raw M, McNeill A, Arnott D. Varenicline: guidance for health professionals on a new prescription-only stop smoking medication. London: Action on Smoking and Health, 2006. Available at: www.newash.org.uk/files/documents/ASH_447.pdf.
24. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. Br J Addict 1991;86:1119–27.
25. Shu-Hong Zhu S-H. Differential cessation rate across populations: what explains it and how to reduce it. Oceania Tobacco Control Conference, Auckland (New Zealand), 4–7 September 2007. Abstract available at: www.smokefreeoceania.org.nz/pdfs/abstracts/ShuHongZhu.pdf.
26. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J Health Promot 1997;12:38–48.
27. Harris M, editor. Smoking, Nutrition, Alcohol and Physical activity (SNAP): a population health guide to behavioural risk factors in general practice. South Melbourne: The Royal Australian College of General Practitioners, 2004.
28. West R, Sohal T. "Catastrophic" pathways to smoking cessation: findings from national survey. BMJ 2006;332:458–60.
29. Silagy C, Mant D, Fowler G, Lancaster T. Nicotine replacement therapy for smoking cessation. In: The Cochrane Library, Issue 2, 1998. Oxford: Update Software.
30. Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. Cochrane Database Syst Rev 2007;1: CD000031.
31. Hughes JR, Stead LF, Lancaster TR. Anxiolytics and antidepressants in smoking cessation. The Cochrane Library, Issue 2, 1998. Oxford: Update Software.
32. Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev 2007;1: CD006103.
33. Wu P, Wilson K, Dimoulas P, Mills EJ. Effectiveness of smoking cessation therapies: a systematic review and meta-analysis. BMC Public Health 2006;6:300.
34. National Institute for Health and Clinical Excellence. Varenicline for smoking cessation, 2007. Available at: www.nice.org.uk/TA123.
35. Aubin H-J, Bobak A, Britton JR, et al. Varenicline versus transdermal nicotine patch for smoking cessation results from a randomised open-label trial. Thorax 2008;63:717–24.

36. Anthonisen NR, Skeans MA, Wise RA, Manfreda J, Kanner RE, Connett JE; Lung Health Study Research Group. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. Ann Intern Med 2005;142:233–9.
37. Action on Smoking and Health Australia. Nicotine replacement therapy: guidelines for healthcare professionals on using nicotine replacement therapy for smokers not yet ready to stop smoking. Woolloomooloo (Australia): ASH, February 2007. Available at: www.ashaust.org.au/pdfs/NRTguide0702.pdf.
38. New Zealand Ministry of Health. New Zealand smoking cessation guidelines. Wellington: MOH, August 2007. Available at: http://www.moh.govt.nz/moh.nsf/pagesmh/6663/$File/nz-smoking-cessation-guidelines.pdf.
39. Gonzales D, Rennard SI, Nides M, Oncken C, Azoulay S, Billing CB et al. Varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. JAMA 2006;296:47–55.
40. Jorenby DE, Hays JT, Rigotti NA, Azoulay S, Watsky EJ, Williams KE et al. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation. JAMA 2006;296:56–63.
41. Cahill K, Stead L, Lancaster T. A preliminary benefit-risk assessment of varenicline in smoking cessation. Drug Safety. 2009;32:119–35.
42. Tonstad S, Tønnesen P, Hajek P, Williams KE, Billing CB, Reeves KR. Effect of maintenance therapy with varenicline on smoking cessation : a randomized controlled trial. JAMA 2006;296:64–71.
43. Pfizer Australia Pty Ltd. CHAMPIX®: varenicline tartrate. Product information. West Ryde (Australia): Pfizer Australia, September 2007.
44. National Institute for Health and Clinical Excellence. Smoking cessation – bupropion and nicotine replacement therapy: the clinical effectiveness and cost effectiveness of bupropion (Zyban) and nicotine replacement therapy for smoking cessation. London: NICE, March 2002. Report No.: TA39.
45. Richmond R, Zwar N. Therapeutic review of bupropion slow release. Drug Alcohol Rev 2003;22:203–20.
46. Evins AE, Cather C, Deckersbach T, Freudenreich O, Culhane MA, Olm-Shipman CM et al. A double-blind placebo-controlled trial of bupropion sustained-release for smoking cessation in schizophrenia. J Clin Psychopharmacol 2005;25:218–25.
47. Hurt RD, Sachs DP, Glover ED, Offord KP, Johnston JA, Dale LC et al. A comparison of sustained-release bupropion and placebo for smoking cessation. N Engl J Med 1997;337:1195–1202.
48. Jorenby DE, Leischow SJ, Nides MA, Rennard SI, Johnston JA, Hughes AR et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. N Engl J Med 1999;340:685–91.
49. Hughes JR, Lindsay F, Stead LF, Lancaster T. Nortriptyline for smoking cessation: a review. Nicotine Tob Res 2005;7:491–9.
50. Wagena EJ, Knipschild P, Zeegers MP. Should nortriptyline be used as a first-line aid to help smokers quit? Results from a systematic review and meta-analysis. Addiction 2005;100:317–26.
51. Foulds J, Steinberg MB, Williams JM, Ziedonis DM. Developments in pharmacotherapy for tobacco dependence: past, present and future. Drug Alcohol Rev 2006;25:59–71.
52. Siu EC, Tyndale RF. Non-nicotinic therapies for smoking cessation. Annu Rev Pharmacol Toxicol 2007;47:541–64.
53. Hall WD. Will nicotine genetics and a nicotine vaccine prevent cigarette smoking and smoking-related diseases? PLoS Med 2005;2:e266.
54. Cahill K, Ussher M. Cannabinoid type 1 receptor antagonists (rimonabant) for smoking cessation. Cochrane Database Syst Rev 2007;3:CD005353.
55. Etter J. Cytisine for smoking cessation: a literature review and a meta-analysis. Arch Intern Med 2006;166:1553–9.

Smoking cessation pharmacotherapy: an update for health professionals

The Royal Australian College of General Practitioners

The Pharmacy Guild of Australia

apna Australian Practice Nurses Association

Quit Victoria

ASH Action on Smoking and Health

The Cancer Council Australia

Pharmaceutical Society of Australia

TSANZ The Thoracic Society of Australia & New Zealand Inc