

Review of smoking cessation interventions • background report for the Department of Health and Human Services, Tasmania

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The executive summary

Executive summary

This document summarises the current evidence for the effectiveness of interventions for smoking cessation. The intent of the review document is to give background information on what is already known about best practice in cessation service to help guide commissioning of smoking cessation services.

Brief advice to stop smoking

There is good evidence [1++] from randomised controlled trials that brief advice to stop smoking from a doctor improves 6-month abstinence rates. All doctors should provide brief advice to quit smoking to all their patients who smoke. Although more intensive intervention may result in higher abstinence rates the marginal benefit may not be worth the extra time. Doctors would be better to provide more advice to more smokers.

The evidence for the effectiveness of brief advice delivered by other healthcare workers is less clear. However, there is no reason to believe that clear advice from dentists, dental hygienists, nurses, pharmacists and all other health care professionals would not have some benefit. Given the relatively small amount of time and skill required to deliver brief advice, it should be provided by all healthcare workers.

Self help interventions

There is good evidence [1++] from randomised controlled trials that self-help materials make a small improvement in 6-month abstinence rates. However self-help materials have only a small effect on abstinence when compared with no intervention. Tailored self-help materials are likely to be more effective than non-tailored materials.

Telephone support

There is good evidence [1++] from randomised controlled trials that shows that proactive telephone smoking cessation counselling improves 6 months abstinence rates. Proactive telephone support for smoking cessation increases long-term abstinence rates. Adding telephone support to pharmacotherapy increases abstinence rates over that of pharmacotherapy alone.

Face-to-face support

(a) Individual support

There is good evidence [1++] from randomised controlled trials that individual smoking cessation support improves 6-month abstinence rates. There is no evidence that more intensive interventions are better than low intensity interventions. There is no direct evidence that

more intensive interventions are better than low intensity interventions. However correlational evidence suggests better outcome with more intensive support.

(b) Group support

There is good evidence [1++] from randomised controlled trials that group-based smoking cessation treatment improves six-month abstinence rates. There is no evidence that group-based interventions are better, or worse, than one-to-one interventions, and there is currently insufficient evidence to ascertain which components of group-based treatment are most important.

Nicotine replacement therapy

There is good evidence [1++] from randomised controlled trials that nicotine replacement therapy improves 6-month abstinence rates. There is evidence to support its use in combination with other NRT products, and its use in cutting down prior to quitting. NRT is safe to use in smokers with a history of cardiovascular disease, although consultation with a physician should occur if the smoker has suffered a recent (within the past 2 weeks) cardiovascular event or has unstable cardiac disease. Robust evidence is lacking for the effectiveness of NRT use in adolescents. However given that there are no safety concerns it can be considered for use in this group. There is no strong evidence for the effectiveness of NRT in pregnant women who smoke. It is also unknown to what degree nicotine adversely affects the pregnancy and fetus. However, in comparison with continued smoking NRT is safer. Therefore the use of NRT in pregnancy may be considered, but it is recommended that a risk benefit assessment be undertaken.

Bupropion

There is good evidence [1++] from randomised controlled trials that bupropion improves 6-month abstinence rates. Bupropion is well tolerated by most people, but consideration needs to be given to the contraindications and side effects associated with this medication.

Nortriptyline

There is good evidence [1++] from randomised controlled trials that nortriptyline improves 6-month abstinence rates. Overall, nortriptyline is a well-tolerated medication however consideration needs to be given to the contraindications and side effects associated with this medication.

Varenicline

There is good evidence [1++] from randomised controlled trials that varenicline improves 6-month abstinence rates. Varenicline has few contraindications and no known drug interactions and therefore appears to be a suitable medication for a large number of smokers. The main side effect of varenicline is nausea.

Young people

There is currently inconsistent evidence concerning whether behavioural interventions aimed specifically at smoking cessation in young people improve continuous 6-month abstinence rates. Overall there are still few data that confirm the effectiveness of interventions specifically aimed at helping young people quit smoking. Although some intervention models may show promise there is insufficient evidence to recommend that any of these be integrated into standard practice. However results from randomised controlled trials suggest that behavioural interventions show promise and further research is warranted. There is insufficient evidence to recommend that

pharmacotherapies be provided to all young smokers that want to quit. Given the lack of clear evidence on specific interventions for young smokers it is recommended that interventions that have efficacy in helping adult smokers be used – this means interventions that use multi-session behavioural support.

Indigenous Australians who smoke

There is insufficient evidence on smoking cessation interventions for indigenous Australians. There are few studies assessing the outcome of smoking cessation interventions for indigenous Australian smokers. There is no evidence to support the assertion that the effectiveness of interventions known to work in the general population such as individual or group based behavioural support and pharmacotherapies should be any different in indigenous Australians. Though the findings of various reports suggest these interventions must be acceptable to these people if they are to engage and fully benefit.

Pregnant women who smoke

There is evidence [1++] from randomised controlled trials that multi-session behavioural interventions to help pregnant women stop smoking improve 6-month abstinence rates, particularly those using CBT. There is insufficient evidence on the use of NRT in pregnancy, although it is likely to assist some women and to be less dangerous than continuing to smoke in pregnancy for those women who are unable to stop without it.

Hospitalised smokers

There is good evidence [1++] from randomised controlled trials evidence to support hospital-based cessation services, however, to be effective inpatient smoking cessation programmes need to include follow-up for at least a month post-discharge.

Pre-operative smoking cessation

There is evidence [1+] from randomised controlled trials that pre-operative smoking cessation interventions improve short-term abstinence rates. However there is insufficient evidence to draw any conclusion regarding 6-month abstinence. All smokers should be encouraged to stop smoking, and supported in their attempt prior to surgery. While any time is likely to be beneficial in comparison to continued smoking, the earlier they stop the lower the post-operative risk is likely to be. There is insufficient evidence that temporary abstinence increases the risk of complications.

People with mental health illness

There is currently inconsistent evidence concerning whether smoking cessation services aimed specifically at smoking cessation in people with mental illness improve continuous 6-month abstinence rates. There are few randomised controlled trials assessing the outcome of smoking cessation interventions for smokers with mental illness. Smokers with mental illness are typically highly dependent smokers and find stopping smoking very difficult. Therefore it is likely that they will benefit from more intensive smoking cessation interventions. These should include multi-session behavioural support and pharmacotherapy. Combination pharmacotherapy may be associated with a superior outcome. Most smokers will not experience a worsening in the symptoms of their mental illness when they stop smoking. In fact in some cases their symptoms may improve. Components of tobacco smoke cause induction of some liver enzymes. Smoking cessation may therefore affect the metabolism of a number of medications.

People with other addictions

There is inconsistent evidence on smoking cessation interventions for those with substance use disorders to draw any conclusion. Overall there is evidence that smoking cessation interventions can be effective at increasing short-term quit rates in people with substance use disorders. However, effectiveness of interventions in aiding long-term abstinence is inconsistent.

People who make repeated quit attempts

There is evidence from randomised controlled trials [1++-] that bupropion and NRT can be used successfully in people who have tried pharmacotherapies in the past but failed. There is insufficient evidence to recommend a minimum time between quit attempts. People who relapse should be encouraged to return for treatment. However, repeat treatment may need to address factors such as high nicotine dependence. Bupropion and NRT can be used again in people that have tried pharmacotherapies in the past but failed. Treatment choice should be guided by learning from prior failures, and individual preference. It is likely that a more intensive treatment is required on a subsequent attempt.

Relapse prevention

There is inconsistent evidence on relapse prevention interventions to draw any conclusion. Despite a number of studies, there is no conclusive evidence for the efficacy of specific interventions for preventing relapse.

Cost-effectiveness

There is good evidence (based on randomised controlled trials) for the cost effectiveness of telephone and face-to-face smoking cessation support and pharmacotherapies such as NRT, bupropion, nortriptyline and varenicline. Smoking cessation interventions are among of the most cost-effective interventions available to healthcare systems.

Other interventions

There are a number of other interventions that have not demonstrated any effect on increasing long-term cessation rates in randomised controlled trials (e.g. acupuncture, hypnosis, anxiolytics) or for which insufficient data is available (e.g. Allen Carr method, Nicobrevin, Nicobloc). These interventions should not be recommended to smokers as smoking cessation methods.

Introduction to the report

Background

The Department of Health and Human Services (DHHS), Tasmania, has contracted Global Public Health (GPH) to review smoking cessation interventions in Tasmania. The intent of the review is to give guidance in how to apply what is already known about best practice in cessation service to the Tasmania service delivery context.

Globally tobacco smoking remains a major public health problem. In Australia it is the largest preventable cause of death and disability. Tobacco smoking is directly responsible for more than 19,000 deaths every year in Australia.¹ It affects not only individuals who smoke but also others exposed to second hand smoke.

Australia has long been at the forefront of tobacco control and over the past two decades has seen a substantial drop in smoking prevalence. Between 1990 and 2005 smoking prevalence dropped in Tasmania by 3.4%. However, a recent (2006) health survey shows that approximately a quarter of Tasmanians aged 18 years and older still smoke.² In 2001, smoking prevalence was 1% lower although this change is not statistically significant. Survey results show patterns of smoking similar to those seen in other countries such as a higher prevalence in men and in those aged 18-34 years of age. In a 2004 household survey the national prevalence in Australia was found to be 17%.³ In the same survey smoking prevalence was 21.5% (22% of males and 21% of females) in Tasmania.

Stopping smoking confers immediate benefits for those who already have smoking-related diseases and future health benefits for all smokers. Helping people who smoke to stop is a leading health goal. The Department of Health and Human Services *Reducing Smoking In Tasmania – A Framework for Action* lists cessation services and treatment as a key strategy area.⁴

The purpose of this report

The purpose of this report is to review the international, national and regional smoking cessation, tobacco control, mental health, and aboriginal networks literature on interventions for smoking cessation.

The report includes information on the effectiveness and, where available cost –effectiveness, of smoking cessation interventions, both behavioural and pharmacological, with an additional focus on priority population groups such as young people, indigenous Australians, pregnant women and people with mental illness. Also included is information on the effectiveness of a selection of other interventions widely promoted as effective smoking cessation aids, such as acupuncture and hypnosis.

The information provided will help guide policy makers and purchasers to determine the most effective and efficient ways of providing cessation services.

Understanding smoking and smoking cessation

The primary reason why many smokers find stopping difficult is nicotine dependence. When deprived of nicotine a withdrawal syndrome involving both physical symptoms and mood disturbances such as irritability, increased appetite, poor concentration, and urges to smoke, results. These withdrawal symptoms, especially urges to smoke and depressed mood, make stopping an extremely unpleasant experience and lead to a high rate of relapse early in a quit attempt.⁵

Healthcare workers need to be aware of these matters. They should understand that the level of support a person trying to stop smoking needs is related to their degree of nicotine dependence, the existence of conditions that may make the quit attempt more difficult, and their ability to cope with the changes associated with quitting.

Armed with appropriate skills and knowledge, healthcare workers should do all they can to assist people to stop by either providing cessation support, prescribing or recommending an effective smoking cessation medication, or referring those interested in quitting to evidence-based smoking cessation services. A number of documents from the US⁶ and the UK⁷ outline core competencies for smoking cessation workers that can be used to guide appropriate training and practice.

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Summary of the methodology

Methodology

Literature search

The literature search was the same as that undertaken for the literature review underpinning the 2007 New Zealand Smoking Cessation Guidelines. This used two key data sources: systematic reviews published by the Cochrane Collaboration and a systematic review undertaken by the US Department of Health and Human Services (USDHHS) to inform the US Treating Tobacco Use Guidelines.⁸ These sources are the most comprehensive and current international systematic reviews relevant to this review and were conducted to the highest, most rigorous standards. Both assess studies that make a direct comparison of the intervention being examined with appropriate controls, as opposed to looking at differences between studies. They use strict and relatively consistent inclusion criteria (e.g. randomised controlled trials that report at least 6 months abstinence rates), provide descriptions of the included studies and are regularly updated. In most cases these reviews reach the same conclusions. The most recent Cochrane reviews used in this report have been updated in the last two years.

We supplemented these reviews with findings from other systematic reviews and randomised controlled trials (published in English from January 2002 until March 2006) and unpublished data where appropriate. Data from publications prior to 2002 are included in the Cochrane reviews.

Studies reporting non-randomised trials were included only when limited higher-level evidence was available. A systematic search of the 'grey literature' was not undertaken.

A list of the databases searched, and the search strategy is found in Appendix 1.

Quality Appraisal and level of evidence

Additional systematic reviews and studies not already included in the Cochrane and USDHHS reviews were assessed for their methodological rigor and quality against the critical appraisal checklists provided by the UK National Institute of Clinical Excellence (NICE; Appendix B of the *Public Health Guidance. Methods Manual – version 1*).

The level of evidence was classified according to NICE guidelines (see table 1).

Reporting results and presentation of findings

Smoking cessation studies generally report **absolute quit rates**. Where an intervention group is compared to a control group, the **odds ratio (OR)**¹ is often used to show the size of the effect of the intervention. The **number needed to treat (NNT)** is also used in this report.²

For each smoking cessation intervention we summarise the evidence and provide an evidence statement.

Table 1: Levels of evidence

Level of evidence	Type of evidence
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs (including cluster RCTs) with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs (including cluster RCTs) with a low risk of bias
1–	Meta-analyses, systematic reviews of RCTs, or RCTs (including cluster RCTs) with a high risk of bias*
2++	High-quality systematic reviews of, or individual, non-randomised controlled trials, case-control studies, cohort studies, controlled before-and-after (CBA), interrupted time series (ITS), correlation studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted non-randomised controlled trials, case-control studies, cohort studies, controlled before-and-after (CBA), interrupted time series (ITS), correlation studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2–	Non-randomised controlled trials, case-control studies, cohort studies, controlled before-and-after (CBA), interrupted time series (ITS), correlation studies with a high risk of confounding bias, or chance and a significant risk that the relationship is not causal*
3	Non-analytic studies (for example, case reports, case series)
4	Expert opinion, formal consensus

*Studies with a level of evidence '–' should not be used as a basis for making a recommendation (see section 7.4) NICE Guideline Development Methods: Chapter 7 Reviewing and grading the evidence (www.nice.org.uk/pdf/GDM_Chapter7_0305.pdf)

¹ The odds ratio is the odds of quitting in the intervention group compared to that in a control group. An OR of greater than 1 indicates that the odds of quitting smoking are greater with the intervention than the control.

² NNT indicates how many people need to be treated for every one person who stops smoking. The NNT is the inverse of the absolute risk (risk difference): $NNT = 1 / \text{risk difference}$. For example, if the risk difference of brief advice from a physician is 2.5% then: $NNT = 1 / 0.025 = 40$. So, for every 40 people that receive brief advice to stop smoking one will stop smoking that would have otherwise not have managed to do so on their own.

The evidence for brief advice

Brief advice to stop smoking

Brief advice to quit smoking given opportunistically by a doctor is an effective smoking cessation intervention. Whilst the effect is small, if delivered to all people who smoke it has great potential to have an impact at a population level.

Brief advice can be given quickly and easily.⁹ Assessment of stage of change is unnecessary as advice can be provided to *all* smokers irrespective of whether they express a wish to stop smoking or not. Advice may be strengthened if linked to an existing smoking related medical condition.

The *Transtheoretical (Stages of Change) model* has been extensively applied to smoking cessation, resulting in an ever increasing amount of evidence that a subject's allocated stage of change is related to outcome and dropout from treatment.¹⁰ The model essentially assesses smokers as belonging to one of six stages of change (precontemplation, contemplation, preparation, action, maintenance, and relapse). There has been recent debate on the usefulness and place of this model in smoking cessation treatment.^{11 12} One of the main criticisms is that it draws arbitrary lines to delineate stages. If, for example, a smoker is thinking of quitting within the next 30 days then she is classified as a contemplator, but if s/he was thinking of quitting in the next 35 days then she would be categorised as a precontemplator. Furthermore, the model assumes that people have to move through each of the stages before moving to the next. In fact people can move from precontemplation to action within a day. The model also ignores the importance of factors that influence human motivation such as plans, beliefs, wants and urges¹¹. Perhaps most importantly there is no evidence that smoking cessation interventions based on this model are any more effective than other interventions.

The Cochrane systematic review of physician advice to stop advice identified 17 studies that compared brief or minimal advice with a control group.¹³ Combining the results of these studies shows a beneficial effect of brief advice (OR=1.74; 95 % CI: 1.48-2.05). This gives an overall risk difference of 2.5% (95% CI: 2-3%) and a number needed to treat of 40.

Brief advice appears to work by triggering a quit attempt rather than by increasing the chances of success of an individual quit attempt.¹⁴ It also seems to have its greatest effect on lighter smokers.¹³ Therefore, for more dependent smokers, brief advice should be followed by a recommendation to use pharmacotherapy or referral to a smoking cessation service.

There is no evidence that adding self-help materials to brief advice confers any additional benefit, nor is there evidence regarding how brief advice should be provided. Direct comparisons of higher intensity versus lower intensity advice show little difference in outcome (OR=1.24; 95% CI: 1.02-1.50).¹³

More doctors should therefore provide low intensity (quick or minimal) advice to stop smoking rather than fewer doctors providing more intensive advice.

Summary	All doctors should provide brief advice to quit smoking to all their patients who smoke. Assessment of stage of change is unnecessary as advice should be provided to <i>all</i> smokers irrespective of whether they want to stop smoking or not. Although more intensive intervention may result in higher abstinence rates the marginal benefit may not be worth the extra time. Doctors would be better to provide more advice to more smokers.	
Strength of evidence	1++	Evidence statement There is good evidence from randomised controlled trials that brief advice to stop smoking from a doctor improves 6-month abstinence rates.

Brief advice from other healthcare workers

The evidence for the effectiveness of brief advice delivered by other healthcare workers is not as strong as advice from physicians.¹⁵⁻¹⁷ However, there is no reason to believe that clear advice from dentists, dental hygienists, nurses, pharmacists and all other health care professionals would not have some benefit. Given the relatively small amount of time and skill required to deliver brief advice, it should be provided by all healthcare workers.

The evidence for self-help materials

Self-help materials

Self-help materials, such as leaflets and books, are a relatively inexpensive means of communicating cessation advice to a potentially large number of smokers. However, the content of these materials is of widely differing quality.¹⁸

The Cochrane review¹⁹ identified sixty studies that examined the efficacy of self-help materials, including written, audio and video materials, that could be tailored or non-tailored, plus internet-based smoking cessation interventions that now enable personalised advice to smokers in a way that traditional written materials could not.²⁰

Seventeen studies examined the efficacy of self-help materials compared to 'no treatment' in nearly 20,000 smokers. Pooling the results of these studies showed a small but significant benefit of self-help materials (OR=1.33; 95% CI: 1.18-1.51). When the results of all studies examining written materials are combined the overall effectiveness of written materials is small (OR=1.11; 95% CI: 1.00-1.22), increasing long-term quit rates by approximately 1% (95% CI: 0-1%).¹⁹ This equates to a number needed to treat of 100.

Adding self-help materials to other effective interventions, such as brief advice, face-to-face or telephone support, and medications, does not appear to increase the effectiveness of those interventions.²¹

Tailored self-help materials

Tailored self-help materials are more effective than no intervention at all (OR=1.38; 1.15-1.66). Tailored self-help materials are more effective than non-tailored materials but the effect size is relatively small (OR=1.50; 95% CI: 1.12-2.02. RD=2%; 95% CI: 0-3%).¹⁹ The number needed to treat is 50. A recent study, not included in the Cochrane review, supports these findings.²²

Internet-based self-help

Some internet based interventions have reported impressive differences between intervention and control groups (e.g. Strecher, 1999 23% versus 18% 12 week continuous abstinences rates²⁰) but there is lack of long-term (6-months or longer) follow-up to be able to conclude that they are truly effective.

Summary	Self-help materials have a small effect on abstinence when compared with no intervention. Tailored self-help materials are likely to be more effective than non-tailored materials.	
Strength of evidence	1++	Evidence statement There is good evidence from randomised controlled trials that self-help materials make a small improvement in 6-month abstinence rates.

An introduction to cessation support

Introduction to cessation support

The term cessation support is used in this review to describe all behavioural and pharmacological treatments for aiding smoking cessation.

Behavioural interventions refer to all cessation support that imparts knowledge about smoking and quitting, provides assistance and teaches skills and strategies for changing behaviour. There are a number of different methods (e.g. motivational interviewing and cognitive behavioural therapy; CBT) and formats that can be used (e.g. telephone and face-to-face counseling, the latter of which can be delivered individually or in group settings). The different methods of behavioural counseling are not discussed in detail in this review, but are very briefly summarized below. Overall there is no evidence to suggest a significant difference in smoking cessation outcome between methods.

There are now a number of pharmacotherapies available to help people stop smoking. Some (e.g. nicotine replacement therapy; NRT) are available over-the-counter, while others can only be obtained on prescription (e.g. bupropion, nortriptyline, and varenicline).

Methods of behavioural treatment for smoking cessation

Motivational interviewing and cognitive behavioural therapy (CBT) are commonly used in smoking cessation although there is no evidence for the superiority of one method over the other. Motivational interviewing typically involves dialogue to engage the individual to motivate and sustain long-term behaviour change. Through discussion with the counselor the individual is prompted to identify their 'risky' situations and develop strategies for coping.²³ CBT is a technique which assists the individual to identify and then utilise strategies to help deal with urges to smoke and other difficult situations that arise during a quit attempt. These strategies combine both cognitive approaches, such as identifying triggers and risk situations, and behavioural approaches, such as distraction, avoidance and relaxation.²⁴ Another method that is used is Withdrawal Oriented Therapy,²⁵ which focuses on assisting smokers through the early stages of a quit attempt with the aim of preventing early relapse. The key components of treatment are intensive behavioural support during the time when withdrawal symptoms are most intense, supervision of medication and emphasizing the importance of trying to achieve total abstinence. Whatever behavioural treatment approach is used there are two key components that are common to most methods; that is (1) setting a firm quit date and (2) repeated contacts for at least four weeks following the quit date. Added to this are general counseling techniques such as getting smokers to recognise risky situations that lead to relapse (e.g. being around other smokers, getting drunk, low mood); developing skills to avoid or cope with these situations; and providing information about smoking and stopping smoking. The latter may include information about tobacco dependence, the risk of relapse associated with even a single puff, and occurrence and expected time course of tobacco withdrawal symptoms.

The evidence for telephone support

Telephone support

Telephone support is an effective method for smoking cessation,²⁶ and also has demonstrated cost-efficacy.²⁷ It can be reactive or proactive and it is the latter technique that has the strongest evidence for efficacy. Reactive telephone support relies on the smoker initiating the calls whereas a proactive service involves the counsellor initiating the calls to the client, usually at prearranged times. Proactive telephone support can also increase the frequency of calls at times when the risk of relapse is at its greatest (i.e. the first few days and weeks of a quit attempt).

Telephone smoking cessation services have the potential to reach more people (i.e. they can be delivered to many people over a large geographical area) than face-to-face support. There is some evidence that some smokers would prefer telephone to face-to-face support.²⁸ There is also evidence that Quitlines provide a service for smokers who may not be reached by other smoking cessation services.²⁹

The Cochrane review of telephone support for smoking cessation showed the most common delivery format was three calls over three months.²⁶ People calling Quitlines and receiving additional proactive calls were significantly more likely to quit smoking for at least 6 months than those in control groups (OR=1.41; 95% CI: 1.27-1.57). The difference in effect between the groups is 3% (95% CI: 2-4%) giving a NNT of 33.²⁶

A recently published randomised controlled trial undertaken in the UK failed to show an effect of proactive telephone counselling compared to usual care on 6-month abstinence rates (9.3% vs. 9.5%, NS).³⁰ One of the reasons cited by the authors for this lack of effect was a non-structured counselling protocol and client-led counselling. Compared to other trials of a similar nature (e.g. Zhu 1996³¹) clients were not allocated to a single counsellor and so there was no continuity of care. This may be an important factor in outcome, although there are no studies that look directly at this comparison.

As yet there is no evidence that telephone follow-up after intensive support reduces relapse rates.³²

Use of telephone counselling in specific groups

- There is evidence from one study that an enhanced telephone support service that provides more personalised advice (e.g. tailored to potential barriers to success) may be better for men.³³

- One randomised controlled trial specifically investigated the effectiveness of telephone counselling in young adults (aged between 18 and 25) and demonstrated that telephone support produced higher six month (2 day self report point prevalence) abstinence rates than written self help materials (9% vs. 2%, $p < 0.005$).³⁴
- Telephone counselling has been shown to be superior to standard care (self-help materials) in a primary care setting. Those patients who received telephone support (7 calls over 2 months) versus those randomised to standard care were more likely to be abstinent for 6-months when follow-up at 12 months after randomisation (self reported).³⁵
- Results of RCT of a tailored telephone counselling programme (up to four brief, <15 minutes, motivational calls over 6 months) in women with a recent abnormal cervical smear showed significantly higher abstinence rates (7-day point prevalence) at 6-months than a usual care control (20% vs. 12%, $p < 0.05$), although this difference was lost at 12 months.³⁶

Combined telephone and face-to-face counselling

There is no advantage of adding telephone support to concurrent face-to-face support.²⁶ However when the intensity of face-to-face counselling is low, for example, a single session for hospital in-patients, additional follow-up with telephone counselling has been shown to have a positive effect.³⁷

Adding telephone support to pharmacotherapy

There is evidence that adding telephone support to pharmacotherapy increases short³⁸ and long-term³⁹ abstinence rates over that of pharmacotherapy alone.

Telephone follow-ups to treatment

To date there is no evidence that telephone counselling following intensive treatment reduces relapse rates.³² However, ongoing telephone contact may reduce the number of people that are lost to follow-up when smoking cessation outcome is measured (usually at six or twelve months) and can identify clients that have relapsed - these clients can then be supported in making another quit attempt.

Reactive telephone counselling

Reactive telephone counselling, which includes help lines, has not been so rigorously evaluated. This is partly due to methodological difficulties in doing this (e.g. the control group would have to be refused any help). However there is indirect evidence that suggests that these may be helpful.²⁶

Summary

Proactive telephone support for smoking cessation increases long-term abstinence rates. Adding telephone support to face-to-face support (concurrently) has not been shown to increase abstinence rates over face-to-face support alone. However, in situations where face-to-face support is limited (e.g. a one-off session) the addition of follow-up telephone support may be advantageous.

Strength of evidence 1++	Evidence statements	<ol style="list-style-type: none">1. There is good evidence from randomised controlled trials that proactive telephone smoking cessation counselling improves 6 months abstinence rates.2. There is evidence that adding telephone support to pharmacotherapy increases abstinence rates over that of pharmacotherapy alone.3. There is insufficient evidence on reactive telephone helplines to draw any conclusions.
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The evidence for face-to-face support

Face-to-face support

There is good evidence that face-to-face cessation support is effective, regardless of the type of provider or the type of therapy they use. Approximately 1 in 20-25 people receiving face-to-face support will stop smoking for at least 6 months who would not have done so on their own. This is usually more intensive and therefore more costly than cessation support delivered via telephone or within the context of a visit to the doctor.

Individual support

A Cochrane review²⁴ included 21 studies assessing the efficacy of individual support based smoking cessation interventions. The interventions differed by level of intensity, counselling methods, study populations, and components of the interventions.

- When the results of 17 studies investigating the effects of minimal counselling compared to no treatment (minimal contact) control are pooled there is a clear benefit of counselling (OR=1.56; 95% CI: 1.32-1.84). The effect size was shown to be 4% (95%CI: 2-5%) giving a NNT of 25. These findings are similar to those of the meta-analysis undertaken for the US guidelines,⁸ showing that individual counselling was more effective than no intervention (OR=1.7; 95% CI: 1.4-2.0).
- Absolute quit rates varied and were generally higher when pharmacotherapy was used in addition to counselling. As one would expect they were lower when delivered to groups that are typically more dependent and harder to treat.
- Three studies that compared brief with more intensive counselling. The pooled results of these studies showed no additional benefit of intensive counselling.
- There is also no evidence for a difference in effectiveness of different counselling approaches.

Although there is no direct evidence showing a difference in smoking cessation outcome by variation of intensity of the support provided there is correlational evidence showing that more intensive behavioural support (e.g. more time spent with smokers) is associated with higher abstinence rates.⁸ The few studies that have made direct comparisons of high and low intensity support²⁴ have not demonstrated a difference in outcomes. However, the US Guidelines subgroup analysis showed a general trend of increasing success with increasing number of sessions provided. Based on this they subsequently recommended that services should aim to see smokers at four or more sessions.⁸

Summary

Smoking cessation support delivered on a one-to-one basis by smoking cessation counselors increase the chances of smokers stopping for at least 6 months. There is no direct evidence that more intensive interventions are better

than low intensity interventions. However correlational evidence suggests better outcome with more intensive support.

Strength of evidence

1++

Evidence statement

There is good evidence from randomised controlled trials that individual smoking cessation support improves 6-month abstinence rates.

Group-based support

Group-based treatment is a method that is used in a number of other therapeutic areas and one that has frequently been used in smoking cessation. The methods are described in more detail elsewhere.^{40 41} One of the main advantages of treating smokers in groups is cost-effectiveness. For example, a group of 20 smokers can be counselled in the same time it takes to counsel two smokers individually. Therefore group-based treatments can be advantageous for healthcare professionals with limited time who face a high demand from smokers wanting help in stopping. Where therapists treat large numbers of smokers' individual treatment can become repetitive and treatment 'failures' can knock their confidence. Groups, on the other hand, generate substantial interest and enthusiasm and the focus is on those clients maintaining abstinence and not those who continue to smoke.

A Cochrane review⁴² considered a total of 55 studies covering a number of different types of group programmes. Most contained an element of cognitive behavioural therapy, but also included skills training, mood management, manipulation of group dynamics (e.g. social support, didactic format, self-control, nicotine fading, altering smoking behaviour before the quit date). The meta-analysis showed:

- the superiority of group-based interventions over self-help in achieving at least 6 months of abstinence (OR=2.04; 95% CI: 1.60-2.60; effect size= 5% 95%CI: 3-6%; NNT=20)
- no evidence that specific components of group treatment are better than others, however more complex interventions seem to provide a small increase in abstinence rates over more simple group based treatments (OR=1.36; 95% CI: 1.03-1.79)
- no difference in the efficacy of group versus individual smoking cessation treatments (OR=0.86; 95%CI: 0.66-1.12)

The conclusion drawn from the meta-analysis is that there is clear and consistent evidence that group-based smoking cessation treatment increases smoking cessation rates over that of self-help or no treatment. The meta-analysis undertaken for the US guidelines comes to similar conclusions, (OR for the group-based treatment compared to no treatment 1.3; 95% CI: 1.1-1.6).⁸

Summary

Group-based smoking cessation treatment is effective in increasing the chances of smokers stopping for at least 6 months compared to no treatment or self-help. There is no evidence that group-based interventions are better, or worse, than one-to-one interventions. There is insufficient evidence to ascertain which components of group-based treatment are most important.

<p>Strength of evidence 1++</p>	<p>Evidence statements</p>	<ol style="list-style-type: none"> 1. There is good evidence from randomised controlled trials that group-based smoking cessation treatment improves six-month abstinence rates. 2. There is insufficient evidence of the comparative efficacy of group versus individual smoking cessation treatments. 3. There is insufficient evidence to draw definitive conclusions about the cost-effectiveness of group-based treatments over individual treatments. However, if treatments produce similar outcomes then it is logical to assume that group-based treatments are likely to be more cost-effective.
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Who is best placed to provide support

Who is best placed to provide support

The US guidelines identified 29 studies that compared the effectiveness of interventions delivered by various types of clinicians. There were a total of 39 arms where the intervention was delivered by a clinician that was not a physician (e.g. nurse, dentist dental hygienist, and pharmacist). Data from these arms was entered into a meta-analysis and this confirmed that these clinician led interventions were significantly more effective than no intervention (OR=1.7; 95% CI: 1.2-2.1). The guidelines subsequently made the recommendation that **“Treatment delivered by a variety of clinician types increases abstinence rates. Therefore, all clinicians should provide smoking cessation interventions.”**⁸

Evidence for the effectiveness of interventions delivered by particular groups of healthcare professionals is presented below.

Dentists

Smoking and oral tobacco use is associated with an increased risk of dental pathology including periodontal disease and oral cancer. Smokers are also more likely to suffer with halitosis, stained teeth and problems of altered taste. Tobacco use is of direct relevance to many dental treatments and surgery and the benefits of stopping smoking can contribute to better outcomes.⁴³

Because of their oral health problems many smokers have contact with dental services. Therefore dentists, and dental hygienists and therapists, are in an ideal position to provide brief advice to stop smoking and in some situations may be able to provide smoking cessation treatment. However, for many dentists, providing brief advice to stop smoking has not become part of normal routine.⁴⁴

There are only a small number of published studies that examine the long-term efficacy of interventions provided by dentists, and most of these focus on the cessation of oral, rather than smoked, tobacco. Interventions range from identification of tobacco users within the practice and provision of brief advice to quit to more intensive cessation-based interventions. The Cochrane review¹⁵ pooled the results of six studies which show that interventions provided within the dental setting are effective in aiding cessation of tobacco use (OR=1.67; 95% CI: 1.09-2.57). However, only one of these studies tested an intervention aimed at cigarette smokers and this failed to show a significant benefit.⁴⁵

These results suggest that dentists and allied staff can deliver interventions that are effective in helping tobacco users to stop smoking. There is no reason to believe that interventions aimed at helping smokers to stop would not be effective, but more research is needed to verify this.

Nurses

Patients often have greater contact time with nurses and may even develop better relationships with nurses than with their doctor (especially in hospital settings). All nurses are well placed to give general advice on stopping smoking and even to provide more intensive smoking cessation interventions.

Systematic reviews^{16 46} showed that nurse based smoking cessation interventions were effective in helping people to stop smoking for at least 6 months (OR=1.59; 95% CI: 1.22-1.67).¹⁶ Subgroup analysis by intensity showed the superiority of higher intensity interventions (OR=1.52; 95% CI: 1.30-1.78) compared to the low intensity interventions, which failed to show a significant effect over no advice (OR=1.19; 95% CI: 0.98-1.44). However, the results of the higher intensity interventions need to be considered with some caution because of the marked heterogeneity among the studies.

Pharmacists

Community pharmacists are freely accessible to most communities, and visitors to community pharmacies tend to be both well and ill people, providing the opportunity for the provision of both preventive advice and treatment. An example of the role pharmacists can play can be found in the UK where they make up an important part of the Stop Smoking Service, and provide both multi-session behavioural support and pharmacotherapy as part of this role.⁴⁷ Hospital pharmacists are an integral part of the clinical team, and have specialist clinical roles. One of the key roles of hospital pharmacists is to assess medication history and so they are required to interact with the majority of inpatients. This means that they are ideally positioned to provide brief smoking cessation advice to smokers. In recognition of the role pharmacists have to play, UK Guidelines were developed especially to aid the provision of smoking cessation advice and treatment for smokers from pharmacists.⁴⁸

There are a small number of trials that aim to assess the effectiveness of smoking cessation interventions provided by pharmacists and their staff. The Cochrane review on community pharmacy personnel interventions for smoking cessation identifies two studies^{49 50} meeting their inclusion criteria.¹⁷ The conclusions that can be drawn from these data are limited. Interventions delivered by community pharmacists have the potential to help smokers quit. Evidence from the UK stop smoking services suggests that many pharmacists are ideally placed to do this.⁴⁷ The most effective type of intervention delivered by pharmacy staff cannot be determined from current data. However, it is likely that a combination of multi-session behavioural support and pharmacotherapy will be the best approach.

The evidence for nicotine replacement

Nicotine replacement therapy

Nicotine replacement therapy has been used to help smokers stop for over 20 years. It is both safe and effective and the most widely used and available proven treatment. There are now six NRT products available on the global market and more are in development. Its primary mechanism of action is to reduce the severity of withdrawal symptoms associated with smoking cessation. Although it does not completely alleviate the unpleasant effects associated with withdrawal, quitting is made more tolerable and the attempt is more likely to succeed.⁵¹ Products typically provide less nicotine than the average smoker obtains from smoking the time to reach peak plasma concentration is longer than with cigarette smoking. NRT is not a 'magic bullet' but unquestionably aids quit attempts making a successful outcome more likely.

Efficacy of NRT

The Cochrane review on nicotine replacement therapy for smoking cessation identifies 105 randomised controlled trials assessing the efficacy of NRT, together involving approximately 40,000 smokers.⁵¹ The meta-analysis showed that the odds of successfully quitting for at least six months using NRT were significantly greater than for placebo (OR=1.77; 95% CI: 1.66-1.88). Long-term abstinence rates achieved in the NRT groups were on average 6% higher than in the controls. This gives a NNT of 17. It is effective in both men and women.⁵²

Does it work in smokers of less than 10 cigarettes per day?

Most studies have examined the use of NRT in dependent smokers of over 10 cigarettes per day. NRT does not appear to be more effective than placebo in light smokers.⁵¹ However, these findings must be considered with caution when treating smokers who have recently cut down.

Is one product better than another?

The odds ratios for each product vary, but overlapping 95% confidence intervals suggest no superiority of any one product over another.

Strength of products

Gum and lozenge: There is a clear advantage in using higher dose products (e.g. 4mg compared to 2mg gum) in highly dependent³ smokers.

³ Shiffman et al (2002) defined high dependency as a person smoking the first cigarette of the day within 30 minutes of waking.⁵³ Shiffman S, Dresler CM, Hajek P, Gilbert SJ, Targett DA, Strahs KR. Efficacy of a nicotine lozenge for smoking cessation. *Arch Intern Med* 2002;162(11):1267-76.

Nicotine patches: Available in two forms, 21mg/24 hour and 15mg/16 hour each with lower strength patches (14mg & 7mg 24 hour and 10mg & 5mg 16 hour) that are marketed for weaning. The odds ratios for long-term abstinence in the studies using 16 and 24-hour patches are the same (1.82). Only one study has directly compared the efficacy of these two patches and found no difference in self reported abstinence at 6 months. Full strength patches are more effective than their lower strength preparations in smokers of more than 10 cigarettes per day.⁵⁴ There is some evidence that the 24 hour patch may be more effective in relieving morning urges to smoke,^{55 56} although there is currently no evidence that this translates into higher abstinence rates. There is no advantage of slowly reducing the patch dose (OR=1.71 95% CI: 1.52-1.92) over stopping abruptly (OR=2.60 1.83-3.71). Two studies directly compared abrupt withdrawal and weaning and found no difference between the groups.⁵¹

There is some evidence for the use of even higher dose patches. Cochrane identified six studies comparing higher dose patches (44/42mg 24 hour and 25mg 16 hour) with their standard doses. The odds ratio from the pooled results showed a small but significant benefit of using a higher dose product (OR=1.21, 95% CI: 1.03-1.42).⁵¹

Long-term effectiveness of nicotine products relative to placebo ⁵¹			
Product	Odds ratio	95% confidence interval	NNT
Gum	1.66	1.51-1.81	17
Patch	1.84	1.65-2.06	17
Nasal Spray	2.35	1.63-3.38	8
Inhaler	2.14	1.44-3.18	13
Sublingual tablet or lozenge	2.05	1.62-2.59	13
Overall	1.77	1.66-1.88	17

Is there an advantage of combining NRT products?

The evidence shows a moderate advantage of using a combination of NRT products over single product use (OR=1.42, 95% CI: 1.14-1.76).⁵¹ Safety concerns with combining products are unfounded.

Is there an advantage of combining NRT with bupropion?

Combining bupropion and nicotine patch produced significantly greater abstinence rates compared to treatment with placebo (OR=4.86; 95% CI: 2.33-10.14).⁵⁷ The abstinence rates in this study for a combination of patch and bupropion were significantly greater than patch alone (OR=2.65, 95% CI: 1.58-4.45) but not compared to bupropion alone (OR=1.28 95% CI: 0.82-1.99).

Use of NRT in pregnancy

There is insufficient evidence that the use of NRT in pregnant women improves abstinence rates during pregnancy.⁴⁶ Expert opinion suggests that NRT can be used in pregnancy following a risk-benefit assessment. When assessing the risks and benefits, healthcare workers should balance the significant risks of continued smoking against the risks of providing NRT to aid a quit attempt.

Cigarette smoke delivers thousands of chemicals, some of which are known to be toxic to the developing fetus, such as carbon monoxide and cadmium.⁵⁸⁻⁶⁰ Carbon monoxide impairs oxygen availability to fetal haemoglobin, while nicotine may contribute to fetal ischaemia by its effects on the placental circulation. Animal studies suggest that nicotine has effects on the development of the fetal central nervous system. Nicotine may also play a role in sudden infant death syndrome (SIDS).⁶⁰ Experts have concluded that the abnormalities produced by various toxins in cigarette smoke are probably responsible for the numerous adverse outcomes associated with smoking in pregnancy and although nicotine might be implicated it is unlikely to be primarily responsible for these adverse outcomes.⁶⁰

Few studies that have investigated the safety of NRT use in human pregnancy, and all have small sample sizes.⁶¹⁻⁶³ However, none have demonstrated any significant adverse effects on the women or fetus. In one RCT of nicotine patch babies born to women who used the patch had significantly higher birth weights than those who used placebo.⁶⁴ This would suggest that nicotine is not the main cause of intra-uterine growth restriction. Even if nicotine is associated with adverse effects in pregnancy there are differences between NRT and smoking as methods of nicotine exposure.⁵⁸ For example, peak venous as well as arterial plasma nicotine concentrations in individuals using smokeless nicotine products are lower than those when smoking, and the rate of delivery from the currently available nicotine products is slower than that of cigarettes.⁶⁵ NRT delivers only nicotine, without the many other substances contained in tobacco smoke. Therefore, current expert opinion is that NRT can be considered safe to use in pregnancy following a risk: benefit assessment.^{60 58} In general NRT products, such as gum, lozenges, sublingual tablets and inhaler, should be used in preference to patches.^{60 66}

Regarding breastfeeding and NRT use, nicotine freely passes in and out of breast milk depending on the concentration of nicotine in maternal blood (in turn affected by cigarette consumption, frequency of breastfeeding and time between smoking and breastfeeding).⁶⁰ NRT typically provides less nicotine than tobacco smoke, and due to the relatively low oral bioavailability of nicotine⁶⁷ it is unlikely that this low level of exposure is harmful to the infant.⁵⁸ Second-hand tobacco smoke also has known adverse effects on young children, therefore risk: benefit assessment overwhelmingly favours the use of NRT to aid smoking cessation. The importance of continuing to breastfeed should be stressed.

Use of NRT in smokers with cardiovascular disease

The safety of NRT in patients with cardiovascular disease (CVD) is well documented.⁶⁸⁻⁷⁰ There is evidence of effectiveness of NRT in this group of patients,^{71 72} however in the past there has been some reluctance to provide NRT to this group. Nevertheless given the risks of continued smoking, experts agree that NRT should be made available to smokers with CVD who are motivated to stop.^{5 8 73 74}

Guidelines on the use of NRT in smokers with cardiovascular disease recommend that:⁷³ (1) NRT can be recommended to smokers with CVD, (2) NRT can be used with smokers who have experienced a serious cardiovascular event, or hospitalisation for a cardiovascular complaint in the previous two weeks, or where they suffer with uncontrolled hypertension, but that the consulting physician should be involved in the decision to recommend NRT, (3) dosages should not exceed manufacturers' recommended dose and patients should stop

NRT if they relapse back to smoking, and (4) wherever possible the provision of NRT should be accompanied with behavioural support. In addition, physicians dealing with acutely ill patients may consider using oral dosing forms rather than patches. There are a number of theoretical reasons for this: (a) nicotine levels can be reduced more rapidly in the event of problems;⁷⁵ (b) nicotine exposure produced by 24-hour patches is different from smoking; and (c) concurrent patch use and smoking may lead to nicotine levels higher than when smoking only.⁷⁶ However, more recently US data on 194 smokers admitted with acute coronary syndrome who received nicotine patches had no increase in short- or long-term mortality when compared to a matched sample who did not use patches.⁷⁷ This suggests that patches may also be appropriate to use in this group of patients.

Use of NRT in young smokers

There is also insufficient evidence to confirm the effectiveness of NRT in young people who want to stop smoking.⁷⁸ However, given that NRT is less harmful than smoking, safety concerns should not be a barrier to use. Expert opinion is that NRT may be considered for use in nicotine dependent adolescents who want to stop smoking.⁶⁶

Pharmacotherapies are not usually recommended for use in those under the age of 18, not so much because of specific safety concerns but usually due to lack of clinical data. There is no evidence to suggest that these medications are harmful. The UK Medicines and Healthcare products Regulatory Agency and Committee on Safety of Medicines also assessed NRT use in adolescents and made the following statement and recommendation:⁶⁶ *“...although data in children and adolescents were limited, there was evidence of efficacy and no indication that NRT used in this population would raise specific safety issues, particularly as their underlying health was likely to be much better than that in older smokers. In addition, when considering possible abuse of NRT by adolescents, the Working Group was of the opinion that there was no evidence for this. Consequently, they recommended that the lower age limit for NRT should be changed to include 12- to 18-year olds but that the product information should indicate that the data in this group were limited and that if treatment was required for longer than 12 weeks this should be discussed with a healthcare professional (eg a doctor, pharmacist or nurse).”*

Pre-treatment with NRT

There are now a number of studies that examine the technique of pre-treatment (or pre-loading) with NRT prior to quitting. The rationale for this is that providing nicotine from an alternative source may decrease the need to obtain nicotine from cigarettes and render cigarettes that are smoked less pleasurable. In a study that randomised 200 smokers to use active or placebo patches for two weeks prior to quitting those using active patches were more likely to be abstinent at follow-up (22% vs. 12%) although this did not reach statistical significance (OR=2.07, 95% CI: 0.96-4.45).⁵¹ There appear to be no safety concerns when NRT is used in this way.^{51 79}

Long-term use

Nicotine replacement therapy is generally used for up to three months. Most users will not need it for longer, although a small number do. Of those who start on NRT some 5% may continue to use it for up to a year.⁸⁰ Products that deliver nicotine faster seem to have a greater chance of long-term use (e.g. percentage of clients using NRT for a year or more by product are: patch (2%), sublingual tablet (7%), lozenge (8%), inhalator (8%), chewing gum (9%), nasal spray (13%).⁸⁰ Furthermore the clients that use NRT for longer are typically more highly dependent smokers and long-term NRT may be necessary to maintain long-term abstinence. There are no safety concerns regarding long-term use of NRT; deciding factors are more likely to be financial, or the client's worries about using it long term.

Using NRT to reduce cigarette consumption prior to quitting (NRT aided reduction prior to quitting)

NRT is currently being marketed to help people reduce the number of cigarettes smoked before quitting. This strategy is not for everyone, but may be useful for people who are not ready to quit right now. If using this strategy the person should aim to *reduce consumption by at least 50% in the first 6 weeks*, and then over the next 18 weeks this reduction can either be maintained, they can continue to reduce or quit completely. NRT should be used as normal once the quit attempt has started. The suggested time periods in which they should reduce consumption by at least 50% is 6 weeks and they should aim to stop smoking completely within 6 months.⁸¹

If a reduction of at least 50% is not achieved in the first 6 weeks then little may be gained in continuing this treatment strategy.⁸¹ At the present time only Nicorette® gum and inhaler have been licensed for this method. However there is no reason why a lozenge, sublingual tablet, or gum produced by other manufacturers could not be used.⁸¹

There are no safety concerns when using this strategy in a general population of people who smoke. However, there is no evidence to recommend its use in those with unstable cardiovascular disease or in those who have suffered a recent cardiac event, or in pregnant women who smoke. It should be noted that decreasing smoking without quitting might not reduce the risks of smoking.

Summary

Nicotine replacement therapy is safe and effective in aiding smoking cessation. There is evidence to support its use in combination with other NRT products, and its use in cutting down prior to quitting. NRT is safe to use in smokers with a history of cardiovascular disease, although consultation with a physician should occur if the smoker has suffered a recent (within the past 2 weeks) cardiovascular event or has unstable cardiac disease. Robust evidence is lacking for the effectiveness of NRT use in adolescents. However given that there are no safety concerns it can be considered for use in this group. There is no strong evidence for the effectiveness of NRT in pregnant women who smoke. It is also unknown to what degree nicotine adversely affects the pregnancy and fetus. However, in comparison with continued smoking NRT is safer. Therefore the use of NRT in pregnancy may be considered, but it is recommended that a risk benefit assessment be undertaken.

Strength of evidence

1++

Evidence statement

There is good evidence from randomised controlled trials that nicotine replacement therapy improves 6-month abstinence rates.

The evidence for bupropion

Bupropion

Bupropion, an atypical antidepressant, was the first non-nicotine treatment specifically licensed for smoking cessation. Unlike NRT (and varenicline) this medication was not specifically designed for smoking cessation. Its action in helping people to stop smoking is independent of its antidepressant effects and works in those without a history of depression. The precise mechanism of action for aiding smoking cessation is unknown, but it is thought to act via its ability to inhibit the neuronal reuptake of dopamine and noradrenaline, both important in nicotine dependence and withdrawal. It may also have some action as a non-competitive inhibitor of the nicotinic acetylcholine receptor, and perhaps by way of its effect on serotonin reuptake.

Efficacy of bupropion

Bupropion is effective in aiding smoking cessation. The Cochrane Review pooled the results of 31 studies, with more than 9000 smokers, which compared the efficacy of bupropion versus placebo or no treatment.⁸² The meta-analysis showed that compared to control, bupropion approximately doubled long-term abstinence rates (OR=1.94; 95%CI: 1.72-2.19). Approximately 1 in 13 people receiving bupropion will stop smoking for at least 6 months who would not have otherwise done so. Another randomised placebo controlled trial comparing bupropion with placebo in 509 smokers that has not been included in the Cochrane Review shows similar outcomes (6-month CO validated continuous abstinence rates were 25% for bupropion and 13% for placebo, OR=2.2; 95% CI: 1.3-3.6).⁸³ Furthermore bupropion is effective for both men and women,⁸⁴ and in those with stable cardiovascular disease⁸⁵ and mild to moderate COPD.^{86 87} However studies to date have not shown any benefit of using bupropion to help adolescents to quit,^{88 89} or in preventing.^{90 91}

How does bupropion compare to other medications?

Evidence that bupropion is more or less effective than NRT or nortriptyline is limited.^{82 92} However, evidence from three randomised controlled trials suggests that it is less effective than varenicline.

Is bupropion a safe medication to use?

Bupropion is a safe treatment when used correctly.⁹³ There are contraindications to be checked when prescribing this medication. In addition some precautions need to be considered. Smokers with a predisposition to seizures should not take bupropion unless the benefit of smoking cessation outweighs any risks associated with using the medication. Bupropion however has been found safe to use in smokers with stable cardiovascular disease, without adverse effects on blood pressure or heart rate.

Summary	Bupropion is safe and effective in aiding smoking cessation.	
Strength of evidence	1++	Evidence statement There is good evidence from randomised controlled trials that bupropion improves 6-month abstinence rates.

The evidence for nortriptyline

Nortriptyline

Nortriptyline is a tricyclic antidepressant that has been shown to be as effective as bupropion and NRT for smoking cessation. Its action in helping people to stop smoking is independent of its antidepressant effects and works in those without a history of depression. Nortriptyline is currently regarded as a second-line therapy by some smoking cessation guidelines,⁸ and not recommended at all by others.⁹⁴

Efficacy of nortriptyline

The Cochrane meta-analysis (of six RCTs) shows an advantage of using nortriptyline over placebo in assisting smokers to abstain long-term (OR=2.34; 95% CI: 1.61 - 3.41). This represents an effect size of 10% (95%CI: 6-15%), and number needed to treat of 10.⁸² These findings are replicated in two other systematic reviews.^{95,96} One of these suggests that nortriptyline should be a first-line aid to help smokers quit.⁹⁶ Their reasoning for this is that (1) nortriptyline appears to be as efficacious as bupropion; (2) data from the six randomised controlled trials show that it is safe and well tolerated; and (3) it is inexpensive. The other review⁹⁵ agrees that nortriptyline is an effective medication for smoking cessation, and notes the advantages of this medication, i.e. it is inexpensive and therapeutic blood levels can be monitored. However they raise some concerns regarding its safety. The first is that although the nortriptyline studies show that it is safe it has only been tested in approximately 500 people. This compares to some 4,000 participants in bupropion studies and 35,000 in NRT studies. The second is that there is good data regarding adverse events when nortriptyline is used to treat depressed patients, showing that it can produce significant adverse events especially when used in higher doses. Nortriptyline has a number of common side effects, for example dry mouth, light-headedness, shakiness, and blurred vision. Urinary retention, constipation, sexual difficulties, and seizure risk are also reported. In addition to these, an overdose of nortriptyline is commonly fatal.

Summary	Nortriptyline is safe and effective in aiding smoking cessation. However consideration needs to be given to the contraindications and side effects associated with this medication. There remains some debate as to whether this drug should be listed as a first or second line treatment for smoking cessation.	
Strength of evidence	1++	Evidence statement There is good evidence from randomised controlled trials that nortriptyline improves 6-month abstinence rates.

The evidence for varenicline

Varenicline

Varenicline is the latest medication to be licensed for smoking cessation and was developed especially for this indication. A nicotinic acetylcholine receptor (nAChR) partial agonist it also possesses antagonist properties, competing with nicotine for the same receptor site. The main receptor targeted is the alpha4 beta2 subtype but it also acts as a full agonist at alpha7 neuronal nicotine receptors.⁹⁷ The agonist effect on the nAChR produces dopamine release, but less than that seen with nicotine.

Varenicline is effective in aiding smoking cessation. It approximately triples the chances of long-term abstinence.⁹⁸ Its mode of action in aiding smoking cessation is primarily by reducing the severity of tobacco withdrawal symptoms (via its agonist effects) but it also reduces the rewarding properties of nicotine (via its antagonistic effects). The later effect may be beneficial in extinguishing smoking behaviour for the week it is used prior to quitting and helping to protect against complete relapse if a smoker lapses.

Efficacy of varenicline

To date the efficacy of varenicline for smoking cessation has been examined in five published placebo controlled trials, with approximately 5000 smokers of 10 or more cigarettes per day and aged between 18 and 65.⁹⁸ Pooling the results of these studies show the superiority of varenicline over placebo in assisting long-term abstinence (OR=3.22; 95% CI: 2.43-4.27). This represents an approximate tripling of 1-year abstinence rates and a NNT of 7.

One study investigated the benefit of extended (24 vs. 12 weeks) varenicline use in people that were abstinent at the end of the 3-month treatment period. There was a small but significant benefit of using varenicline for the extended period.⁹⁹

How does varenicline compare to other medications?

Three studies have found it to be more effective than bupropion (OR=1.66; 95% CI: 1.28-2.16).⁹⁸ Indirect comparisons suggest that it is also more effective than NRT (OR=1.66; 95% CI: 1.17-2.36).⁹² No comparisons (direct or indirect) have yet been made with nortriptyline.

Safety

Varenicline has demonstrated a good safety profile so far. However, adverse event data from general use in the population are not yet available. There are no clinically significant drug interactions. It has a half-life of approximately 24 hours and is not extensively metabolised with 92% excreted in urine unchanged. No significant differences in pharmacokinetics by sex, age, smoking status, ethnicity, or use of other

medications has been observed. The most common side effect associated with this medication is nausea and this appears to be dose dependent. The titration period prior to quitting helps limit the occurrence of nausea.

Summary	Varenicline is safe and effective in aiding smoking cessation.		
Strength of evidence	1++	Evidence statement	There is good evidence from randomised controlled trials that varenicline improves 6-month abstinence rates.

The evidence for smoking cessation interventions in young people

Young people

It is a misconception to believe that young smokers are not addicted or that they do not want to quit. Tobacco dependence can develop early in an individual's smoking career¹⁰⁰ and many experience symptoms of tobacco withdrawal on smoking cessation.¹⁰¹ Until recently most smoking cessation interventions have focussed on adult smokers and interventions for adolescents have typically been of a preventative nature. It is now generally acknowledged that interventions aimed at young smokers need to be different than those developed for adults given the differences in lifestyle and attitudes, for example.

A recent systematic review undertaken by the Cochrane collaboration⁷⁸ identified only 15 randomised controlled trials that examined smoking cessation interventions in a total of 3,605 young (<20 years old) smokers. Two studies examined interventions based on the Stages of Change model^{102 103} which essentially delivered material appropriate to the young smokers' stage of change and compared results to a control group (health education). Both these studies reported 30-day point prevalence abstinence, neither attempted to validate self-reports. At 12 months more participants in the intervention groups had stopped smoking compared to controls (OR=1.70; 95% CI: 1.25-2.33).

The remaining studies assessed in this review all utilised interventions that aimed to enhance motivation (e.g. motivational interviewing), cognitive behavioural therapy, and an older study based the intervention on an educational approach (facts, scare tactics and attitudinal).¹⁰⁴ The combined results of the three trials that used motivational interviewing (MI) show a positive outcome (OR=2.05; 95% CI: 1.10-3.80), however the authors urge caution when interpreting the results as the studies included other behavioural components and not MI alone.

The Not on Tobacco intervention deserves mention.¹⁰⁵ This study recruited a total of 673 young smokers from 84 schools across three American states (Florida, North Carolina and West Virginia). The intervention involved small same-gender groups that met for 50 minutes once a week and covered nicotine dependence, health consequences of smoking, preparing for quitting, dealing with urges and cravings, and general healthy lifestyle topics. The control groups received brief advice. Although at each state level the intervention was not effective when compared to control groups, the pooled results do not rule out an effect (OR=1.87; 95% CI: 1.00-3.50). However, it is important to note that their outcome measure was one day or more of abstinence at 6-month follow-up, and it needs to be asked if this measure is meaningful. We identified one further abstract whose results from an Alabama arm are similar to those described above and therefore are unlikely to change the results of the meta-analysis.¹⁰⁶

Pharmacotherapies are discussed in the previous sections. None of the studies to date have shown these medications (NRT and bupropion) to be effective in helping young people to stop smoking.

One New Zealand study targeted recruitment at older adolescents (16yrs+) and young adults (although there was no upper age limit) for a text message mobile phone-based smoking cessation intervention.¹⁰⁷ This was a 6-month programme of regular personalised messages including cessation advice, support and distraction. The intervention was found to double self-reported quit rates at 6 weeks. However the 6 months results were less impressive due to methodological problems leading to an increase in quit rates in the control group and a differential loss to follow-up between intervention and control groups. In an analysis of results for 16-19 year-olds, those in the intervention group were more likely to have quit at 6 weeks (OR=2.92 95% CI 1.95, 4.39) and 12 weeks (OR=1.72 95% CI 1.28, 2.31), but not at 24 weeks (OR=0.93 95% CI 0.70, 1.22).

<p>Summary</p>	<p>Overall there are still few data that confirm the effectiveness of interventions specifically aimed at helping young people quit smoking. Although some intervention models may show promise there is insufficient evidence to recommend that any of these be integrated into standard practice. There is also insufficient evidence to recommend that pharmacotherapies be provided to all young smokers that want to quit. The US guidelines recommend that healthcare professionals provide advice to stop smoking to young smokers and assist those interested in stopping. Given the lack of clear evidence on specific interventions for young smokers it is recommended that interventions that have efficacy in helping adult smokers be used – this means interventions that use multi-session behavioural support.</p>	
<p>Strength of evidence 1+</p>	<p>Evidence statement</p>	<ol style="list-style-type: none"> 1. There is currently inconsistent evidence concerning whether behavioural interventions aimed specifically at smoking cessation in young people improve continuous 6-month abstinence rates. However results from randomised controlled trials suggest that behavioural interventions show promise and further research is warranted. 2. There is insufficient evidence that the use of pharmacotherapies in young people improves continuous 6-month abstinence rates.

The evidence for smoking cessation interventions in indigenous Australians

Indigenous Australians

Data from 2004/05 show that 50% of the indigenous Australian adult population smoke on a daily basis (51% of men and 49% of women).² Across all age groups smoking prevalence is highest in indigenous Australians than any other ethnic group,² and smoking initiation is at a younger age.¹⁰⁸ Furthermore smoking prevalence amongst indigenous Australians has not declined over time at the same rate as in other Australian ethnic groups. Indigenous Australians die earlier than other Australians, and suffer considerable smoking related ill health. In other priority groups such as pregnant women who smoke, smoking prevalence in indigenous Australians is at least twice that of other Australian women.^{109 110} These high rates of smoking, combined with the poorer health outcomes associated with smoking in this population make smoking cessation a priority.

Many of the reasons for why indigenous Australians smoke are similar to that of the general population. However there are others that need to be considered including the effects of colonisation, dispossession, socio-economic status, and cultural beliefs.¹¹¹ There is also some evidence to suggest that the knowledge of the harm associated with smoking may be less in some groups of indigenous Australians.¹¹² There are also cited differences in the proportion of smokers who are ready to quit, make a quit attempt, and who achieve long-term abstinence. These proportions are all lower in indigenous Australian people who smoke compared to other groups. Recent Australian research has suggested that cessation rates may be lower among indigenous Australians because of multiple life stressors experienced by this group.¹¹³

In a review by Ivers (2001) it is noted that there is little research regarding smoking cessation interventions in this population. Since this review few other data for smoking cessation interventions in indigenous Australians have been published. This is highlighted in a systematic review of tobacco interventions for Indigenous Australians published in 2003.¹¹⁴ None of the four published studies identified in this review measured smoking cessation as an outcome.

In further work by Ivers a study (non-randomised) was undertaken to assess the use of free nicotine patches by Indigenous people in addition to a brief smoking cessation intervention. It involved 111 indigenous smokers, but only 40 of these people chose to use the patches in free nicotine patches, the remainder opted for the brief intervention only. At 6 months more of the patch users had quit smoking (10% CO validated) compared to those who received the brief intervention only (1% CO validated).¹¹⁵ The cessation rates achieved are similar to that seen in other populations.

A recently published Australian pre/post study assessed the effect of community tobacco interventions in Aboriginal communities. The interventions were mainly tobacco control related activities (e.g. sports sponsorship, health promotion campaigns) but did involve training healthcare professionals in the delivery of smoking cessation advice. The interventions did result in a decrease in tobacco consumption in one community compared to a control community, but had no effect on smoking prevalence.¹¹⁶

Ivers suggests an evidence based approach to smoking cessation interventions for indigenous Australians and sees no reason as to why interventions that are effective in a general population (e.g. brief advice, NRT, bupropion, and behavioural support) should not be effective in indigenous Australians who smoke. These interventions should be used as a starting point, however it needs to be acknowledged that interventions based on mainstream approaches, and costs of others (e.g. pharmacotherapy) may make these inaccessible to many people in this group.^{111 117} Factors highlighted above, such as reasons why indigenous Australians smoke, need to be addressed when designing smoking cessation programmes.

Summary	There are few studies assessing the outcome of smoking cessation interventions for indigenous Australian smokers. There is no evidence to support the assertion that the effectiveness of interventions known to work in the general population such as individual or group based behavioural support and pharmacotherapies should be any different in indigenous Australians. Though the findings of various reports suggest these interventions must be acceptable to these people if they are to engage and fully benefit.	
Strength of evidence	2-	Evidence statement There is insufficient evidence on smoking cessation interventions for indigenous Australians.

The evidence for smoking cessation interventions in pregnant women

Pregnant women

Smoking during pregnancy poses risks to the pregnancy (e.g. premature delivery, spontaneous abortion, placenta previa, placental abruption), the newborn (e.g. low-birth weight) and the infant (sudden infant death syndrome, otitis media, learning difficulties).^{118 119} The proportion of pregnant women that continue to smoke throughout pregnancy has decreased in line with the drop in smoking prevalence in the general population.¹²⁰ However, smoking rates in indigenous Australian women remain high and are at least twice that of other Australian women.^{109 110 121} While around 20% of women smokers stop smoking when they become pregnant, they tend to be less dependent smokers and with better resources to help them quit. Conversely, women that continue to smoke throughout their pregnancy are typically socially disadvantaged with less support, are more likely to have a partner who smokes and are generally young.¹²² However, the majority of these women would like to stop smoking.^{123 124} Helping pregnant women to stop smoking benefits both mother and child. Cessation efforts should be encouraged in all women who smoke of child-bearing age and at anytime throughout the pregnancy, from as early in the pregnancy as possible and into the post-partum period.¹²⁵

Smoking cessation interventions

There is modest evidence for the effectiveness of interventions among pregnant women who smoke, resulting in a 5% (95% confidence interval 4-7%) increase in absolute long-term success above that of control groups (mostly usual care).¹²⁰ The most successful interventions use elements of cognitive behavioural therapy (effect size 5%; 95% CI: 3-7%). Others using the Stages of Change model have not demonstrated any efficacy in aiding smoking cessation in pregnant women^{126 127} or their partners.¹²⁸ Another well conducted randomised controlled trial failed to demonstrate the benefit of a home-based motivational interviewing intervention.¹²⁹ A cluster-randomised controlled trial of self-help materials also failed to show any efficacy in helping pregnant women to quit smoking.¹³⁰

Possible reasons for the lack of efficacy in some studies are that the interventions are not intensive enough for this population of smokers, midwives could not deliver the intervention effectively in the time available to them, or other barriers, such as fear of damaging their relationship with their clients, prevented them from intervening effectively. There is also some evidence of deficits in knowledge of smoking cessation interventions among maternity staff.¹³¹ However, all midwives should be providing brief advice to stop smoking, although there is evidence suggesting that few provide this advice.¹²⁴ There is some evidence that brief advice from midwives/nurses and doctors can improve cessation rates in this group of smokers.^{132 133} Provision of advice to stop smoking is not associated with increased stress in pregnant women who smoke.¹³⁴ This may be contrary to the belief of some healthcare professionals.

There is limited evidence of the effectiveness of NRT to help pregnant women stop smoking. The safety of NRT use in pregnancy is discussed in the section on NRT.

A small number of high quality studies have tested programmes aimed at reducing relapse to smoking in the post-partum period but none have shown any benefit. However, most interventions have focused on the traditional skills-based approach to preventing relapse (see relapse prevention section) and it may be that this approach on its own is not enough.³²

Summary	There is evidence to support the effectiveness of interventions to help pregnant women to smoke, particularly those using CBT. There is insufficient evidence on the use of NRT in pregnancy, although it is likely to assist some women and to be less dangerous than continuing to smoke in pregnancy for those women who are unable to stop without it.	
Strength of evidence 1++	Evidence statements	<ol style="list-style-type: none"> 1. There is evidence from randomised controlled trials that multi-session behavioural interventions to help pregnant women stop smoking improve 6-month abstinence rates. 2. There is insufficient evidence on whether NRT improves 6-month abstinence rates in pregnant women.

The evidence for smoking cessation interventions in hospitalised smokers

Hospitalised smokers

Smoking is directly responsible for many hospital admissions, medical procedures and surgical operations. Being admitted to hospital brings smokers into direct contact with healthcare professionals who can advise on giving up smoking. The consequences of smoking are directly relevant, the smokefree environment provides few smoking cues and for some there will be less desire to smoke when feeling ill. Hospitalisation therefore is an important opportunity to assist people to stop smoking.

To be effective, smoking cessation interventions (that is interventions aimed at helping smokers to stop as opposed to brief advice to stop – covered in Brief Advice section) delivered within hospital settings need to be more than merely a short one-off session delivered by a busy healthcare professional. A Cochrane review⁷² identified 16 studies and categorised them according to levels of intensity as follows: (1) single contact in hospital of less than 15 minutes duration; (2) one or more contacts each of more than 15 minutes duration; (3) any number of contacts in hospital plus outpatient follow-up of less than one month; and (4) any number of contacts in hospital with at least one month of follow-up as an outpatient. Only the last category showed a significant effect, increasing six months abstinence by 9% (95% CI: 6-12%) with an odds ratio of 1.82 (95% CI: 1.49-2.22) compared to a control group. Interventions were largely effective regardless of the use of NRT; however, the results are compatible with other data showing that adding NRT increases quit rates.

The studies included in the Cochrane review⁷² showed a number of different ways to deliver a hospital based smoking cessation intervention. One that relied on cardiac rehabilitation nurses delivering a single session had no significant effect on helping patients give up smoking after myocardial infarction.¹³⁵ This outcome is consistent with the need for smoking cessation interventions in this group to include outpatient follow-up. This may be achieved by having a dedicated hospital based smoking cessation specialist who can see people who smoke as inpatients and outpatients, or having systems which allow seamless referral of inpatients to community based smoking cessation interventions (e.g. Quitlines, smoking cessation counsellors).

In the past there has been concern regarding the use of NRT in smokers with a history of cardiovascular disease⁶⁹ but NRT is generally safe to use in these smokers.⁷³ This is discussed in more detail in the section on NRT.

Summary There is evidence to support hospital-based cessation services, however, to be effective inpatient smoking cessation programmes need to include follow-up for at least a month post-discharge.

Strength of evidence 1++	Evidence statement There is good evidence from randomised controlled trials that high intensity behavioural interventions that include at least one month of follow-up contact improve 6-month abstinence rates in hospitalised patients.
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The evidence for smoking cessation interventions in pre-operative smokers

Pre-operative smokers

Complications following surgery are not uncommon, especially following major procedures.¹³⁶ Smokers have an increased risk of cardio-pulmonary complications, poorer wound and bone healing and a greater chance of being transferred to other hospital departments and a longer length of hospital stay than non-smokers.¹³⁷ The risk of developing complications is dependent on both the acute and chronic effects of smoking. The pre-operative period is thus an opportunity to give advice and provide support to stop, not just for the immediate peri-operative period but also permanently.

The available evidence confirms that interventions aimed at assisting smokers to stop prior to surgery are effective.¹³⁷ Preoperative smoking cessation decreases post-operative risks such as wound infection, delayed wound healing, pulmonary and cardiac complications.¹³⁶

The timing of cessation appears to be important in reducing the risk of post-operative complications. While difficult to achieve in acute situations, stopping smoking at least eight weeks prior to surgery appears to be optimal, and is feasible for elective surgery where waiting lists are often long

There is currently a lack of evidence for the efficacy of pre-operative smoking cessation interventions on long-term abstinence. Cessation interventions that are effective in the general population should be at least as effective in this group. Nevertheless, smokers with a smoking related disease may be a more dependent group, and some who manage to stop pre-operatively may have only committed to abstain for a short period of time (in the same way that some women stop when pregnant then start smoking again).

Summary	All smokers should be encouraged to stop smoking, and supported in their attempt prior to surgery. While any time is likely to be beneficial in comparison to continued smoking, the earlier they stop the lower the post-operative risk is likely to be. There is insufficient evidence that temporary abstinence increases the risk of complications.	
Strength of evidence	Evidence statement	There is evidence from randomised controlled trials that pre-operative smoking cessation interventions improve short-term abstinence rates. However there is insufficient evidence to draw any conclusion regarding 6-month abstinence.

The evidence for smoking cessation interventions in people with mental illness

Mental health service users

Tobacco use among people with mental illness is higher than in the general population.¹³⁸ For example, the odds of being a smoker if diagnosed with schizophrenia is six times that of people without schizophrenia.¹³⁹

Encouraging people with a mental illness to stop smoking is often overlooked, not seen as an important intervention or even resisted by health professionals.¹⁴⁰ Smokers with a mental illness typically have lower abstinence rates than those without psychiatric comorbidities.¹⁴¹ A number of differences in demographics, dependence and smoking history between smokers in the general population and those with mental illnesses may account for this. For example, people with a mental illness tend to be more dependent smokers^{139 142-144} and have a higher cigarette consumption.^{139 145}

There may also be resistance from healthcare professionals working with people with mental illnesses to promote quitting. Reasons include a lack of confidence that quitting will be successful. For instance, depressed mood, a common feature of much mental illness is a predictor of relapse.¹⁴⁶ Furthermore, there are potential risks of exacerbating mental illness when smokers quit. Depressed mood is a tobacco withdrawal symptom¹⁴⁷ and major depressive episodes following cessation have been reported.¹⁴⁸

One of the hypotheses for why people with mental illness have higher rates of smoking than the general population is that smoking may alleviate some psychiatric symptoms.¹⁴⁹ However, stopping smoking improves some psychiatric symptoms such as anxiety and stress,^{142 150} depressive symptoms,¹⁵¹ and can lead to a general improvement in mental health.¹⁵² Smoking may also reduce the side effects of some neuroleptic medications.¹³⁸ Conversely it has also been reported that nicotine may improve cognitive function,¹³⁸ but the evidence for this is not strong.

There are limited data regarding the effectiveness of smoking cessation interventions in smokers with mental illness. Despite this, the US guidelines recommend that patients with mental illness be offered treatment that is of proven effectiveness in the general population.⁸ These recommendations are echoed in a recent systematic review.¹⁵³

There is limited evidence on who should deliver smoking cessation treatment to people with mental illness, however, it has been suggested that cessation treatment delivered in an integrated approach (e.g. involving all healthcare professionals who provide care) may be more likely to engage smokers and encourage compliance with medication.¹⁵⁴

Pharmacotherapy

There is no doubt that pharmacotherapies increase long-term success rates. While there are limited data from randomised controlled trials regarding the use of pharmacotherapies in smokers with mental illness, the US guidelines suggest that bupropion and nortriptyline be considered for treating smokers with a history of depression.⁸

It is likely that smokers with mental illness may benefit from more aggressive pharmacological treatment including higher doses and longer length of treatment.^{155 156} Bupropion has been safely used for smoking cessation in people with schizophrenia, although there are insufficient data on long-term efficacy.^{157 158} It should be noted that caution needs to be applied when using bupropion concomitantly with other psychoactive medications such anti-depressants as there is an increased risk of seizure.

Effect of stopping smoking on mood and medication side effects

Smoking tobacco causes induction of the liver enzyme cytochrome P450 (CYP1A1, CYP1A2).¹⁵⁹ This is largely an effect of the polycyclic aromatic hydrocarbons present in tobacco smoke, not an effect of nicotine. CYP1A2 is responsible for the breakdown of a number of medications, so in a smoker medications metabolised by this enzyme are metabolised faster. On stopping smoking these enzymes return to a normal level of activity, so that a number of medications are metabolised more slowly and may need a dosage adjustment.¹⁵⁹

Summary	There are few randomised controlled trials assessing the outcome of smoking cessation interventions for smokers with mental illness. Many studies still have methodological problems such as small sample size. Smokers with mental illness are typically highly dependent smokers and find stopping smoking very difficult. Therefore it is likely that they will benefit from more intensive smoking cessation interventions. These should include multi-session behavioural support and pharmacotherapy. Combination pharmacotherapy may be associated with a superior outcome. Most smokers will not experience a worsening in the symptoms of their mental illness when they stop smoking. In fact in some cases their symptoms may improve. Components of tobacco smoke cause induction of some liver enzymes. Smoking cessation may therefore affect the metabolism of a number of medications.	
Strength of evidence	1+	Evidence statement There is currently inconsistent evidence concerning whether smoking cessation services aimed specifically at smoking cessation in people with mental illness improve continuous 6-month abstinence rates.

The evidence for smoking cessation interventions in other addictions

Addiction service users

In international research it is often reported that drug users who smoke tend to have started smoking at a younger age, be more dependent, more likely to be heavy smokers, have more cognitive deficits and more medical problems, and therefore may be more likely to experience greater difficulty quitting.¹⁶⁰ However, a higher smoking prevalence does not mean that people with substance use disorders are less likely to quit smoking. For example, people with alcohol dependence, despite having higher nicotine dependence, do not appear to have more difficulty quitting on a given attempt than smokers without alcohol problems.¹⁶¹ People who use addiction services should have access to smoking cessation services that combine multi-session support and pharmacotherapy.

Smoking cessation is often not included in substance abuse treatment programmes, for reasons such as reported low success rates, the less immediate negative consequences of smoking compared to other drugs, and drug substitution with tobacco. Clinicians and patients often believe that people with multiple substance use disorders should only tackle one addiction at a time. However admission for treatment of other dependencies is an opportune time to address tobacco dependence. Furthermore, it has been suggested that it would be best to provide a consistent message and to treat the underlying addiction with quitting all dangerous substances.¹⁶⁰

Two major reviews of smoking cessation treatment with addiction service users have been reported.^{160 162} Overall there is evidence that smoking cessation interventions can be effective at increasing short-term quit rates in people with substance use disorders.

Smoking and drinking alcohol are co-cues and use of one can trigger cravings for the other. Smoking cessation uncommonly precipitates a relapse of substance use disorder^{163 164} but this is not a sufficient reason to discourage a person from trying to stop smoking. A more appropriate response would be to support the quit attempt and provide close monitoring. People with substance use disorders are likely to benefit from more intensive smoking cessation interventions that include multi-session contact and pharmacotherapy.

Summary	Overall there is evidence that smoking cessation interventions can be effective at increasing short-term quit rates in people with substance use disorders. However, effectiveness of interventions in aiding long-term abstinence is inconsistent.	
Strength of evidence	1+	Evidence statement There is inconsistent evidence on smoking cessation interventions for those with substance use disorders to draw any conclusion.

The evidence for repeated quit attempts

People who make repeated attempts to stop smoking

Unfortunately most smokers who attempt to stop smoking will not achieve long-term abstinence.¹⁶⁵ Furthermore, a failed quit attempt, especially if relapse occurs shortly after the quit day, may predict future failed attempts.¹⁶⁶ However, previous failure is likely to indicate greater tobacco dependence and potentially other factors, such as a history of mental illness, that are negative predictors of abstinence.¹⁶⁷ It is also important to note that there are many other factors associated with a failed quit attempt, such as stress, social cues, and urges to smoke.

It is a fallacy to believe that repeat quitters would not be interested in a repeat quit attempt. Fu et al followed up 951 patients six months after they had received a prescription for smoking cessation treatment.¹⁶⁵ Although two thirds had relapsed 65% said that they would like to make another quit attempt in the next month. Furthermore, 64% stated that they wanted to quit using a combination of pharmacotherapy and behavioural support.

Most of the studies investigating the treatment of repeat quitters have specifically examined the use of pharmacotherapies.¹⁶⁸ Some studies investigating the use of pharmacotherapies in repeat quitters found little to no effect on long-term cessation.¹⁶⁹⁻¹⁷² One study investigated the use of telephone support for repeat quitters, but failed to show a benefit.¹⁷³ However, other studies demonstrate that pharmacotherapies such as bupropion and NRT have equally good outcomes on active treatment despite previous failure with pharmacotherapies.^{166 174 175}

Lessons can be learned from previous quit attempts, and factors associated with a failed attempt should be addressed at re-treatment. It is likely that a more intensive treatment is required on a subsequent attempt. Regarding pharmacotherapy, client preference, ease of use, and contraindications should guide treatment selection.¹⁶⁶

There is some debate regarding the length of time that a client should be made to wait between quit attempts. For example, guidance issued by the NHS National Institute of Clinical Excellence (NICE) suggested that the NHS would not normally fund another quit attempt within six months of a quit attempt.¹⁷⁶ However, there are only limited data to support this cut-off. In fact, given that there is some evidence that the majority of successful quit attempts are unplanned or spontaneous, smokers should be enabled to quit whenever they are ready.¹⁷⁷

Summary	People who relapse should be encouraged to return for treatment. However, repeat treatment may need to address factors such as high nicotine dependence. Bupropion and NRT can be used again in people that have tried pharmacotherapies in the past but failed. Treatment choice should be guided by learning from prior failures, and individual preference. It is likely that a more intensive treatment is required on a subsequent attempt.	
Strength of evidence	1++	Evidence statement <ol style="list-style-type: none"> 1. There is evidence from randomised controlled trials that bupropion and NRT can be used successfully in people who have tried pharmacotherapies in the past but failed. 2. There is insufficient evidence to recommend a minimum time between quit attempts.

The evidence for relapse prevention

Relapse prevention

Smoking is a chronic relapsing condition. Given the high relapse rates following short-term smoking cessation, interventions aimed at helping people to remain abstinent long-term are extremely important. Unfortunately the evidence for the effectiveness of these interventions is lacking. Typically relapse prevention programmes have employed a skills-based approach where by recent ex-smokers are taught to recognise ‘high risk’ situations (such as when drinking alcohol) and then to learn skills to resolve the desire to smoke. Other programmes have utilised cue exposure techniques, aversive smoking, exercise, extending the duration of the treatment period and long-term pharmacological treatment.

The Cochrane review identified a total of 40 studies that met its inclusion criteria.³² Pooling the results of those studies that reported long-term follow-up has so far not provided any evidence for the effectiveness of relapse prevention programmes.³²

Although there is little positive news there are a number of factors that need to be taken into consideration. Many of the studies had an inadequate sample size to detect a difference between the intervention and control groups. There is lack of originality in the interventions tested with most focusing on the skills-based approach. The possibility that this approach does not work must be considered. Alternatively, the approach may work but the skills are not being taught effectively. Finally, many of the interventions were brief and one-off. Given the nature of tobacco dependence this may not be enough. If the goal is to increase the number of recent ex-smokers abstaining for a year or more innovative approaches to relapse prevention are needed. Suggestions include maintenance of motivation to remain abstinent, maintaining the awareness of the hazards of a lapse and how it can lead to complete relapse, the use of NRT as needed, ongoing social support, and contingency contracting.

Summary	Despite a number of studies, there is no conclusive evidence for the efficacy of specific interventions for preventing relapse.	
Strength of evidence	1++	Evidence statement There is inconsistent evidence on relapse prevention interventions to draw any conclusion.

The evidence for other pharmacotherapies

Other pharmacotherapies

There are a number of other products that have been or are currently used for smoking cessation. Some have been subjected to randomised controlled trials and others have not been sufficiently studied. Some of these are summarised below. Brief evidence statements are provided in square brackets in the headings.

Clonidine [evidence of effectiveness but not routinely used]

Clonidine is an alpha-2 adrenoceptor agonist that reduces noradrenaline release, and is generally used as an anti-hypertensive and for the prevention of recurrent migraine. Clonidine has been used to treat opioid and alcohol dependence,^{178 179} and has been shown to reduce the symptoms of tobacco withdrawal, and increase abstinence rates.¹⁸⁰ A Cochrane review of clonidine in smoking cessation identified 21 studies, many with only short-term follow-up.¹⁸⁰ With six studies meeting the inclusion criteria the pooled results showed an odds ratio of 1.89 (95% CI: 1.30 – 2.74). However, despite this positive result, because of its extensive adverse effect profile it is not recommended for use.

Anxiolytics [evidence of no effectiveness]

Medications used for treating anxiety have been examined as possible smoking cessation aids. A Cochrane Review of anxiolytics for smoking cessation showed no evidence of effectiveness of any of these medications.¹⁸¹

Nicobrevin [insufficient evidence of effectiveness]

Nicobrevin is a 'natural' product developed in Germany in the late 1960's and marketed for smoking cessation since then in many countries. Each of four main ingredients is alleged (without any supporting evidence) to facilitate smoking cessation: (1) menthyl valerate, to help via its sedative and anxiolytic effects, (2) quinine, to relieve withdrawal, (3) camphor and (4) eucalyptus oil, to relieve 'airway symptoms'. The Cochrane review of Nicobrevin¹⁸² identified two studies^{183 184} but as neither provided six-month or longer follow-up they were not entered into the meta-analysis. Two trials suggest that Nicobrevin may have an effect on short-term outcome but both were methodologically weak, so the data must be regarded with caution.

NicoBloc [insufficient evidence of effectiveness]

NicoBloc is marketed in a number of countries as a smoking cessation aid and often sold through community pharmacies.¹⁸⁵ It comes in the form of a liquid, containing a sugar compound, which is dropped onto the filter of the cigarette. It then dries and forms an occlusive barrier

to nicotine and tar thereby reducing the delivery of these substances to the smoker. The proposed mechanism of action of this product is that of gradual reduction of cigarette consumption and nicotine intake. NicoBloc aims to stop the compensatory smoking that usually occurs with reduction in cigarette consumption. The manufacturer suggests that smokers reduce their cigarette consumption over a six-week period, as they increase the number of drops of NicoBloc solution applied to the filter. This substance has been used by large number of smokers and two cohort follow-up studies report success rates of 42% to 58% at the end of a course of treatment (6 weeks).¹⁸⁶ However, the study methodology and outcome criteria in both studies are poorly described, so these results need to be interpreted with caution. One small, but well-designed, randomised double blind placebo controlled trial showed no benefit of NicoBloc over placebo.¹⁸⁷

The evidence for other interventions

Other interventions

A number of other interventions for smoking cessation deserve mention. These are summarised below and brief evidence statements are provided in square brackets in the headings.

Hypnosis [evidence of no effectiveness*]

Hypnosis is one of the most widely advertised and best-known alternative treatments for smokers. The Cochrane review of hypnotherapy for smoking cessation included a total of nine studies in their meta-analysis.¹⁸⁸ The results show no benefit in smokers receiving hypnotherapy compared to those receiving a suitable control intervention. There is no advantage of adding hypnosis to other cessation methods. However, it may match some behavioural treatments and it may be superior to no treatment although this statement needs to be treated with some caution. Hypnosis is a safe intervention although it is said that it may worsen symptoms in those suffering from mental illnesses such as schizophrenia and bipolar disorder. Hypnosis may also result in emergence of unpleasant memories in those suffering post-traumatic stress disorder and caution is advised in those with major depression and borderline personality.

*Evidence from a meta-analysis of randomised controlled trials suggests that hypnotherapy does not improve 6-month abstinence rates over that of attention control. Evidence suggests that hypnotherapy may be more effective than no treatment.

Acupuncture [evidence of no effectiveness]

Acupuncture is one of the most widely used complementary treatments for a variety of illnesses, but with varying degrees of effectiveness. Reviews have concluded that acupuncture is effective for nausea and vomiting (particularly post-operative and chemotherapy-induced) and dental pain. There are two main acupuncture-based treatments for smoking cessation. The first typically involves inserting needles at points on the ear (e.g. lung and hunger auricular points) or on the face whilst the patient relaxes for 10-20 minutes. Points on other parts of the body may have needles inserted at the same time and electrical stimulation can also be applied. Secondly, needles may be inserted into points in the ear and secured in place for a length of time (e.g. 1-3 weeks). These can then be pressed whenever there is an urge to smoke. Instead of needles small beads or seeds can be used, usually taped in place, and these can be pushed when the urge to smoke occurs. This is known as acupressure. Additionally, acupuncture needles can be stimulated, by hand or electrically. This is believed to provide more precise stimulation for the release of neurotransmitters. Another variation of acupuncture uses low-level laser.

The Cochrane review of acupuncture and related interventions for smoking cessation shows no evidence of any benefit of acupuncture, over placebo, in aiding long-term smoking cessation (OR=0.99; 95% CI: 0.68-1.44).¹⁸⁹ The US guidelines⁸ carried out a series of meta-

analyses of various interventions for smoking cessation and reached similar conclusions. Five studies that investigated the efficacy of acupuncture compared to 'control acupuncture' were included. There was no difference in the estimated abstinence rates between the two treatments (8.9% vs. 8.3% for acupuncture and control respectively).

Competitions and incentives for smoking cessation [evidence of no effectiveness]

Provision of reward for stopping smoking has been used as an incentive in a number of settings. Of the 15 RCTs included in a Cochrane review, none showed any effect of incentives or competitions on long-term abstinence. One of the key findings, as may be expected, was that these interventions appear to work only as long as participants stand to be rewarded. As soon as incentives cease the normal relapse pattern occurs. Incentives have been shown to improve participation rates in smoking cessation interventions, and this is often assumed to lead to more people quitting smoking. However, this does not seem to be the case. A possible reason for this is that programmes offering incentives may attract smokers with less motivation to quit or those who find it harder to quit. A more obvious disadvantage of these programmes is that there will be a proportion of participants claiming to be smokers, who are in fact non- or ex-smokers at the time of entry into the programme.

Quit and Win Contests [insufficient evidence of effectiveness]

Quit and Win contests as a means of promoting smoking cessation have been used since their inception in the 1980s. Although there are data from non-randomised controlled trials that these contests can result in an increase in 12-month abstinence rates, there is insufficient evidence from randomised controlled trials of the efficacy of quit and win contests to draw any conclusions.¹⁹⁰

Exercise to aid smoking cessation [insufficient evidence of effectiveness]

The current evidence does not show a beneficial effect of exercise on long-term quit rates. However, there is some evidence to suggest that exercise may alleviate some of the symptoms of tobacco withdrawal and thus assist in the short-term.¹⁹¹⁻¹⁹⁴ It may also help by increasing self-esteem and may have a positive effect on managing post-cessation weight gain.¹⁹⁵ Although there is little evidence to support the use of exercise as a stand-alone smoking cessation intervention people should not be discouraged from adopting exercise during their cessation attempt as it has many other health benefits.

Biomedical Feedback [insufficient evidence of effectiveness]

Smokers often see little evidence of the adverse effects of smoking on their bodies until the damage has reached a stage where it causes physical disease. Furthermore, they only rarely experience immediate improvements in their health when they stop smoking. It has been argued that if smokers could see the damage smoking was doing to their bodies then they would be more likely to quit. This idea has been tested by researchers. Measurement of smoke exposure (e.g. with measurement of carbon monoxide in breath; cotinine in saliva or urine), assessment of smoking related harm (e.g. lung function tests), and assessment of risk of developing a smoking-related disease (e.g. genetic susceptibility to the adverse effects of tobacco smoke) have all been assessed. The effect of providing biomedical feedback on smoking cessation outcomes has been the subject of two systematic reviews by the same authors.¹⁹⁶⁻¹⁹⁷ However, currently there are insufficient data to provide a clear answer as to whether measurement and feedback of risk is helpful in aiding smoking cessation.

The evidence for cost effectiveness

Cost effectiveness

The Australian smoking cessation guidelines for general practice¹²¹ states that smoking cessation interventions are cost effective. Whilst international data support this assertion^{27 198-202} there are relatively few Australian-specific data regarding the cost effectiveness of smoking cessation treatments. However, a report estimating the costs and effects of smoking cessation interventions in Australia has recently been published,²⁷ showing that from a population perspective, telephone support was the most cost-effective cessation intervention. In particular, adding proactive telephone support to pharmacotherapy increased the overall effectiveness for low marginal cost. This report also confirmed the cost effectiveness of bupropion and NRT. Bupropion appeared to be more cost effective than NRT, a finding that has also been reported by agencies such as the NHS National Institute of Clinical Excellence (NICE).²⁰³ An earlier report, published in 2000, estimated the cost effectiveness of an Australian physician-based smoking cessation intervention, with baseline costs of AUS\$183 per additional quitter.²⁰⁴

Cost information is often presented in the cessation literature as the cost per person treated or cost per quitter. Cost-effectiveness is better expressed as the expected number of life years saved (LYS). This is affected by the age at which the person stops smoking as the earlier in life a person stops smoking the more life years they are expected to gain. It should be noted that the LYS is a conservative measure of effectiveness because it only considers mortality as an outcome.²⁰⁵ Another measure, quality-adjusted life years saved (QALYs) includes wider benefits (e.g. improvement in health, quality of life) from stopping smoking, not just extra years of life gained. However, because of the difficulty in estimating all of the potential health benefits associated with smoking cessation this measure is less precise.

Many smoking cessation treatments only look at short-term outcome, or at best smoking cessation rates at one year. However, by factoring in known relapse rates, estimates of long-term outcome can be made.²⁰⁶ For example, it is expected that 60-65% of abstainers measured at 4 weeks after quitting will have relapsed by a year. The relapse rate after one year is approximately 35%.²⁰⁷ Therefore subtracting this percentage from one-year abstinence rates gives the number of life-long ex smokers.

The UK smoking cessation guidelines, published in 1998, showed that the cost-effectiveness of smoking cessation interventions ranged from £174 (discounted cost per LYS) for brief advice to £255 for specialist face-to-face interventions.¹⁹⁸ In 1999 the UK National Health Service (NHS) established a national smoking cessation service. This provides multi-session behavioural support and pharmacotherapy to help people to stop smoking. The service is free, although some people have to pay prescription charges. In 2001 an analysis of the cost effectiveness of the NHS stop smoking services found that in the year from April 2000 to March 2001 the NHS had contributed £21.4 million to the set up, running, and monitoring of the service. This figure did not include costs of medication provided on prescription, only nicotine

replacement therapy (NRT) provided by a voucher system. In the same time period 126,800 people made an attempt to stop smoking, with 48% abstinent at the end of 4 weeks of treatment. The cost per person treated was a reasonable £169. The costs of prescribed medication are estimated to be an additional £40 per person on average, giving a total cost of £209 per person treated. The estimated 1-year abstinence rate is approximately 17%, which equates to 11% of all people using the services becoming life-long ex-smokers. Accounting for discounted life-years saved and subtracting the LYS associated with those who would have stopped on their own at some stage without any help, the cost per LYS was calculated to be £601 and £766 for those aged 35-44 and 45-56 years respectively. More recently published data confirm a figure of £684 per LYS.²⁰¹ Even under a 'worst case scenario' the cost per LYS was still well under £3000. NICE has a benchmark cost-effectiveness figure of £20,000 as being acceptable for NHS expenditure.²⁰¹ Smoking cessation treatments fall well below this, demonstrating that smoking cessation services, in general, are extremely cost effective.

The cost effectiveness of medications to aid smoking cessation have also been estimated.^{203 208} In 2002 NICE assessed the cost effectiveness of NRT and bupropion,²⁰³ taking into account all factors associated with the costs of treatment and benefits of stopping smoking. The report concluded that both of these treatments were among the most cost effective of all healthcare interventions. The discounted cost per LYS was calculated at £1700 (range £1000-£2400) for NRT and £1100 (range £640-£1500) for bupropion. An evaluation of the cost effectiveness of the strategy where NRT is used to reduce consumption prior to quitting shows that this method is very cost effective compared to no quit attempt, but not as cost effective as using NRT for abrupt quitting.²⁰⁹

Nortriptyline is an inexpensive medication, but there are few reports on its cost effectiveness. One randomised controlled trial comparing smoking cessation with bupropion, nortriptyline and placebo calculated the cost effectiveness at 1 year finding that Nortriptyline was more cost effective than bupropion although the difference was not statistically significant.²¹⁰

Whilst NICE has not yet completed an economic evaluation of varenicline, there is no doubt that it will also be a cost effective treatment. Using cost effectiveness estimates for bupropion and data from outcome studies comparing bupropion and varenicline Stapleton (2006) calculates the cost per LYS for varenicline to be approximately £900.²¹¹ Despite the small differences between individual medications they all compare very favourably to other medications used for preventing illness. For example, a US study found the cost per LYS for cholesterol lowering drugs to be in the region of US\$56,000-\$440,000).²¹²

More recently in a paper comparing the cost-effectiveness of four interventions to prevent cardiovascular disease (smoking cessation, aspirin, anti-hypertensives, and statins) smoking cessation was found to be the most cost effective.²¹³ It should also be noted that while medications such as aspirin and anti-hypertensives are typically used for the remainder of the person's life, smoking cessation treatments are used for only a short period of time.²¹⁴

Summary Smoking cessation interventions are among of the most cost-effective interventions available to healthcare systems.	
Strength of evidence 1++	Evidence statement There is good evidence (based on randomised controlled trials) for the cost effectiveness of telephone and face-to-face smoking cessation support and pharmacotherapies such as NRT, bupropion, nortriptyline and varenicline.

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Appendix 1

search strategy

Databases searched

We searched the following databases: MEDLINE; Cochrane Database of Systematic Reviews; Cochrane Controlled Trials Register (CENTRAL); DARE; AMED; Embase; PsycINFO. The terms used for the MEDLINE searches are shown.

Search strategy

Each search strategy combined the intervention specific terms with smoking specific terms.

Smoking specific terms

((smoking cessation.mp.) or (smoking cessation/))

Intervention specific terms

Brief advice: (advice.mp)

Written self-help materials: (self-help.mp)

Telephone counselling: (telephone*.mp or quitline*.mp or helpline*.mp)

Face-to-face behavioural support: (counsel*.mp)

Smoking cessation for pregnant and breastfeeding women: (pregnan*.mp or breastfeed*.mp)

Smoking cessation for young people: (youth.mp or young.mp or adolescen*.mp or teen*.mp)

Smoking cessation for inpatients: (inpatient*.mp or secondary care.mp)

Smoking cessation for mental health consumers: ((mental health/) or (mental health.mp))

Smoking cessation for addiction service users: (substance abuse/)

Smoking cessation for repeat quitters: (relapse*.mp)

Nicotine replacement therapy: ((nicotinic agonists/) or (nicotine/) or (nicotine replacement.mp))

Bupropion: ((bupropion/) or (bupropion.mp))

Nortriptyline: ((nortriptyline/) or (nortriptyline.mp))

Varenicline: (varenicline.mp)

Acupuncture: ((Acupuncture Therapy/ or Acupuncture Points/ or Acupuncture/ or Acupuncture, Ear/ or acupuncture.mp.) or (acupressure.mp. or Medicine, Chinese Traditional/ or Acupressure/) or transcranial.mp. or transcutaneous.mp. or (Electric Stimulation/ or Electric Stimulation Therapy/ or electrostimulation.mp.) or electric stimulation.mp. or (electroacupuncture.mp. or Electroacupuncture/) or neuroelectrotherapy.mp. or laser therapy.mp.))

Hypnosis: ((hypnosis.mp. or Hypnosis/) or hypnotherapy.mp.))

NicoBloc: ((nicobloc.mp. or (accu drop.mp.) or (take-out.mp.))

Nicobrevin: Nicobrevin.mp

Appendix 2

assessing nicotine dependence

Measuring the degree of nicotine dependence can help identify those who would benefit from extra assistance to stop smoking. One of the most frequently used tools for assessment of nicotine dependence is the Fagerstrom Test for Nicotine Dependence (FTND). This is a 6 item questionnaire, however the best question to ask is: ***“How soon after you wake up do you usually have your first cigarette?”*** *If the person smokes within 30 minutes of waking then they have a higher degree of nicotine dependence and are likely to benefit from more intensive smoking cessation treatments, particularly those utilising medications.*

Cigarette consumption is often used on its own to measure dependence, but it does not always correlate well with the degree of dependence because of the way people smoke their cigarettes. For example, people can cut down the number of cigarettes they smoke each day but can get a similar amount of nicotine out of fewer cigarettes by taking deeper puffs, blocking the vent holes on the cigarette, increase puff frequency and smoking more of each cigarette.